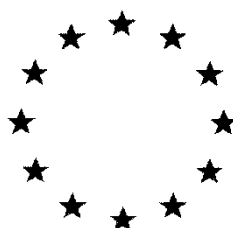


# *European Commission*



**Draft Assessment Report prepared according to the Commission  
Regulation (EU) N° 1107/2009**

## **XDE-729 Methyl (Halauxifen-methyl) Volume 3 – B.7**

**Rapporteur Member State: United Kingdom  
Co-Rapporteur Member State: France**

## Version History

When	What
2013-12-19	Initial DAR

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## CONTENTS

	<b>Page</b>
<b>B.7 Residue data</b>	<b>3</b>
B.7.1 Metabolism, distribution and expression of residues in plants	3
B.7.2 Metabolism, distribution and expression of residues in domestic livestock	37
B.7.3 Definition of the residue	74
B.7.4 Use pattern	75
B.7.5 Identification of critical GAPs	75
B.7.6 Residues arising from supervised trials	79
B.7.7 Stability of residues prior to analysis	202
B.7.8 Effects of industrial processing and/or household processing	235
B.7.9 Livestock feeding studies	261
B.7.10 Residues in succeeding or rotational crops	323
B.7.11 Proposed pre-harvest intervals for envisaged uses, or withholding periods, in the case of post harvest uses	323
B.7.12 Community MRLs and MRLs in EU Member States	323
B.7.13 Proposed EU MRLs and justification for the acceptability of those MRL's	323
B.7.14 Proposed EU Import tolerances and justification for the acceptability of those residues	324
B.7.15 Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRL's	324
B.7.16 Estimates of potential and actual dietary exposure through diet and other means	325
B.7.17 Summary and evaluation of residue behaviour	338
B.7.18 References relied on	338
B.7.19 References used in assessment of data	346

**B.7 RESIDUES DATA****B.7.1 Metabolism, distribution and expression of residues in plants (IIA 6.1, IIIA 8.1)**

**Report:** Ma, M., Smith, K. P., and Jackson, A. U. *A Nature of the Residue Study with [<sup>14</sup>C]-XR-729 Methyl Applied to Wheat with and without the Safener Cloquintocet Mexyl, Unpublished report of Dow AgroSciences, study ID 101080, 28 Oct 2011.*

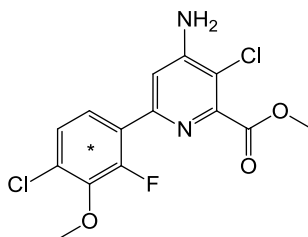
**Guidelines:** OECD Guidance Document 501 for Metabolism in Crops (Issued 8 January 2007)

**GLP:** Yes (certified laboratory)

**B.7.1.1 Wheat**

The Notifier submitted a wheat metabolism study (Ma, M., Smith, K. P., and Jackson, A. U.) completed in 2011. The uptake, distribution and metabolism of XDE-729 methyl was studied in wheat (*var. Hard Red VNS*) grown outdoors in the USA (California). The investigation was carried out in 2010/2011 in accordance with GLP using [<sup>14</sup>C]-phenyl labelled XR-729 methyl and [<sup>14</sup>C]-pyridine labelled XR-729 methyl. In order to investigate the effect of the safener Cloquintocet Mexyl (CQC) on the transformation of XR-729 methyl in wheat, samples from different plots were treated with both [<sup>14</sup>C]-phenyl labelled XR-729 methyl and [<sup>14</sup>C]-pyridine labelled XR-729 methyl with and without Cloquintocet Mexyl (CQC). The radiolabel test substance (with and without CQC) was formulated as an Emulsifiable Concentrate (formulation blank GF-2630) and applied using a R&D wand sprayer pressurised with CO<sub>2</sub>.

Figure B.7.1.1-1 Structure of XDE-729 methyl showing the position of the radiolabels

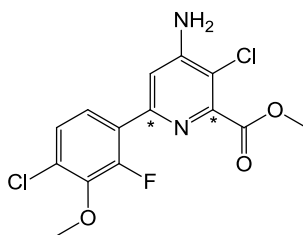


<sup>14</sup>C-PH-XDE-729 methyl

\* Position of <sup>14</sup>C radiolabel

Specific activity: 45.3 mCi/mmol, Radiochemical purity: 97.4%.





<sup>14</sup>C-PY-XDE-729 methyl

\* Position of <sup>14</sup>C radiolabel

Specific activity: 29.6 mCi/mmol, Radiochemical purity: 97.8%.

### Study Design

A single foliar application of [<sup>14</sup>C]-XDE-729 Methyl (methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl) pyridine-2-carboxylate) was made to spring wheat at the maximum Seasonal rate of 10 g a.i./ha (9.6 g a.e./ha) at BBCH 45. The proposed GAP for spring cereals is for 1 application at BBCH 13-45 to be made at 6.25 g a.s/ha, therefore the metabolism study has been conducted at a nominal application rate of 1.6N. However, the proposed GAP for winter cereals is for 2 applications, the first at BBCH 09 to 29 (7.82 g a.s/ha) and the second at BBCH 13 to 45 (6.25 g a.s/ha). Given the metabolism study was carried out with a single application at BBCH 45, the emergence use for winter cereals has not been considered in the metabolism study. Therefore, the notifier was requested to justify how the metabolism study addresses the winter wheat application. The notifier responded with the following case:

*“The application was made at the latest growth stage, and therefore the shortest PHI, for both spring and fall cereals. The residue was defined as parent and three identified metabolites, plus conjugates of metabolite X11406790. The characterized residue is not likely to change due to an earlier application, or a longer PHI. It is likely that the individual residue levels will change, with primarily an increase in conjugated components and bound residues, by the addition of an earlier application”.*

The metabolism study demonstrates that the parent is not extensively metabolized, and the proposed metabolic pathway of XDE-729 methyl in wheat proceeds through dissociation to the acid and/or de-methylation of the methoxy group on the phenyl ring. The resulting metabolites are then rapidly conjugated and metabolism proceeds through natural incorporation of the radiolabeled carbon into natural plant constituents, such as pectin and lignin. Given the results of the study, the RMS agree that the characterised residue is unlikely to change due to a longer PHI, which in addition to the fact that the consumable part (grain) of the plant has not yet developed at BBCH 45, the notifiers case shown above is acceptable.

Normal crop husbandry procedures for the region were followed throughout the growing period. Irrigation water was applied by hand with an inline flow meter. The water was carefully added to the soil in order to prevent washing the test substance off the treated wheat and to minimally disturb the soil. No maintenance chemicals were applied to the wheat. Climatic data were collected from a weather station 5.25 miles Southwest of the test site, with on-site rainfall monitored by a Tru-Check rain gauge during the study. There were no meteorological abnormalities that may have impacted the study.

### Sampling

The wheat was grown outdoors to maturity, with immature forage and hay collected 7 and 24 days after application and mature straw and grain collected 84 days after application.

**Table B.7.1.1-1**

Crop Information					
Crop/ crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested RAC	Harvesting procedure
cereal	<i>Hard Red VNS</i>	BBCH 45 (foliar applications)	BBCH 49	forage	cut by hand
			BBCH 75	hay	cut by hand, dried 12 days in greenhouse
			BBCH 89	straw & grain	cut by hand, separated grain, chaff combined with straw

A small portion of each tissue sample was first milled using a food processor with dry ice, then the processed sample was transferred to a coffee grinder with an additional small amount of dry ice and processed until the sample was a fine powder. Due to the size and nature of grain, the grain samples were only processed through the coffee grinders.

In order to confirm the homogeneity of the processed samples, five replicates (0.2 g) of each processed tissue sample were combusted for two minutes at the trial site, prior to shipment. Processed samples were shipped to Dow AgroSciences (DAS) on dry ice *via* overnight delivery.

### Sample Extraction

In general, the milled samples were analyzed by the sequence of extractions described below and shown in Figure B.7.1.1.1-2.

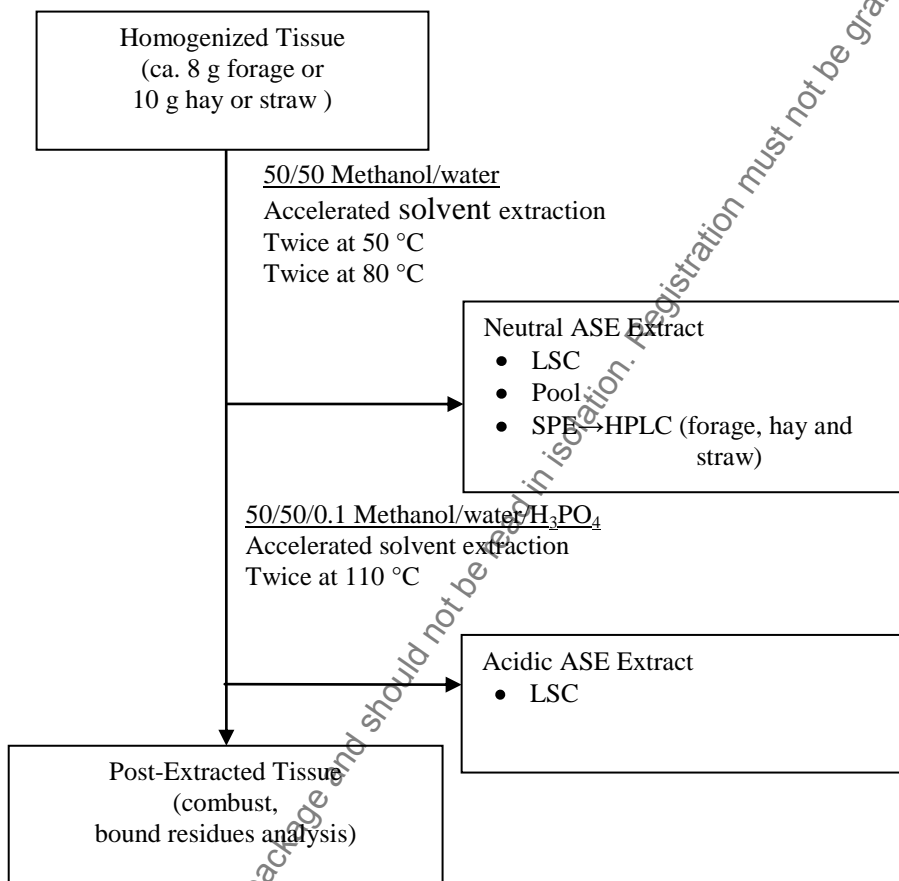
**Accelerated Solvent Extraction (ASE):** An accelerated solvent extractor (Dionex model ASE 350) was used to extract forage, hay and straw samples. A sample (8 to 10 g) was weighed into a 34 mL ASE extraction cell, and approximately 3 g of diatomaceous earth was added on top to fill the cell. Each sample was subjected to six sequential ASE extractions, twice with 50/50 methanol/water at 50 °C, twice with 50/50 methanol/water at 80 °C, and twice with 50/50/0.1 methanol/water/H<sub>3</sub>PO<sub>4</sub> at 110 °C. The six ASE extracts per sample were collected in individual glass vials. All extractions were conducted at approximately 1,500 psi with 5 minutes heating time and 5 minutes static extraction time.

Volumes of each ASE extract were measured and triplicate aliquots (0.25 mL) were analyzed by liquid scintillation counting. The extract volumes were typically 20 mL. The neutral extracts using 50/50 methanol/water at 50 °C and 80 °C were combined and the volume was measured, and triplicate aliquots were analyzed by liquid scintillation counting. Solid phase extraction

(SPE) was conducted on aliquots of the forage, hay and straw combined neutral extracts, and SPE fractions were prepared for HPLC analysis.

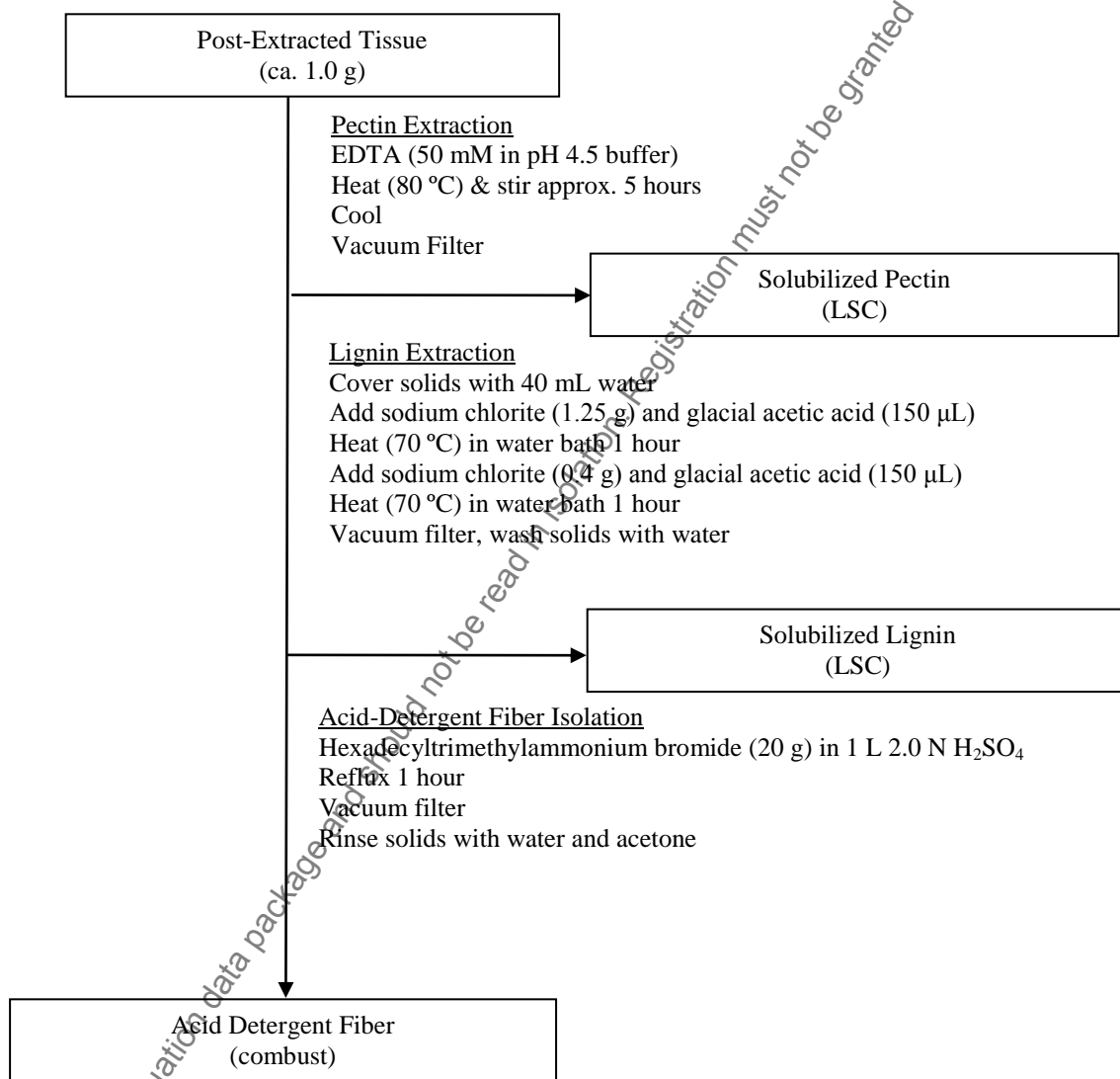
The tissue remaining after the ASE extraction was air-dried and weighed. Triplicate aliquots (0.05 g each) were analyzed by oxidative combustion to determine the amount of non-extractable radioactive residue.

**Figure B.7.1.1-2. Schematic Flowchart for the Analysis of Crop Fractions**



**Bound Residue Determination:** The analytical procedure for the analysis of bound residues in crop fractions is summarised in Figure B.7.1.1.1-3, shown below

**Figure B.7.1.1-3. Schematic Flowchart for the Analysis of Crop Fractions**



#### *Pectin Solubilization*

The pectin substances in the NER were solubilized using ethylenediaminetetraacetic acid (EDTA), 50 mM in pH 4.5 buffer. An aliquot (1 g) of the non-extractable tissue was heated (approx. 80 °C) with 100 mL of the buffered EDTA while stirring for approximately 5 hours. After cooling then vacuum filtering, the solids were transferred back into the original jar. The volume of the extract was measured and triplicate aliquots (1.0 mL) were analyzed by liquid scintillation counting.

### *Lignin Extraction*

The lignin was removed from the solids remaining after the pectin solubilization. First, the solids were transferred to flasks and covered with water (40 mL). Sodium chlorite (1.25 g  $\text{NaClO}_2$ ) and glacial acetic acid (150  $\mu\text{L}$  of  $\text{CH}_3\text{COOH}$ ) were added to each solid sample, stirred, and heated in a hot water bath (approx. 70 °C) for one hour. Additional  $\text{NaClO}_2$  (0.4 g) and acetic acid (150  $\mu\text{L}$ ) were added to each sample, mixed thoroughly, and incubated for another hour. The solids were vacuum filtered and washed several times with water. The total amount of radioactivity in the liquid fraction, which included dissolved lignin, was determined by LSC analysis. After air-drying overnight, the remaining solids were weighed and used in the Acid-detergent Fiber (ADF) Isolation procedure, below.

### *Acid-Detergent Fiber (ADF) Isolation*

The ADF fraction was isolated from the solids remaining after the lignin extraction step. The pellet from the lignin extraction step was refluxed for approximately one hour in acid detergent solution (20 g hexadecyltrimethyl-ammonium bromide in 1 L 2.0 N  $\text{H}_2\text{SO}_4$ ). Following the reflux period, the solids were removed by vacuum filtration through a tared glass fiber filter. The resulting filter cake was washed with water, then acetone. After drying in an oven at 100 °C overnight, the remaining solids (this is the ADF fraction) were weighed and combusted. The ADF fraction consists of cellulose and includes radioactivity encapsulated by cellulose. The total amount of radioactivity in the liquid fraction, which includes hemicellulose and dissolved plant proteins, was determined by LSC analysis.

**Metabolite Identification:** Metabolites were isolated from the combined neutral extracts of the PH-labelled forage tissue. First, an aliquot (50  $\mu\text{L}$ ) of the extract replicate was purified using a Strata X SPE, eluting with 15 mL methanol/water/ $\text{H}_3\text{PO}_4$  (95/5/0.1, v/v/v). The eluate was concentrated to approximately 100  $\mu\text{L}$  on the TurboVap and reconstituted in 2 mL of methanol/0.1% formic acid (35/65, v/v/v). The reconstituted solution was analyzed by HPLC while collecting 30-second fractions. Fractions from six such injections were collected and the fractions with the same retention time were combined. Fraction vials were individually concentrated to dryness and reconstituted in 0.2-0.5 mL of methanol/0.1% formic acid (30/70, v/v). These concentrated fractions were submitted for MS analysis. Metabolites were identified based upon relative retention time and mass spectral matching with the reference standard.

### **Metabolite Quantification:**

The neutral ASE extracts with 50/50 methanol/water at 50 °C and 80 °C were combined, and an aliquot of the extract was concentrated on a Turbovap to remove the majority of the organic solvent. The samples were diluted with 0.1% phosphoric acid (5 mL). The Strata-X SPE cartridges (500 mg, 8B-S100-HDG, Phenomenex Inc., Torrance, California, USA) were conditioned with methanol (5 mL) followed by 0.1% phosphoric acid (2 x 5 mL). The prepared sample was applied to the conditioned SPE cartridge and eluted at approx. 2 mL/min, collecting the eluate. The SPE cartridge was dried for 10 seconds after the SPE had eluted. The sample vial was rinsed with 0.1% phosphoric acid (5 mL), transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. The SPE cartridge was dried under full vacuum for 20 seconds. The Strata-X SPE was eluted with methanol/water/phosphoric acid (95/5/0.1, v/v/v) in three aliquots (3 x 5-6 mL), pooling the elution aliquots.

The elution samples were concentrated to near dryness in a Turbovap. The elution samples were reconstituted in methanol/0.1% formic acid (approx. 30/70, 1.4 mL), and mixed well. Triplicate

aliquots of each load and the reconstituted elution sample were analyzed by LSC. The concentrated elution sample was also analyzed by HPLC.

### **Storage Stability:**

Storage stability data from the study report (A Nature of the Residue Study with [<sup>14</sup>C]-XR-729 Methyl Applied to Wheat with and without the Safener Cloquintocet Mexyl, ID101080) states that tissues were stored at -20°C for 27-71 days. Since this is less than 6 months storage whilst frozen, storage stability does not need to be addressed further. However, for the extracts, the report states that storage at -20°C took place over 386 days. The notifier was requested to provide supporting storage stability data to cover this storage interval; However, the notifier presented further clarification, shown below, which confirmed that further data were not necessary.

*“Initial analyses of extracts occurred within about 2-4 months. HPLC analysis for % TRR determination was completed within 6 weeks of sample extraction. The mass spectral analyses of the forage extracts occurred up to 386 days after the initial extraction; these samples were used for qualitative mass spectral metabolite identification only. Forage and hay were re-analyzed at a later date with similar results, demonstrating stability for the storage interval noted”.*

### **Total Radioactive Residue**

Table B.7.1.1-2 presents TRR levels in immature plants (Forage and Hay) and mature plants (Grain and Straw). The data show that very little XDE-729 methyl is translocated to the grain. Due to the levels of radioactive residues in the edible portions of the crop following treatment as proposed ( $\leq 0.004$  mg/kg XR-729 methyl equivalents) being less than the trigger level of  $< 0.01$  mg/kg (Human food), no characterisation of terminal metabolites had been carried out.

Table B.7.1.1-2

Total Radioactive Residues in Plant Samples Collected for XR-729 Methyl Nature of Residue in Wheat Study		
Sample	dpm/g	mg/kg XR-729 methyl equivalents (ppm)
<b>Forage (immature plants)</b>		
PH-XR-729 ME	27,340	0.094
PH-XR-729 ME + CQC	58,750	0.202
PY-XR-729 ME	26,422	0.139
PY-XR-729 + CQC	27,788	0.146
<b>Hay (immature plants)</b>		
PH-XR-729 ME	81,223	0.279
PH-XR-729 ME + CQC	68,718	0.236
PY-XR-729 ME	67,986	0.357
PY-XR-729 + CQC	78,165	0.411
<b>Grain (mature)</b>		
PH-XR-729 ME	1,181	0.004
PH-XR-729 ME + CQC	1,187	0.004
PY-XR-729 ME	900	0.003
PY-XR-729 + CQC	523	0.002
<b>Straw (mature)</b>		
PH-XR-729 ME	85,555	0.294
PH-XR-729 ME + CQC	55,287	0.190
PY-XR-729 ME	102,762	0.353
PY-XR-729 + CQC	18,128	0.062

### **Distribution of Total Radioactive Residue**

Table B.7.1.1-3 presents the distribution of the total radioactive residues within the harvested crops.

**Table B.7.1.1-3**

Fractionation of the Residues in XR-729 Methyl Treated Wheat RACs (Average of Duplicates)									
Sample ID	TRR	Neutral MeOH/H <sub>2</sub> O Extract <sup>a</sup>		Acidic MeOH/H <sub>2</sub> O Extract <sup>b</sup>		Non-Extractable		Total Recovered	
	mg/kg <sup>d</sup>	% TRR	mg/kg <sup>d</sup>	% TRR	mg/kg <sup>d</sup>	% TRR	mg/kg <sup>d</sup>	% TRR	mg/kg <sup>d</sup>
<b>Forage</b>									
PH	0.094	71.1	0.067	4.4	0.004	29.0	0.027	104	0.098
PH+CQC	0.202	72.6	0.146	2.9	0.006	23.7	0.048	99	0.200
PY	0.139	77.1	0.107	3.4	0.005	23.8	0.033	104	0.145
PY+CQC	0.146	73.0	0.107	3.5	0.005	26.8	0.039	103	0.116
<b>Hay</b>									
PH	0.279	63.3	0.176	3.5	0.010	30.0	0.084	97	0.264
PH+CQC	0.236	63.4	0.149	3.2	0.007	29.1	0.072	96	0.225
PY	0.357	63.7	0.227	3.2	0.012	26.9	0.096	93	0.335
PY+CQC	0.411	62.9	0.258	3.5	0.014	28.8	0.118	95	0.381
<b>Straw</b>									
PH	0.294	68.0	0.200	3.7	0.011	29.2	0.086	101	0.296
PH+CQC	0.190	69.5	0.132	3.3	0.006	25.0	0.047	98	0.186
PY	0.353	67.7	0.239	3.8	0.013	30.8	0.109	102	0.361
PY+CQC	0.062	62.4	0.039	3.5	0.002	39.6	0.025	106	0.066

<sup>a</sup> Four neutral ASE extracts (MeOH/H<sub>2</sub>O at 50 °C and 80 °C) were combined and prepared for HPLC analysis.

<sup>b</sup> Two acidic ASE extracts (MeOH/H<sub>2</sub>O/H<sub>3</sub>PO<sub>4</sub> 50:50:0.1 at 110 °C).

<sup>c</sup> mg/kg = mg/kg XR-729 methyl equivalent.

Approximately 71-77% of the TRR (0.07-0.15 mg/kg XR-729 methyl equivalents) was extracted from the immature forage plants with 50/50 methanol/water at 50 °C and 80 °C. Additional 3-4% of the TRR (0.004-0.006 mg/kg XR-729 methyl equivalents) was further extracted using 50/50/0.1 methanol/water/H<sub>3</sub>PO<sub>4</sub> at 110 °C. Lower levels of radioactivity were extracted from the immature hay (63-64% of the TRR, 0.15-0.26 mg/kg XR-729 methyl equivalents; 3-4% of the TRR, 0.007-0.014 mg/kg XR-729 methyl equivalents) and mature straw (62-70% of the TRR, 0.04-0.24 mg/kg XR-729 methyl equivalents; 3-4% of the TRR, 0.002-0.013 mg/kg XR-729 methyl equivalents) with 50/50 methanol/water and 50/50/0.1 methanol/water/ H<sub>3</sub>PO<sub>4</sub>, respectively.

The grain was not analyzed due to the low TRR levels (See section above, ≤0.004 mg/kg XR-729 methyl equivalents).

For each tissue sample, the four neutral ASE extracts (50/50 methanol/water at 50 °C and 80 °C) were combined and prepared for HPLC analysis. The average SPE recoveries were 86-93% for the forage, hay and straw samples.



HPLC Analysis: HPLC results for the samples described above are summarized in Table B.7.1.1-4

**Table B.7.1.1-4**

XDE-729 Methyl and Metabolite Levels In Neutral Organic Extracts of XDE-729 Methyl Treated Wheat RACs (Average of Duplicates)																		
	XR-729 methyl		X11449757		X11393729		X11861662		X11406790 glucose conj.		X11406790 glucose-malonyl conjugate (X12245409)		X11406790		identified extractable residue		residue characterized but not identified <sup>a</sup>	
Retention time	30.1 min		14.8 min		17.2 min		19.0 min		19.3 min		20.2 min		25.2 min					
Sample ID	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>	% TRR	mg/kg <sup>b</sup>
<b>Forage</b>																		
PH	4.1	0.004	4.8	0.004	0.6	0.001	5.0	0.005	3.0	0.003	6.2	0.006	4.0	0.004	27.5	0.026	27.7	0.026
PH + CQC	5.0	0.010	5.1	0.010	1.6	0.003	4.4	0.009	2.6	0.005	10.3	0.021	2.6	0.005	31.5	0.063	26.5	0.053
PY	8.3	0.011	4.7	0.007	1.8	0.002	3.9	0.005	2.4	0.003	6.1	0.008	3.3	0.005	30.4	0.042	23.1	0.032
PY + CQC	8.3	0.012	4.7	0.007	1.9	0.003	4.7	0.007	1.4	0.002	5.9	0.009	3.8	0.006	30.7	0.045	26.3	0.038
<b>Hay</b>																		
PH	3.2	0.009	1.8	0.005	1.4	0.004	2.6	0.007	3.1	0.009	6.4	0.018	0.9	0.003	19.4	0.054	27.4	0.076
PH + CQC	1.0	0.002	1.9	0.005	1.7	0.004	2.2	0.005	4.4	0.010	5.0	0.012	0.5	0.001	16.8	0.040	33.5	0.079
PY	3.8	0.014	1.8	0.007	1.6	0.006	3.3	0.012	3.7	0.013	6.3	0.022	1.0	0.003	21.5	0.077	25.6	0.091
PY + CQC	5.4	0.022	1.9	0.008	1.8	0.007	1.8	0.007	4.9	0.020	4.8	0.020	0.8	0.003	21.4	0.088	26.4	0.108
<b>Straw</b>																		
PH	3.0	0.009	2.2	0.006	1.5	0.004	2.7	0.008	3.0	0.009	5.7	0.017	0.7	0.002	18.8	0.055	32.9	0.097
PH + CQC	1.2	0.002	2.0	0.004	1.2	0.002	2.7	0.005	3.2	0.006	5.2	0.010	0.9	0.002	16.3	0.031	37.9	0.072
PY	3.4	0.019	1.7	0.009	0.9	0.004	0.5	0.003	3.0	0.014	3.4	0.019	0.6	0.003	13.6	0.070	21.8	0.113
PY + CQC	1.9	0.001	1.7	0.001	1.8	0.001	1.1	0.001	3.0	0.002	3.7	0.002	0.8	0.001	14.0	0.009	30.6	0.019

<sup>a</sup> Extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate. No single component accounted for more than 4% of the TRR, or 0.010 mg/kg XR-729 methyl equivalents.

<sup>b</sup> mg/kg = mg/kg XR-729 methyl equivalents

The neutral ASE extracts of forage, hay and straw consisted of multiple components, including the parent XR-729 methyl, X11449757, X11393729, X11861662, X11406790, X11406790 glucose conjugate, and X11406790 glucose-malonyl conjugate (see Table B.7.1.1-4 above for levels of metabolites). In forage, no other single component accounted for more than 4% of the TRR or 0.01 mg eq/kg. Overall, the average of the TRR identified in forage, hay and straw was 30%, 20% and 16% respectively. Whilst the level of TRR characterized (extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate) was on average 26%, 28% and 31%. It is stated in the study report that the characterised residue is multi-component; however, given that levels in hay and straw are between 0.072-0.113 mg/kg XDE-729 methyl equivalents, the notifier was requested to address whether any single component may exceed the trigger <0.05 mg/kg for animal feed. The notifier responded stating that “No other single component accounted for more than 4% of the TRR or 0.01 mg eq/kg”.

The samples from the four different plots showed a similar chromatographic profile and individual metabolite levels, which indicates there is no significant effect of the safener CQC on the transformation of XR-729 methyl in wheat.

Overall, the metabolite levels in neutral ASE extract of hay and straw are very similar, and both were slightly higher (in terms of mg/kg XR-729 methyl equivalents) than the levels observed in the forage samples. In the animal feed samples analyzed, the conjugates of X11406790 (sum of glucose and glucose plus malonyl) are present at the highest levels, yet below 0.05 mg/kg XR-729 methyl equivalents. The conjugates were present at higher levels than the free X11406790 indicating rapid and preferential conjugation. Metabolites X11449757, X11393729, and X11861662 never exceeded 0.012 mg/kg XR-729 methyl equivalents in any sample harvested.

The 50/50/0.1 methanol/water/H<sub>3</sub>PO<sub>4</sub> extracts were not analyzed by HPLC due to the low levels of radioactivity. Although two combined acidic methanol/water extracts contained up to 0.014 mg/kg XR-729 methyl equivalents, each individual extract contained less than 5% of the TRR and less than 0.01 mg/kg XR-729 methyl equivalents.

### **Bound Residue Determination of the Non-Extractable Residue (NER)**

As shown in Table B.7.1.1-4, the amount of non-extractable, or bound radioactivity, was 24-29% (0.03-0.05 mg/kg XR-729 methyl equivalents), 27-30% (0.07-0.12 mg/kg XR-729 methyl equivalents), and 25-31% of the TRR (0.05-0.11 mg/kg XR-729 methyl equivalents) in forage, hay and straw, respectively.

The bound residues of forage, hay and straw were evaluated, and the results are shown in Table B.7.1.1-4. The results demonstrated broadly similar levels of incorporation or encapsulation of radioactivity into pectin, ADF soluble and ADF of forage, hay and straw tissue. There is slightly more radioactivity associated with lignin in the straw, which is to be expected as the plant grows. The residues in the pectin, lignin, ADF soluble and ADF fractions are below the 0.05 mg/kg trigger value for animal feed, therefore further characterisation of the metabolites is not required.

Table B.7.1.1-4

Fractionation of the Bound Residues in XR-729 Methyl Treated Wheat (Average of Duplicates)											
Sample ID	Bound Residue <sup>a</sup>		Pectin		Lignin		ADF soluble		ADF		Recovery % <sup>b</sup>
	% TRR	mg/kg <sup>c</sup>	% TRR	mg/kg <sup>c</sup>	% TRR	mg/kg <sup>c</sup>	% TRR	mg/kg <sup>c</sup>	% TRR	mg/kg <sup>c</sup>	
Forage											
PH	29.0	0.027	1.8	0.002	9.4	0.009	8.2	0.008	6.7	0.006	90.2
PH + CQC	23.7	0.048	0.6	0.001	7.0	0.014	6.5	0.013	7.6	0.015	91.8
PY	23.8	0.033	1.3	0.002	4.5	0.006	7.3	0.010	6.2	0.009	81.0
PY + CQC	26.8	0.039	1.3	0.002	5.2	0.008	9.1	0.013	8.3	0.012	89.7
Hay											
PH	30.0	0.084	2.3	0.006	7.4	0.021	9.9	0.028	6.7	0.019	87.7
PH + CQC	29.1	0.072	1.8	0.004	7.4	0.018	9.2	0.022	8.6	0.020	92.9
PY	26.9	0.096	2.4	0.009	7.5	0.027	9.2	0.033	6.8	0.024	96.2
PY + CQC	28.8	0.118	2.1	0.009	8.8	0.036	4.7	0.019	6.4	0.026	93.0
Straw											
PH	29.2	0.086	2.1	0.006	10.1	0.030	9.0	0.026	6.6	0.019	95.1
PH + CQC	25.0	0.047	0.7	0.001	8.7	0.017	6.3	0.012	6.9	0.013	90.7
PY	30.8	0.109	2.4	0.009	9.6	0.034	7.1	0.025	7.4	0.026	86.6
PY + CQC	30.3	0.019	0.0	0.000	13.2	0.008	9.8	0.006	7.5	0.005	76.5

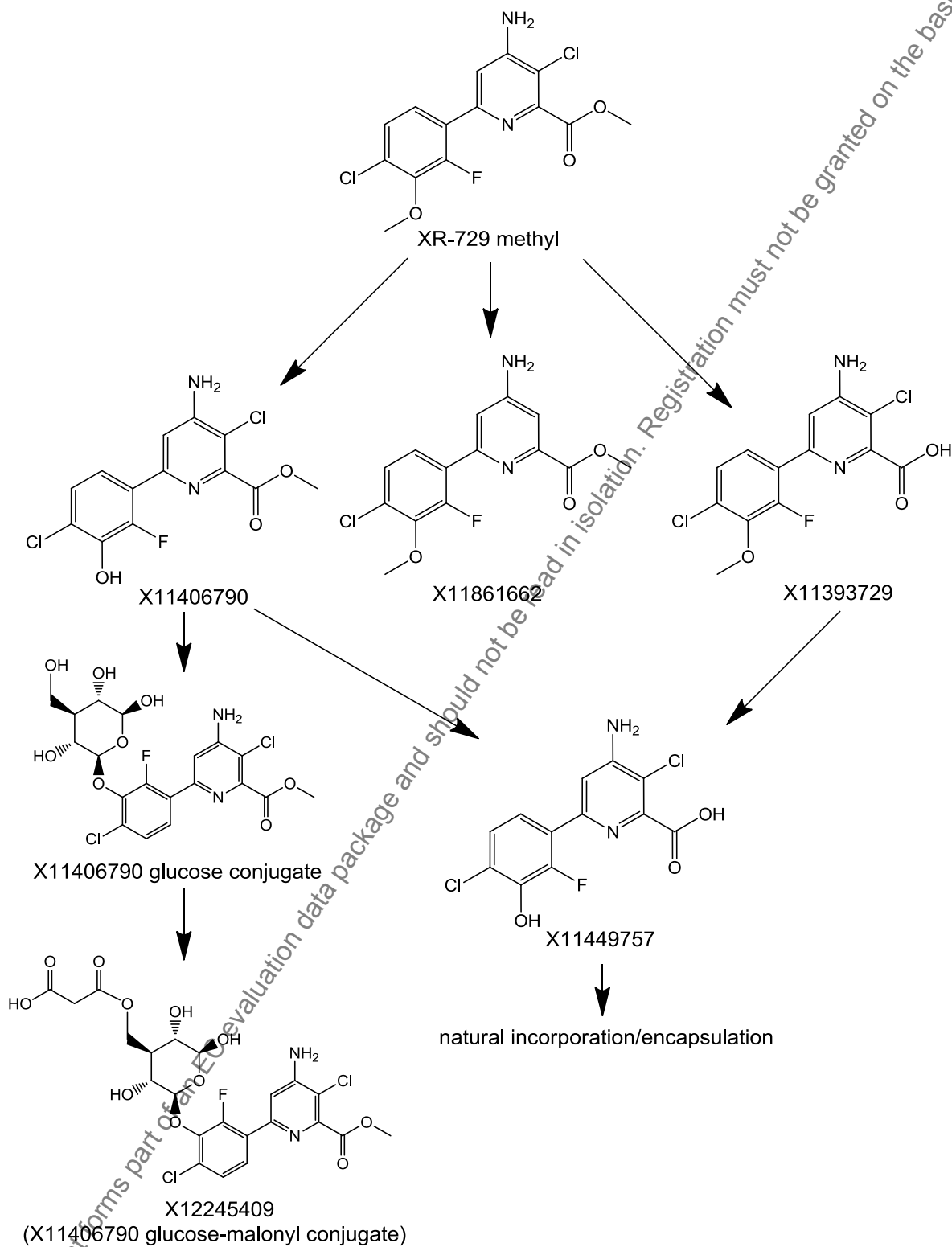
<sup>a</sup> Values from TABLE B.7.1.1-3.

<sup>b</sup> Procedural recovery for the 4-step bound residue process.

<sup>c</sup> mg/kg = mg/kg XR-729 methyl equivalents

### Proposed Metabolic profile

The proposed metabolic pathway is presented in **Figure B.7.1.1-3**. As shown in the diagram, the metabolism of XR-729 methyl in wheat proceeds through dissociation to the acid or de-methylation of the methoxy group on the phenyl ring. The resulting de-methylated metabolite X11406790 is rapidly conjugated with glucose followed by malonylation. Very low levels of free X11406790 compared to conjugated X11406790 indicate that conjugation is rapid and a preferential route of metabolism. Metabolism proceeds through natural incorporation of the radiolabeled carbon into natural plant constituents, such as pectin and lignin. Dechlorination of XR-729 occurs to produce the metabolite X11861662 at very low levels (<0.01 mg/kg XR-729 methyl equivalents in most cases). As dechlorination is an uncommon plant metabolism process and the X11861662 is one of the aqueous photodegradation products (see Section B.8.4.6), it is proposed that X11861662 was formed by photolysis of XR-729 methyl upon the leaf surface.

**Figure B.7.1.1-3 Proposed Metabolic Profile of XR-729 in Wheat**

## Conclusions

A single application of XDE-729 methyl with and without the safener cloquintocet-mexyl at an application rate of 10 g a.s./ha resulted in immature forage, hay and mature straw and grain that contained 0.09-0.20, 0.24-0.41, 0.07-0.35, and  $\leq 0.004$  mg/kg XR-729 methyl equivalents of the TRR, respectively.

The majority of the residues were found to be readily extractable with a mild procedure, and minimal additional residues were extractable with stronger procedures. Typically 62-77% of the residue was extracted from forage, hay and straw samples and was further characterized by HPLC.

The neutral ASE extract of immature forage consisted of multiple components, including parent XR-729 methyl (4-9% of the TRR), X11449757 (approx. 5% of the TRR), X11393729 (0.6-2.0 % of the TRR), X11861662 (4-5% of TRR), X11406790 (3-4% of TRR), X11406790 glucose conjugate (2-3% of the TRR), and X11406790 glucose-malonyl conjugate (X12245409, 6-10% of the TRR). The neutral ASE extract of hay and straw showed a similar HPLC profile to the forage extract. No other single component accounted for more than 4% of the TRR. Overall, the average of the TRR identified in forage, hay and straw was 30%, 20% and 16% respectively. Whilst the level of TRR characterized (extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate) was on average 26%, 28% and 31%. It is stated in the study report that the characterised residue is multi-component; however, given that levels in hay and straw are between 0.072-0.113 mg/kg XDE-729 methyl equivalents, the notifier was requested to address whether any single component may exceed the trigger  $<0.05$  mg/kg for animal feed. The notifier responded stating that "No other single component accounted for more than 4% of the TRR or 0.01 mg eq/kg".

The samples from four different plots showed similar metabolite levels, which indicates there is no significant effect of the safener CQC on the transformation of XR-729 methyl in wheat.

No characterization of radioactivity was performed for the grain samples due to low TRR levels ( $\leq 0.004$  mg/kg XR-729 methyl equivalents).

The amount of non-extractable, or bound radioactivity, was 24-29% (0.03-0.05 mg/kg XR-729 methyl equivalents), 27-30% (0.07-0.12 mg/kg XR-729 methyl equivalents), and 25-31% of the TRR (0.05-0.11 mg/kg XR-729 methyl equivalents) in forage, hay and straw, respectively. The bound residues of forage, hay and straw were evaluated, and the results demonstrated broadly similar levels of incorporation or encapsulation of radioactivity into pectin, ADF soluble and ADF of forage, hay and straw tissue. There is slightly more radioactivity associated with lignin in the straw, which is to be expected as the plant grows. The residues in the pectin, lignin, ADF soluble and ADF fractions are below the 0.05 mg/kg trigger value for animal feed, therefore further characterisation of the metabolites is not required.

Metabolism of XDE-729 methyl in wheat proceeds through dissociation to produce the XDE-729 acid or de-methylation of the methoxy group on the phenyl ring to produce the metabolite X11406790. X11406790 is then conjugated with glucose followed by further conjugation with malonic acid. Metabolism continues through natural incorporation of the radiolabeled carbon into natural plant constituents, such as pectin and lignin. Low levels of the X11861662 are proposed to be as a result of absorption of the photodegradation product by the plant.

### Further consideration of the residue definition

The notifier proposes that XDE-729 methyl and XDE-729 acid are included in the residue definitions for Risk Assessment and Enforcement/Monitoring purposes.

However, given the levels of metabolites formed through the pathway involving demethylation of the methoxy group on the phenyl ring (i.e X11406790, X11406790 glucose conjugate and X11406790 glucose-malonyl conjugate (X12245409)) in comparison to the levels of parent XDE-729 and XDE-729 acid (see Figure B.7.1.1-3), consideration should be given to the metabolites formed through the demethylation pathway (including conjugates and X11449757). Hydrolysis of the conjugates would lead to the formation of X11406790, which ultimately may be hydrolysed to X11449757, which is also formed from the XDE-729 acid (X11393729). X11449757 appears to be formed in equivalent or higher quantities than the XDE-729 acid (X11393729), but again this metabolite does not appear as part of the residue definition. In order to address these concerns about whether these additional metabolites should be included in the residue definition, the notifier presented the following case (shown in italics):

*Given the levels of individual metabolites quantified in wheat commodities from the wheat plant metabolism study, the degree of characterization/identification carried out in the study are acceptable according to trigger values given in the guidance document (OECD 501)*

- 1) *Total Radioactive Residues (TRR) in commodities used for human food (grain) were low ( $\leq 0.004$  mg/Kg) and as such were not required to be characterized according to guidelines. No toxicological concern regarding these low TRRs exist.*
- 2) *The TRR levels in commodities that could theoretically be fed to livestock were also low ( $\leq 0.20$  mg/kg in 7 day PHI forage and  $\leq 0.41$  mg/Kg in 24 day PHI hay). Characterization of the TRR showed the residue to be multi-component and comprised of at least 7 peaks. Quantitation of the radioactive peaks showed that the levels of each metabolite were low (in terms of mg/Kg and % of TRR). In fact, given the maximum level of  $\leq 6.4\%$  TRR, the metabolites were below the 10% AR trigger for requiring "characterization" as outlined in OECD 501. The only exception was the glucose-malonyl conjugate of X11406790 treated with phenyl label/CQC present at 10.3% of the TRR. The levels of the individual metabolites were  $\leq 0.022$  mg/kg which triggers the action of "...Characterize. Only attempt to confirm identity if straight forward..."*

*OECD guideline 501 states "If the extractable radioactivity represents 0.01 mg/kg or less, it will not require further analysis. If the extractable radioactivity is greater than 0.01 mg/kg, refer to (Table 1) for trigger values relating to the identification/characterisation of extractable residues. The exception for this would be toxicology concerns regarding potential residues which might occur at lower levels, including polar fractions. However, low-level individual residues (in terms of both mg/kg and percent of total residues) do not typically need to be identified if the major components of the residue have been identified. For example, if the total radioactivity in a crop part is 3 mg/kg and 75 percent of that has been conclusively identified, it is unlikely that identification of a series of individual residues in the range of 0.05-0.1 mg/kg would be needed. On the other hand, extensive efforts toward identification of 0.05-0.1 mg/kg residues would be expected when the total radioactivity is only 0.3 mg/kg."*

*To assess the relevance of these low level metabolites with respect to human health the "Guidance Document on the Definition of Residue (2009)" which considers 1) the potential for exposure and 2) the relative toxicity is referenced.*

According to current guidance, the plant metabolites of XDE-729 methyl are classified as “minor metabolites” as they individually comprise less than 10% of the TRR. Minor metabolites are typically not included in the dietary risk assessment as they do not contribute significantly to the overall exposure. Minor metabolites may be considered relevant for dietary risk assessments if they are: 1) known or suspected to be significantly more toxic than the parent compound or 2) where no major residues (i.e. >10% of TRR) are present and numerous toxicologically significant metabolites are present. The latter scenario is somewhat akin to XDE-729.

It is acknowledged that the potential exposure of humans to these minor plant metabolites is minimal due to the proposed use pattern and the physical properties of the metabolites. Nevertheless, human exposure to XDE-729 metabolites may arise from two scenarios: 1) consumption of grain based commodities 2) Consumption of meat and milk products from ruminants fed with treated cereal commodities.

#### Exposure to Non-Conjugated Metabolites from Consumption of Grain Based Commodities

The risk to humans from consuming non conjugated metabolites in cereal grain is believed to be insignificant due to the low levels present (Total TRR  $\leq 0.004$  mg/Kg) and the physical properties of the metabolites. The metabolites are more hydrophilic than the parent compound and as such are more likely to be excreted than the parent. This difference in hydrophilic nature is reflected in the QSAR log  $K_{ow}$  values of 3.1, 2.6 and 2.2 for XDE-729 methyl, X11406790 and X11449757 respectively. It is acknowledged that there is a slight chance for hydrolytic conversion of X11406790 to X11449757 in the human GI tract. However, this would lead to an insignificant increase in level of a known rat metabolite. Direct human exposure to crop metabolites in animal feed commodities is not relevant in human health assessments and as such is not addressed here.

#### Exposure to Non-Conjugated Metabolites from Consumption of Meat and Milk Products

Cereal crop commodities are not a significant part of livestock feed, and pasture uses are not anticipated for this product thus there is minimal potential transfer of residues to milk and animal tissues which may contribute to human exposure. A ruminant metabolism study has shown that residues of XDE-729 and metabolites in animal tissues/commodities are likely to be extremely low ( $< 0.01$  mg/Kg) assuming a standard dietary burden calculation. This study also showed no propensity for XDE-729 or its metabolites to bio-concentrate after repetitive dosing, with the majority of the dose excreted as parent or known rat metabolites.

In addition to the case presented by the notifier (shown above in italics), the notifier was also asked to address the relative toxicity of the non-conjugated metabolites X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. If the toxicity of X11406790 is comparable to or more toxic than the XDE-acid (X11393729), then the inclusion of the conjugates (see discussion below (Relevance of Conjugated Residues to Human Health Assessment)) would need to be considered further, as the amount of the X11406790 metabolite formed by degradation by human colonic and bovine rumen microflora could be significant. However, if the metabolite X11406790 was less toxic than X11393729, the case to support non-inclusion of the non-conjugated metabolites (shown above) and their conjugates (see below) in the residue definition would be acceptable.

The notifier responded stating that *“In the case of the 6 metabolites for which limited toxicity data exists, it was decided to address the risk of potential human exposure by utilizing the concept of ‘threshold of toxicological concern’ (TTC) as used in the European regulation of pesticide metabolites (European Commission, 2003) and described in the open literature (Felter et al., 2009) and in an EFSA Scientific Opinion (EFSA, 2012).*

*A dietary exposure assessment for the metabolites X11406790 and X11449757 is also presented as further evidence that the metabolites should not be added to the residue definition for XDE-729 methyl (the proposed residue definition is for XDE-729 methyl and XDE-729 acid only). The toxicological based assessment of the metabolites shows the metabolites to be of no toxicological concern with respect to genotoxicity”.*

A summary of the toxicity studies on metabolites presented by the notifier is reproduced below (sections shown in italics):

*This section addresses the metabolites of XDE-729 methyl.*

*Metabolites of XDE-729 methyl are summarised below.*

*8 molecules were assessed for genotoxicity alerts using QSAR (OASIS and DEREK databases):*

- 1. XDE-729 methyl (parent)*
- 2. XDE-729 acid*
- 3. O-demethyl XDE-729 Acid (X11449757)*
- 4. O-demethyl XDE-729 Methyl (X11406790)*
- 5. Glucuronide conjugate of X11449757*
- 6. Sulfate conjugate of X11449757*
- 7. Glucuronide conjugate of X11406790*
- 8. Sulfate conjugate of X11406790*

*For all 8 molecules:*

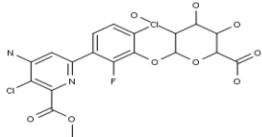
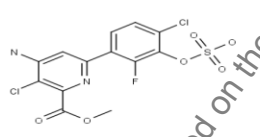
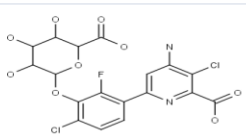
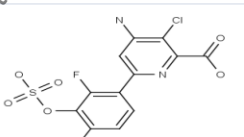
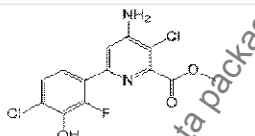
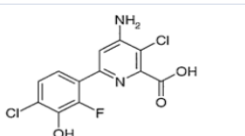
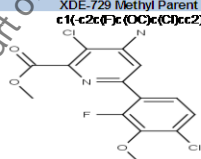
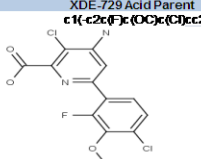
- 1. DEREK did not produce alerts for mutagenicity or chromosome damage;*
- 2. OASIS did not produce alerts for mutagenicity but did produce alerts for chromosome damage. The nitrogen-containing ring, which is present in all 8 molecules, was identified as the structure responsible for these alerts (see Table 5.8.1-2 for full results summary).*

*Testing of 3 of these 8 molecules for in vitro genotoxicity confirmed lack of mutagenicity and chromosome damage indicating that the alert raised by OASIS is a false positive.*



## XDE 729 Methyl (Halaluxifen-methyl)

## Volume 3, Annex B.7

Toxicological Prediction Using DEREK Nexus II (2012) and OASIS TIMES (v. 2.27.5)							
Glucuronide conjugate of the 790 metabolite				Sulphate conjugate of the 790 metabolite			
SMILES	<chem>COC(=O)c1c(cc(n1)c2cc(c(c2F)OC3C(C(C(C3O)O)O)O)O)O)C1</chem>			SMILES	<chem>COC(=O)c1c(cc(n1)c2cc(c(c2F)OS(=O)(=O)C1)O)O)C1</chem>		
Structure				Structure			
Endpoints	DEREK	OASIS		Endpoints	DEREK	OASIS	
Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance	Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance
Mutagenicity	No Alert	Not Mutagen	Uncertain	Mutagenicity	No Alert	Not Mutagen	Uncertain
Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain	Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain
Genotoxicity	No Alert	Not Available	n.a.	Genotoxicity	No Alert	Not Available	n.a.
Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.	Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.
Glucuronide conjugate of the 757 metabolite				Sulphate conjugate of the 757 metabolite			
SMILES	<chem>c1c(c(c(c1c2c(c(c(c2)C(=O)O)C1)F)OC3C(C(C(C3O)O)O)O)O)C1</chem>			SMILES	<chem>c1c(c(c(c1c2c(c(c(c2)C(=O)O)C1)F)OS(=O)(=O)C1)O)O)C1</chem>		
Structure				Structure			
Endpoints	DEREK	OASIS		Endpoints	DEREK	OASIS	
Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance	Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance
Mutagenicity	No Alert	Not Mutagen	Uncertain	Mutagenicity	No Alert	Not Mutagen	Uncertain
Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain	Chromosome Damage	No Alert	CA Parent	Uncertain
Genotoxicity	No Alert	Not Available	n.a.	Genotoxicity	No Alert	Not Available	n.a.
Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.	Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.
X-790				X-757			
SMILES	<chem>c1c(c(c(c1)C(=O)F)c2nc(c(c2)N)C(C(=O)O)O)O</chem>			SMILES	<chem>c1c(c(c(c1)C(=O)F)c2nc(c(c2)N)C(C(=O)O)O)O</chem>		
Structure				Structure			
Endpoints	DEREK	OASIS		Endpoints	DEREK	OASIS	
Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance	Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance
Mutagenicity	No Alert	Not Mutagen	Uncertain	Mutagenicity	No Alert	Not Mutagen	Uncertain
Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain	Chromosome Damage	No Alert	CA Parent	Uncertain
Genotoxicity	No Alert	Not Available	n.a.	Genotoxicity	No Alert	Not Available	n.a.
Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.	Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.
XDE-729 Methyl Parent				XDE-729 Acid Parent			
SMILES	<chem>c1c(c2c(F)c(OC)c(Cl)c2)cc(N)c(C)c(C(=O)OC)m1</chem>			SMILES	<chem>c1c(c2c(F)c(OC)c(Cl)c2)cc(N)c(C)c(C(=O)O)m1</chem>		
Structure				Structure			
Endpoints	DEREK	OASIS		Endpoints	DEREK	OASIS	
Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance	Software Version	Version Nexus Knowledge	TIMES V.2.27.5	Relevance
Mutagenicity	No Alert	Not Mutagen	Uncertain	Mutagenicity	No Alert	Not Mutagen	Uncertain
Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain	Chromosome Damage	No Alert	CA Parent & Metabolite(s)	Uncertain
Genotoxicity	No Alert	Not Available	n.a.	Genotoxicity	No Alert	Not Available	n.a.
Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.	Rapid prototypes: chromosome damage in vitro	No Alert	Not Available	n.a.

Regarding the experimental data:

1. XDE-729 methyl and XDE-729 acid both have negative genotoxicity packages (in vitro and in vivo studies)
2. X11449757 has been tested in an Ames test (IIA 5.8.1/1), a HGPRT (IIA 5.8.1/2) and a HLCAT (IIA 5.8.1/3), all of which were negative.

Therefore, the OASIS QSAR alerts for chromosome damage are considered unreliable for all 8 of these structurally related molecules based on the proven lack of chromosome damage in these guideline-compliant studies.

The RMS conclude that overall no toxicity concerns have been identified for the metabolites.

Full details of the TTC approach and the dietary exposure assessment are given in Section B.7.17.9 (Estimates of potential and actual dietary exposure through diet and other means).

In summary, the QSAR analyses of the metabolites X11406790 and X11449757 and the interpretation of the results with supporting experimental data showed that the metabolites and their associated conjugated forms are not genotoxic.

The initial Tier I TTC value used was 1.5 µg/person per day (0.02 µg/kg bw/day) for non-genotoxic chemicals (EC, 2003; Kroes *et al.*, 2005; Felten *et al.*, 2009). Estimated dietary intake was at 198% of the TTC (see Section B.7.17.9 for full details). Following decision trees used in a number of publications (Kroes *et al.*, 2005; Felten *et al.*, 2009, EFSA, 2012) if exceedances of the Tier I TTC is observed the next relevant TTC value to be used for non-carbamate/organophosphate compounds is the TTC value for Cramer structural class III compounds at 90 µg/person per day (1.5 µg/kg bw/day). Based on this TTC the estimated intake of any of the individual metabolites (or all of the metabolites combined) was at 3% of the TTC (see Section B.7.17.9 for full details). Once again, referring to the decision tree that is generally used, if a compound has an estimated intake below the Cramer class III TTC, then the 'substance would not be expected to be a safety concern'. As the worst-case estimated exposure was 33-fold lower than the relevant TTC, it is possible to conclude that the exposure is of no concern with respect to human safety.

Full details are given in Section B.7.17.9; however, in summary, the metabolites X11406790 and X11449757 and their conjugates are not considered to be of toxicological concern or a risk in terms of potential dietary exposure, and should not be included in the residue definition for XDE-729 methyl.

#### Relevance of Conjugated Residues to Human Health Assessment

The DEFRA project (PS2510) provides a comprehensive overview of the behavior of conjugated residues in mammalian systems and their impact on human health assessments. This literature and laboratory study was initiated to understand the behavior of common pesticide conjugates under conditions typically found in the GI tract of humans and livestock. Findings of the project are outlined below where relevant to the XDE-729 discussion:

- 1) Based on the model conjugates studied, β-D-glucoside conjugates of phenols (like X11406790) are stable to the pH levels found in the human and ruminant GI tract.
- 2) The model conjugates were also stable to digestive enzymes present in the human stomach and small intestine.

- 3) *In vivo* studies with the rat demonstrated that  $\beta$ -D-glucosides were absorbed and excreted unchanged in the urine i.e. they were not de-conjugated or further metabolized in the intestine or liver.
- 4)  $\beta$ -D-glucosides are completely degraded by human colonic and bovine rumen microflora releasing the exocon moiety.

From the above research it may be concluded that the conjugated metabolites of XDE-729 are likely to be readily absorbed and rapidly excreted and as such are of limited significance in a human health assessment. Conjugated metabolites not absorbed in the stomach/intestines are likely to be de-conjugated, with the release of metabolites whose toxicology has been assessed alongside the parent compound in toxicological studies.

The notifier states that attempts to hydrolyze the conjugates with strong acids and heat (data not reported) during the residue method development were not satisfactory. Hydrolysis experiments led to significant degradation of parent and known metabolites and formation of  $^{14}\text{C}$  HPLC peaks to which structures could not readily assigned. As a result of the above, the data generation method does not employ a hydrolysis step to hydrolyze conjugates.

**To conclude, the opinion of the RMS is that the notifier has provided sufficient evidence to support non-inclusion of the metabolites X11406790 and X11449757 and their conjugates in the residue definition. The proposed residue definition XDE-729 methyl and XDE-729 acid is acceptable.**

#### B.7.1.2 Turnip (Root Crop)

**Report:** Rotondaro, S. L., Taylor, J. A., Balcer, J. L., Grotenhuis, A. N., and Graper, L. K. *A Nature of the Residue Study with [ $^{14}\text{C}$ ]-XDE-729 Methyl Applied to Turnips, Unpublished report of Dow AgroSciences, study ID 110413, 23 July 2012.*

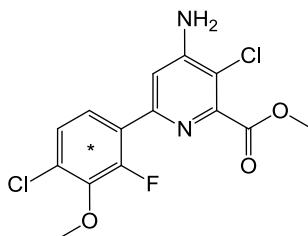
**Guidelines:** OECD Guidance Document 501 for Metabolism in Crops (Issued 8 January 2007)

**GLP:** Yes (certified laboratory)

The Notifier submitted a turnip metabolism study (Rotondaro, S. L., Taylor, J. A., Balcer, J. L., Grotenhuis, A. N., and Graper, L. K.) completed in 2012. The uptake, distribution and metabolism of XDE-729 methyl was studied in turnip (*var. Brassica rapa*) grown outdoors in the USA (Ricerca Biosciences, 7528 Auburn Road, Concord, OH 44077, USA). The investigation was carried out in 2011/2012 in accordance with GLP using [ $^{14}\text{C}$ ]-phenyl labelled XR-729 methyl and [ $^{14}\text{C}$ ]-pyridine labelled XR-729 methyl. The radiolabel test substance was formulated as an Emulsifiable Concentrate (formulation blank GF-2630) and applied using a hand-held trigger sprayer. Unlike the wheat metabolism study evaluated above, the effect of the safener Cloquintocet Mexyl (CQC) on the transformation of XR-729 methyl in turnip was not investigated. Given that evaluation of the current study has demonstrated that the metabolic pathway for root crops is very similar to wheat, and the effect of the safener

was evaluated as part of the wheat metabolism study, the RMS concludes that the root crop metabolism study carried out in the absence of the safener is acceptable.

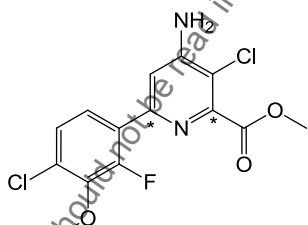
Structure of XDE-729 methyl showing the position of the radiolabels



<sup>14</sup>C-PH-XDE-729 methyl

\* Position of <sup>14</sup>C radiolabel

Specific activity: 45.3 mCi/mmol, Radiochemical purity: 97.4%.



<sup>14</sup>C-PY-XDE-729 methyl

\* Position of <sup>14</sup>C radiolabel

Specific activity: 30.6 mCi/mmol, Radiochemical purity: 98.6%.

### Study Design

A single foliar application of [<sup>14</sup>C]-XDE-729 Methyl (methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl) pyridine-2-carboxylate) was made to the crop at 10 g a.i./ha (9.6 g a.e./ha) at BBCH 17. The growth stage at harvest for immature crops was 14 days after application, BBCH 75, or 28 days after application, BBCH 79 for mature harvest. During harvest, the crops are removed from the soil, the tops are separated from the roots and the roots are brushed clean of soil. The representative use for authorisation of XDE-729 is for use on cereals, therefore there is no proposed GAP for root crops.

After planting, the plots were observed routinely throughout the study to look for any developing problems with fertilization, irrigation, insect infestation, etc. The study report states that plots were maintained as close as possible to normal agronomic practices for crop production in the region. No maintenance pesticides were applied during the growing season. The turnip plants developed normally throughout the study period and were at the predicted state of maturity

at the time of harvest. No disease or damage due to excessive pest pressure was observed throughout this experiment.

Outdoor climatic data was obtained from The U.S. Department of Commerce National Oceanic and Atmospheric Administration National Weather Service, Cleveland, Ohio, Cleveland Station. The data was collected from April through November 2011 and included the following: temperature data (maximum and minimum daily temperatures) and rainfall data including date and amount. There were no meteorological abnormalities that may have impacted the study.

### Sample Handling and Preparation

For each control and treated turnip sample of the 14 DAT harvest, the entire roots or foliage sample was processed. For the 28 DAT turnip harvest at least 10 grabs of the total sample were taken, approximating 700 grams of either roots or foliage, to form a representative subsample for processing. The remaining 28 DAT turnip non-processed harvest was double bagged, labeled, and stored frozen.

The 14 DAT and the 28 DAT control and treated turnip root samples were cut into smaller pieces and then ground using dry ice and a Robot Coupe Blixer® 5V Mixer (Robot Coupe USA, Inc., Jackson, MS). The 14 DAT and 28 DAT control and treated turnip tops (foliage) were ground using dry ice and a Robot Coupe Blixer® 5V Mixer.

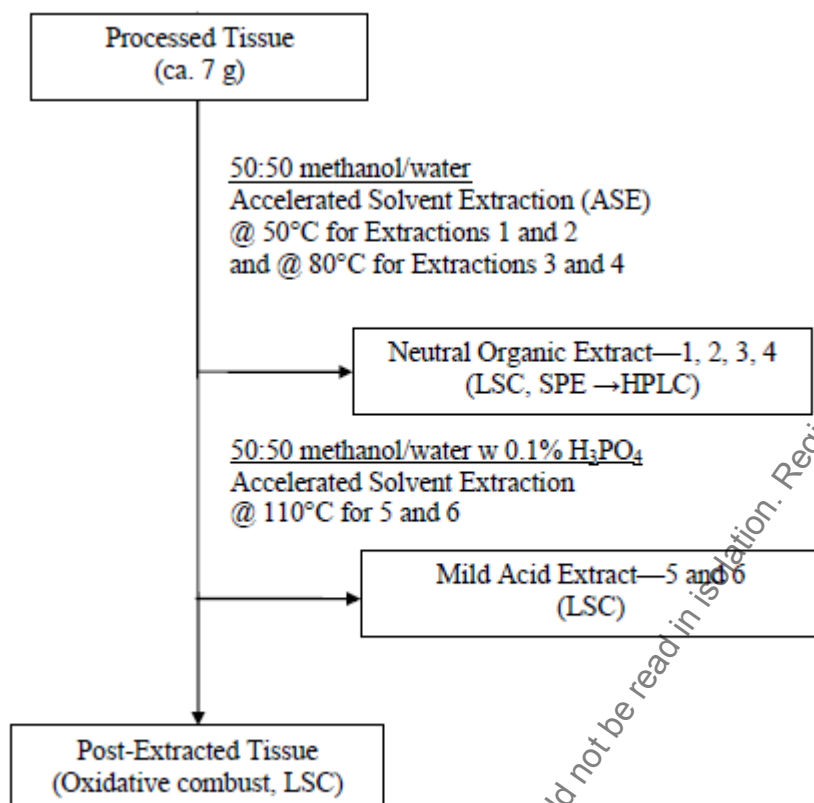
Aliquots (5 x approximately 0.3 g) of the milled samples were analyzed by oxidative combustion to determine the radioactive residues in the samples.

### Analytical Methodology

The turnip roots were not analysed due to the low TRR levels ( $\leq 0.006$  mg/kg XDE-729 Methyl equivalents). An accelerated solvent extractor (Dionex model ASE 350) was used to extract the turnip tops (foliage) samples. A sample of the turnip tops, approximately 7 grams, was weighed into a 50 mL conical vial, and diatomaceous earth (inert filler, DE) was added on top of the sample to fill the vial to approximately the 34 mL mark. The vial was then shaken, and the matrix and DE were then transferred to a corresponding 34 mL ASE extraction cell for extraction. Each sample was subjected to six sequential ASE extractions, twice with 50/50 methanol/water at 50 °C, twice with 50/50 methanol/water at 80 °C, and twice with 50/50 methanol/water with 0.1%  $\text{H}_3\text{PO}_4$  at 110 °C. The six ASE extracts per sample were collected in individual vials. Volumes of each ASE extract were calculated by mass and density. Triplicate aliquots (0.5 mL) were analyzed by LSC. The extract volumes were typically 40 mL. The four neutral extracts using 50/50 methanol/water at 50 °C and 80 °C were combined and two 50 mL portions of each extract were evaporated to aqueous. After evaporation to aqueous, triplicate aliquots were analyzed by LSC.

The tissue typically remaining ASE was air-dried and weighed. Triplicate aliquots (0.2 g) were analyzed by oxidative combustion to determine the amount of non-extractable radioactive residue.

**Bound Residue Determination:** Bound residue determinations were not necessary because  $<0.025$  mg eq/kg remained unextractable (see comment under the heading Bound Residues in the following section **Characterisation of Radioactive Residues**).

**Figure B.7.1.2-1****Schematic Flowchart for the Analysis of Turnip Tops****Metabolite Identification Procedures**

After extraction and clean-up, the samples were analyzed by HPLC. The metabolites observed in the HPLC radio-chromatograms were compared to reference standards analyzed *via* the same HPLC method. In order to identify metabolites that did not match a reference standard, the samples were submitted for analysis *via* mass spectrometry. Metabolites were identified *via* mass spectrometry using the turnip tops samples.

**SPE:** The general clean-up procedure for the extracts was with a Strata-X SPE (500 mg, 8B-S100-HDG, Phenomenex Inc., Torrance, California, USA). The ASE neutral extracts using 50/50 methanol/water at 50 °C and 80 °C were combined, and two 50 mL aliquots were evaporated to aqueous separately. Once the extracts were aqueous, 5 mL of 0.1% H<sub>3</sub>PO<sub>4</sub> was added to the sample. The SPE cartridges were conditioned with methanol (1 x 5 mL) followed by water containing 0.1% H<sub>3</sub>PO<sub>4</sub> (2 x 5 mL). The prepared sample was applied to the conditioned SPE and eluted at approx. 2 mL/min, collecting the eluate. The SPE was dried for 10 seconds after the sample had eluted. The sample vial was rinsed with water containing 0.1% H<sub>3</sub>PO<sub>4</sub> (5 mL), transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. The SPE cartridge was dried under full vacuum for 20 seconds. This pooled eluate was designated as 'load/wash'. The Strata-X SPE was eluted at approximately 1 mL/min with three 5 mL aliquots of 95:5 methanol/water containing 0.1% H<sub>3</sub>PO<sub>4</sub>, these elution aliquots were pooled to create the sample designated as 'elution'.

After the addition of 100 µL of a 80:20 methanol/glycerol solution, the elution samples were concentrated to approximately 100 µL. The elution samples were reconstituted in 600 µL of water with 0.1% formic acid and swirled, vortexed and sonicated for about a minute. Then, 30 µL of methanol was added to the sample and it was swirled, vortexed, and sonicated for about 1 minute. The sample was transferred to an eppendorf tube and centrifuged at about 14,000 rpm for approximately 10 min. The supernatant was then transferred to an HPLC vial. Triplicate aliquots of each load and reconstituted elution sample were analyzed by LSC. The concentrated elution sample was also analyzed by HPLC.

**HPLC:** The primary HPLC system used a flow-through radioactivity detector (β-RAM model 5) to quantify the amount of radioactivity present in each peak. A UV detector at 254 nm wavelength was used to determine the retention times of the non-radiolabeled standards. The HPLC column used was a Synergi Hydro-RP, 4 µm 80A 150 x 4.6 mm (Phenomenex). The solvent system used was gradient elution with the following mobile phases: Solvent A 0.1% formic acid in water, Solvent B 0.1% formic acid in acetonitrile. A direct spike of each sample analyzed by HPLC was compared to the sum of the radioactivity eluted from the column and used to determine the chromatographic recovery.

## RESULTS AND DISCUSSION

### Storage Stability

All samples and extracts were stored frozen at approximately -20 °C when not in use. Initial analyses of extracts occurred within 2 weeks. Repeat analyses of HPLC samples and extracts stored frozen showed results that were qualitatively similar to the initial analyses, demonstrating stability of the HPLC sample and extracts under these storage conditions. Some quantitative differences were observed between HPLC samples, however the chromatographic profiles were similar.

**Table B.7.1.2-1**

Summary of Storage Conditions			
Matrix (RAC or Extract)	Storage Temp. (°C)	Actual Study Duration (days or months)	Interval of Demonstrated Storage Stability (days or months)
tissues	-20	60-101 days	not re-extracted
extracts, % TRR levels	-20	83 days	83 days (~2 months)
extracts, MS analysis	-20	215 days	215 days (~7 months)

### Dosing and In-life Summary

The plots received 100.6% and 103.4% of the target amount of formulated [<sup>14</sup>C]-PY labelled XDE-729 Methyl and [<sup>14</sup>C]-PH labelled XDE-729 Methyl, respectively. Overall, the [<sup>14</sup>C]-PY labelled XDE-729 Methyl foliar applied plot received 1.40 mg, equivalent to 10.1 g a.i./ha (9.65 g a.e./ha). The [<sup>14</sup>C]-PH labelled XDE-729 Methyl foliar applied plot received 1.44 mg, equivalent to 10.3 g a.i./ha (9.92 g a.e./ha). Both foliar applications were applied at a seasonal 1X rate.

Radiochemical purity and stability of the formulated application solution post-application averaged 99.2% for the [ $^{14}\text{C}$ ]-PY labelled XDE-729 Methyl and 99.0% for the [ $^{14}\text{C}$ ]-PH labelled XDE-729 Methyl. Pre-application retainer sample analyses were similar, with an average of 99.1% for the [ $^{14}\text{C}$ ]-PY labelled XDE-729 Methyl and 98.8% for the [ $^{14}\text{C}$ ]-PH labelled XDE-729 Methyl. This indicates stability of [ $^{14}\text{C}$ ]-PH labelled XDE-729 and [ $^{14}\text{C}$ ]-PY labelled XDE-729 Methyl during storage and application.

### Identification, Characterization, and Distribution of Residues

TRR levels are shown in the table below. In all cases, samples of the turnip tops (foliage) contained higher residue levels than the turnip roots. Roots contained less than 0.010  $\mu\text{g equiv./g}$  tissue, and the TRR levels were lower in mature roots than in immature roots, presumably due to size dilution. The 14 DAT foliage contained approximately 0.08  $\mu\text{g equiv./g}$  tissue, while the mature foliage contained approximately 0.1  $\mu\text{g equiv./g}$  tissue. TRR levels were similar irrespective of radiolabel position.

**Table B.7.1.2-2**

Total Radioactive Residues (TRRs) in Pea Matrices.				
Matrix	Number of Applications	PHI (days)	XDE-208 equivalents	
			dpm/g	mg/kg (ppm)
PY-label				
immature roots	1	14	1,122	0.006
immature tops	1	14	16,163	0.082
mature roots	1	28	366	0.002
mature tops	1	28	21,517	0.109
PH-label				
immature roots	1	14	1,382	0.005
immature tops	1	14	23,127	0.079
mature roots	1	28	406	0.001
mature tops	1	28	26,514	0.091

### Characterization of Radioactive Residues

The turnip roots were not analyzed due to the low TRR levels ( $\leq 0.006$  mg/kg XDE-729 Methyl equivalents). As shown in the table below, an average of approximately 80-85% of the TRR was extracted from the immature and mature turnip tops (foliage) plants with 50/50 methanol/water at 50 °C and 80 °C (combined per sample). An additional amount <3% of the TRR was removed using 50/50/0.1 methanol/water/ $\text{H}_3\text{PO}_4$  at 110 °C; this was not analyzed further. For each tissue sample, the four neutral ASE extracts (50/50 methanol/water at 50 °C and 80 °C) were combined and prepared for HPLC analysis.

In the 14 DAT turnip top samples, five larger components and multiple minor components were present. The overall profile did not change significantly in the 28 DAT samples. Both radiolabels appeared to contain the same major components, indicating that bridge cleavage did not occur. In general, the neutral organic extracts contained multiple components, including parent XDE-729 Methyl, X11393729, X11406790, and glucose and/or malonyl-glucose



conjugates of these components, and other low-level metabolites. No individual metabolite was present at greater than 0.019 mg equiv./kg tissue. The highest individual metabolite was found to be an N-glucose conjugate of XDE-729 methyl, of which two anomers are possible and observed. The combined free plus conjugated XDE-729 methyl averaged 0.028-0.037 mg equiv./kg tissue. HPLC results are summarized in the table below. The radiolabeled metabolites were the same irrespective of radiolabel, indicating no evidence of bridge cleavage. No other metabolites were observed at levels greater than 5% of the TRR.

Table B.7.1.2-3

Distribution of the Residue in Turnip Tops (Foliage) after Application of <sup>14</sup> C-labeled XDE-729 Methyl.							
Fraction	Neutral Organic Extraction <sup>a</sup>		Mild Acid Extraction <sup>a</sup>		Post-Extracted Tissue		Recovery %TRR
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
<b>PY-label</b>							
14 DAT Immature	80.2	0.066	2.6	0.002	14.3	0.012	97.1
28 DAT Mature	81.3	0.089	1.1	0.001	20.9	0.023	103.3
<b>PH-label</b>							
14 DAT Immature	84.2	0.067	2.8	0.002	15.8	0.013	102.9
28 DAT Mature	80.3	0.073	0.9	0.001	23.2	0.021	104.3

<sup>a</sup> These six extractions were completed on the same day: four using 50:50 methanol/water and two using 50:50 methanol/water with 0.1% H<sub>3</sub>PO<sub>4</sub>.

Table B.7.1.2-4

<b>Summary of Characterization and Identification of Radioactive Residues in Plant Matrices Following Application of Radiolabeled XDE-208 to Peas</b>								
	<sup>14</sup> C-PY 14 DAT Turnip Tops TRR 0.082 mg/kg		<sup>14</sup> C-PH 14 DAT Turnip Tops TRR 0.079 mg/kg		<sup>14</sup> C-PY 28 DAT Turnip Tops TRR 0.109 mg/kg		<sup>14</sup> C-PH 28 DAT Turnip Tops <sup>d</sup> TRR 0.091 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
<b>Total Radioactive Residue (TRR)</b>	100	0.082	100	0.079	100	0.109	100	0.091
<b>Total extractable</b>	82.8	0.068	87.0	0.069	82.4	0.090	81.1	0.074
<b>Total analyzed by HPLC</b>	80.2	0.066	84.2	0.067	81.3	0.089	80.3	0.073
Parent XDE-729 ME	12.2	0.010	13.5	0.011	7.3	0.008	6.7	0.006
Polar radioactivity	--	--	--	--	--	--	--	--
Low Level Metabolite: RT 13.7 min	3.0	0.002	3.5	0.003	4.7	0.005	6.5	0.006
X11393729 glucose conjugate	12.6	0.010	12.5	0.010	14.1	0.015	12.9	0.012
X11393729	3.5	0.003	3.1	0.002	3.3	0.004	2.9	0.003
X11406790 malonyl glucose conjugate	7.2	0.006	5.9	0.005	7.1	0.008	7.0	0.006
XDE-729 Methyl N- glucose conjugate (1)	21.4	0.018	19.0	0.015	17.4	0.019	14.9	0.014
XDE-729 Methyl N- glucose conjugate (2)	7.3	0.006	7.4	0.006	9.1	0.010	9.9	0.009
X11406790	1.5	0.001	2.2	0.002	1.5	0.002	2.5	0.002
<b>Total Identified</b>	65.7	0.054	63.7	0.051	59.7	0.065	56.9	0.052
<b>Total characterized<sup>b</sup></b>	14.4	0.012	20.5	0.016	21.6	0.024	22.8	0.021
<b>Total unextractable</b>	14.3	0.012	15.8	0.013	20.9	0.023	23.2	0.021
<b>Accountability<sup>c</sup></b>	97.1	0.080	102.9	0.082	103.3	0.113	104.3	0.095

-- Not observed

<sup>a</sup> mg/kg XDE-729 methyl equivalents

<sup>b</sup> Extractable radioactivity that analyzed by HPLC and was multi-component and did not co-elute with any known reference compound or identified conjugate; "low level metabolite: RT 13.7 min" is included in the characterized total.

<sup>c</sup> Accountability (% TRR) =  $\frac{\text{extractable} + \text{unextractable}}{\text{TRR}}$ .

<sup>d</sup> Sample had no duplicate for HPLC analysis.

**Bound Residues:** The notifier stated that "Bound residue determinations were not necessary because less than 0.025 mg XDE-729 Methyl equivalents/kg remained unextracted". The RMS note that although the % TRR of total unextractable residue is relatively high (14-23.2%), the actual residue is less than 0.05 mg/kg, the trigger for animal feed, therefore it is agreed that further work is not required.

**Degradate and Metabolite Isolation and Identification:** The metabolites were identified in all four turnip top samples. The glucose conjugate of X11393729 was identified by accurate mass

and MS/MS fragmentation. The X11393729 peak in the mass spec report was identified by comparison to a known standard. The peak for the malonyl glucose conjugate of X11406790 was identified by accurate mass and MS/MS fragmentation and comparison to a non-GLP standard. The peaks representing the N-glucose conjugates of XDE-729 methyl were identified by accurate mass and MS/MS fragmentation. The notifier states that HPLC separation of two glucose anomers ( $\alpha$ - or  $\beta$ - conjugated) should be possible, and therefore explain the identical accurate mass of two mass spectral peaks. The peaks representing X11406790 and XDE-729 methyl were identified by comparison to standards.

### Proposed Metabolic Profile

The proposed metabolic pathway is presented in Figure B.7.1.2-2 below. As shown in the diagram, the metabolism of XDE-729 methyl in turnips proceeds through N-conjugation with glucose, or dissociation to produce X11393729, or de-methylation of the methoxy group on the phenyl ring to produce the metabolite X11406790. X11406790 is then conjugated with glucose (theorized) followed by further conjugation with malonic acid. X11393729 is also conjugated with glucose, through either the nitrogen or the oxygen. The higher amounts of conjugates to primary metabolites indicates that conjugation is a preferential route of metabolism.

Previous plant metabolism studies conducted on wheat also concluded that the initial metabolism forms X11393729 and X11406790, with glucose and glucose plus malonic acid conjugation of X11406790. In the case of the longer life-cycle of wheat, metabolism continues through natural incorporation of the radiolabeled carbon into natural plant constituents such as pectin and lignin.

Overall, the  $^{14}\text{C}$ -residues in the turnips were similar to those observed on wheat.

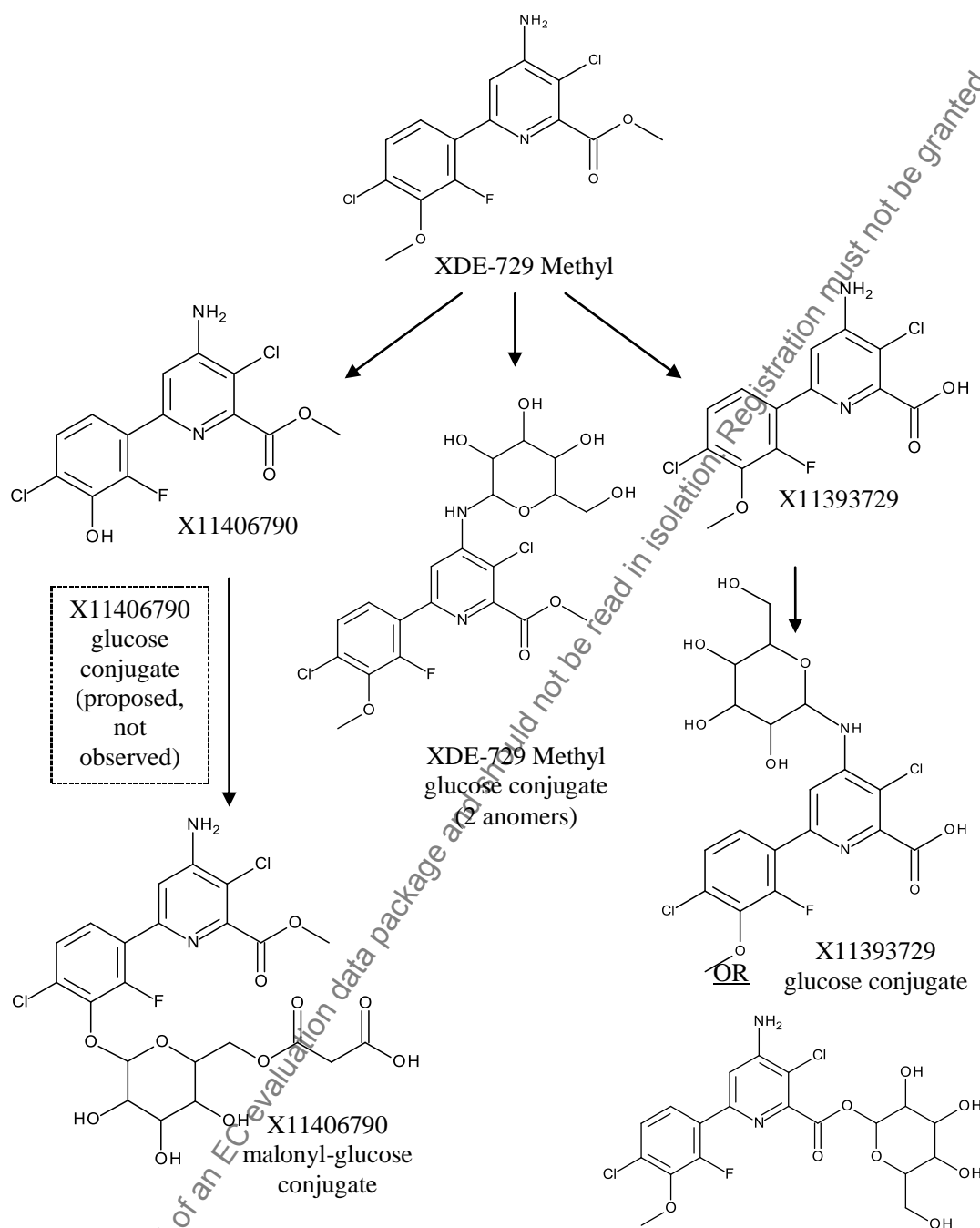
### CONCLUSIONS

A foliar application of XDE-729 Methyl at the maximum proposed seasonal application rate resulted in mature PH-labeled roots and tops that contained 0.001 and 0.091  $\mu\text{g/g}$  XDE-729 Methyl equivalents, respectively. The PY-labeled mature roots and tops contained 0.002 and 0.109  $\mu\text{g/g}$  XDE-729 Methyl equivalents, respectively.

Due to the low levels of radioactivity, the roots were not analyzed further. Immature and mature foliage contained consistent metabolites at similarly low levels. In the mature foliage, the radioactive residue was identified as XDE-729 Methyl (parent) (7% of the TRR, 0.006-0.008  $\mu\text{g/g}$ ), X11393729 (Acid) (3% of the TRR, 0.003-0.004  $\mu\text{g equiv./g}$ ), glucose conjugate of X11393729 (13-14% of the TRR, 0.012-0.015  $\mu\text{g equiv./g}$ ), a malonyl glucose conjugate of X11406790 (7% of the TRR, 0.006-0.008  $\mu\text{g equiv./g}$ ), two N-glucose conjugates of XDE-729 Methyl (anomer 1: 15-17% of the TRR, 0.014-0.019  $\mu\text{g equiv./g}$ , anomer 2: 9-10% of the TRR, 0.009-0.010  $\mu\text{g equiv./g}$ ), and X11406790 (2-3% of the TRR, 0.002  $\mu\text{g equiv./g}$ ). The radiolabeled metabolites were the same irrespective of radiolabel, indicating no evidence of bridge cleavage.

In summary, individual metabolite levels were low, with the majority of the radioactive residue identified as parent XDE-729 methyl, primarily conjugated through the nitrogen. Additionally, de-methylation metabolites X11393729 and X11406790, and glucose or malonyl-glucose conjugates of these metabolites were also observed. The higher amounts of conjugates to primary metabolites indicates that conjugation is a preferential route of metabolism. The overall metabolic pathway is consistent with the metabolic pathway observed in wheat.

Figure B.7.1.2-2 Proposed Metabolic Profile of XDE-729 Methyl in Turnips



**B.7.1.3 Metabolism, distribution and expression of the residue in rotational crops**

**Report:** Rotondaro, S. L. *A Confined Rotational Crop Study with [<sup>14</sup>C]-XDE-729 Methyl Ester, Unpublished report of Dow AgroSciences, study ID 101635, 09-DEC-2011.*

**Guidelines:** OECD Guidance Document 502 for Metabolism in Rotational Crops (Issued 8 January 2007)

**GLP:** Yes (certified laboratory)

The amount, nature and distribution of residues in the raw agricultural commodities from three rotational crops (a cereal, a leafy vegetable, and a root crop) planted 14, 90 and 270 days after treatment (DAT) of a single bare soil application of <sup>14</sup>C-XDE-729 methyl (labelled at the phenyl ring <sup>14</sup>C-PH-XDE-729 methyl and at the pyridyl ring <sup>14</sup>C-PY-XDE-729 methyl) were investigated. The <sup>14</sup>C-XDE-729 methyl was formulated as an emulsifiable concentrate (EC), and applied at a target rate of 10 g a.e./ha. The proposed GAP on Spring cereals is 1 application of 6.25 g a.s./ha, therefore the study rate represents 1.6N. The GAP for winter cereals proposes two applications, the first 7.82 g/a.s./ha (BBCH 09 to 29), and the second 6.25 g/a.s./ha (BBCH13 to 45), therefore resulting in a maximum total dose of 14.07 g/a.s./ha. This maximum total dose equates to 0.7N. Since 25% of the maximum total dose would be 3.5175 g a.s./ha ± 25% from the application rate would be 10.55-17.59 g a.s./ha. Therefore the application rate used in the study is just below the minimum application rate. The metabolism study however demonstrated that all crop fractions harvested contained less than 0.01 mg/kg XDE-729 methyl equivalents. Furthermore, the study involved application of the active substance to bare soil, whereas in practical use, XDE-729 methyl is a foliar treatment to be applied to a cereal crop and not directly to the bare soil. Therefore, it is expected that the crop will intercept the applied XDE-729 methyl, such that the soil will only receive a portion of the application. Therefore application to bare soil may be considered a worst-case scenario. It is noted that for spring cereals the study is acceptable, with a rate of 1.6N, without considering crop interception; However, for winter cereals, the additional consideration of crop interception, as discussed above, makes it reasonable to conclude that although the application rate does not accurately reflect the proposed maximum total application rate proposed by the DAR for winter or spring cereals, the study is fit for purpose in this instance. Finally, from the soil photolysis study submitted for evaluation by fate, it would appear that soil photolysis is unlikely to influence the speed of metabolism or the metabolic pathway, compared to the metabolism observed from the active substance applied to the crop at a later growth stage (where metabolism will occur in the plant rather than in the soil). Therefore the study in which the active substance is applied to bare soil is also fit for purpose to address metabolism in rotational crops when application is at the later growth stage, and where there will be greater crop interception.

This study was conducted between 2010 and 2011 in confined conditions in sandy loam soil in the USA.

**Table B.7.1.3-1****Test Site and Crop Information**

<b>Test Site Information</b>				
Testing Environment*	Soil characteristics**			
	Type	%OM	pH	CEC
Outdoor test plots for 1 <sup>st</sup> 140 DAT , then greenhouse until 361 DAT (only wheat (for hay and mature collection) returned outdoors)	sandy loam	3.1	4.6	9.1

365 outdoor test plots, greenhouse, plant growth chambers, etc

\*\* Only required for studies involving a soil treatment

There were no meteorological abnormalities that may have impacted the study.

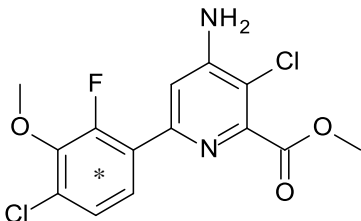
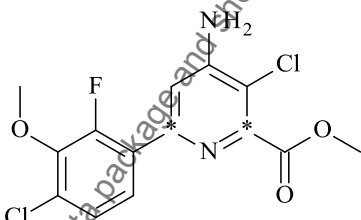
**Table B.7.1.3-2**

<b>Crop Information</b>					
Crop/ crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested RAC	Harvesting procedure
Lettuce /leafy vegetable	Grand Rapids	14-, 90- and 270-day plant-back*	BBCH 41-43	immature	cut by hand
			BBCH 49	mature	cut by hand
Radish/ root crop	Cherry Belle	14-, 90- and 270-day plant-back*	BBCH 49	mature tops and roots	pulled by hand, tops & roots separated
Wheat/ cereal	Coker 9553	14-, 90- and 270-day plant-back*	BBCH 25	forage	cut by hand
			BBCH 61-85	hay	cut by hand, dried 3-6 days in greenhouse
			BBCH 89	straw & grain	cut by hand, separated grain, chaff combined with straw

\*14, 90 and 270 days after application.

Nominally 0.81 mCi of  $^{14}\text{C}$ -PH-XDE-729 methyl was received in 1:1 methanol:acetonitrile and diluted to 5 mL with acetonitrile. Nominally 0.53 mCi of  $^{14}\text{C}$ -PY-XDE-729 methyl was received in 1:1 methanol:acetonitrile and diluted to 5 mL with acetonitrile. The test substances were analyzed for amount of radioactivity and purity. The specific activity was not adjusted. The solvent was removed from a nominal 5.65 mg of each radiolabeled test substance separately, under a gentle stream of nitrogen. The dried test substances were shipped to the contract laboratory.

Table B.7.1.3-3

Test Material Characteristics	
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>
Common Name	$^{14}\text{C}$ -PH-XDE-729 methyl
Lot No.	INV031089-0003
Purity	97.4% (18 Jun 2009), FAPC-G-09-23
Specific activity	45.3 mCi/mmole
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>
Common Name	$^{14}\text{C}$ -PY-XDE-729 methyl
Lot No.	INV027098-0002
Purity	97.8% (18 Jun 2009), FAPC-G-09--22
Specific activity	29.6 mCi/mmole

Upon receipt at the contract laboratory, 0.67 mL EC formulation blank GF-2630 was added to each radiolabeled test substance, carefully mixed, and refrigerated pending application. On the day of application, 04 June 2010, the formulated test materials were removed from the refrigerator. Approximately 200 mL water was added to an amber glass bottle. The test material was quantitatively transferred to the mixing container using five sequential 2-mL portions of water, and a total of 410 mL of water was added to the mixing container. Aliquots (0.25 mL) were taken to determine the concentration of the spray solution and confirm homogeneity. The remainder of the spray solution was then divided into four portions, 102 mL each, for application

to each of the four prepared boxes per radiolabel. In general, the bare soil applications were made using a hand-held trigger sprayer in which the container was covered with aluminum foil, evenly spraying per box. The spray solution container was then rinsed with 25 mL of water, swirled, then sprayed evenly onto the same plot. Two boxes were left untreated.

## **Identification/ Characterization of Residues**

### **Sample Handling and Preparation**

Following harvest, plant samples were stored frozen. In general the frozen plants were homogenized using a Robot Coupe with dry ice. The milled samples were stored in a freezer (approximately -10°C) while the dry ice was allowed to sublime.

Aliquots (5 x approximately 0.25 g) of the milled samples were analyzed by oxidative combustion to determine the radioactive residues in the samples. Combustion analysis occurred within 15 days of harvest.

### **Analytical Methodology**

The total radioactive residue levels in all crops at all plant-back intervals were well below 0.01 mg/kg XDE-729 methyl equivalents, and were therefore not analyzed.

### **Storage Stability**

Since all samples were stored frozen at or below approximately -10 °C when not in use, and combustion analysis occurred within 15 days of harvest, assessment of storage stability was not necessary.

### **Application and In-life Summary**

Radiochemical purity of the PH- and PY-labelled XDE-729 methyl prior to application was determined to be 99.59% and 99.31%, respectively, by HPLC. The specific activity was unchanged at 291,361 and 194,664 dpm/μg for the PH- and PY-label, respectively.

Four boxes were treated per radiolabeled test substance at a rate of 9.8 g acid equivalents (a.e.)/ha. Each box received 98% of the target amount of formulated XDE-729 methyl to the test plot.

Aliquots of the application solutions were collected before and after application, and shipped to DAS for analysis. HPLC analysis demonstrated that the <sup>14</sup>C-PH-XDE-729 methyl averaged 98.3% radiopurity before and after application. HPLC analysis demonstrated that the <sup>14</sup>C-PY-XDE-729 methyl averaged 98.4% radiopurity before application and 99.0% after application. Therefore, the test substance did not degrade during the application.

## **Identification, Characterization, and Distribution of Residues**

### **TRR Levels**

TRR levels are shown in **Table B.7.1.3-4**. All samples from all plant-back intervals contained well below 0.01 mg XDE-729 methyl equivalents/kg.



Table B.7.1.3-4

Total Radioactive Residues (TRRs) in CRC Tissue Matrices.					
Raw Agricultural Commodity	plant-back (days)	PH TRR		PY TRR	
		(dpm/g)	(mg/kg) <sup>a</sup>	(dpm/g)	(mg/kg) <sup>a</sup>
radish tops	14	56	<LOQ <sup>b</sup>	64	<LOQ <sup>b</sup>
radish roots	14	90	<LOQ	83	<LOQ
immature lettuce	14	178	0.001	227	0.001
mature lettuce	14	68	<LOQ	50	<LOQ
wheat forage	14	95	<LOQ	55	<LOQ
wheat hay	14	197	0.001	234	0.001
wheat grain	14	194	0.001	144	<LOQ
wheat straw	14	229	0.001	193	0.001
radish tops	90	93	<LOQ	65	<LOQ
radish roots	90	55	<LOQ	77	<LOQ
immature lettuce	90	131	<LOQ	101	<LOQ
mature lettuce	90	127	<LOQ	181	0.001
wheat forage	90	137	<LOQ	91	<LOQ
wheat hay	90	164	0.001	140	<LOQ
wheat grain	90	104	<LOQ	85	<LOQ
wheat straw	90	141	<LOQ	131	<LOQ
radish tops	270	110	<LOQ	95	<LOQ
radish roots	270	79	<LOQ	93	<LOQ
immature lettuce	270	172	0.001	113	<LOQ
mature lettuce	270	311	0.001	141	<LOQ
wheat forage	270	111	<LOQ	122	<LOQ
wheat hay	270	158	<LOQ	166	0.001
wheat grain	270	242	0.001	240	0.001
wheat straw	270	98	<LOQ	64	<LOQ

<sup>a</sup> mg XDE-729 methyl equivalents/kg tissue

<sup>b</sup> Less than the limit of quantitation (LOQ), where LOQ = 0.00055 mg/kg for the PH-label and LOQ = 0.00082 mg/kg for the PY label

Due to the very low TRR levels, none of the tissue samples were characterized further.

### Summary/assessment

XDE-729 methyl radiolabeled in either the phenyl or pyridine ring was applied to plots of bare sandy loam soil at the rate of 10 g a.e./ha. At three plant-back intervals (14, 90, and 270 days) radishes, lettuce, and wheat were sown. The crops were grown outdoors to maturity at Ricerca, Ohio, USA. Plot maintenance simulated typical cultural practices.

From each plant-back interval, immature lettuce, mature lettuce, mature radish tops, mature radish roots, wheat forage, wheat hay, and wheat grain and straw were harvested. The harvested crops were milled and combusted to determine Total Radioactive Residue levels. All crop fractions harvested contained less than 0.01 mg/kg XDE-729 methyl equivalents, and were therefore not analyzed further.

It is unlikely that crops rotated into wheat fields treated with XDE-729 at 10 g a.e./ha would result in detectable levels of XDE-729 methyl or metabolites in any Raw Agricultural

Commodity. Because of the low residue levels in all crops at all plant-back intervals, a metabolic pathway has not been proposed, and a succeeding residue trials crop study and tolerance/MRL are not necessary for succeeding crops.

It is noted that the Environmental Fate assessment (Section B.8.3 iv) has concluded that high levels of unextracted residues may accumulate at up to 3.83 times the initial parent dose (although there is some uncertainty about this level of accumulation). Uniform Principles relating to unextracted residues state that no authorisation can be granted in the case of high unextracted residue, unless it can be scientifically demonstrated that there is no accumulation in soil at such levels that unacceptable residues in succeeding crops occur. In this instance, given the results of the rotational crop metabolism study confirmed that levels of TRR in all crop samples were very low, and at a level that did not need further characterisation, it can be concluded that, despite accumulation in the soil, it is reasonable to conclude that unacceptable residues will not occur in succeeding crops.

## **B.7.2 Metabolism, distribution and expression of the residues in livestock (AII 6.2, IIIA 8.1)**

### **B.7.2.1 Cattle**

A metabolism study in cattle has not been submitted, but the ruminant metabolism is addressed through the submission of the goat metabolism study evaluated below.

### **B.7.2.2 Goats**

**Report:** [REDACTED] *A Nature of the Residue Study in the Ruminant with [14C]-XDE-729 Methyl Ester, Unpublished report of [REDACTED] study ID 101389, 27 October 2011.*

**Guidelines:** *OECD Guidance Document 503 for Metabolism in Livestock (Issued 8 January 2007)*

**GLP:** *Yes (certified laboratory)*

In a metabolism study performed in 2011 goats were orally dosed (a single gelatine capsule, no absorbent) once a day for five consecutive days with either  $^{14}\text{C}$ -PH-XDE-729 methyl (radiochemical purity 97.4%, specific activity 9.63 mCi/mmol) or  $^{14}\text{C}$ -PY-XDE-729 methyl (radiochemical purity 97.8%, specific activity 9.50 mCi/mmol).

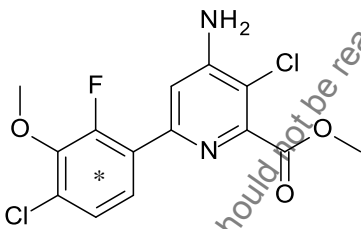
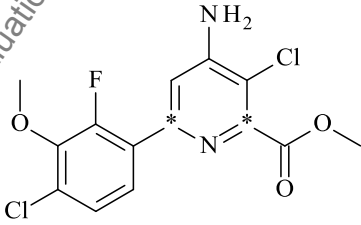
#### Preparation of Test Materials

The  $^{14}\text{C}$ -PH-label-XDE-729 methyl was prepared by combining 59 mg non-radiolabeled test substance and 16 mg radiolabeled test substance (9.970 mL) for a final specific activity of 9.63 mCi/mmol (61,968 dpm/ $\mu\text{g}$ ). The procedure was repeated with the  $^{14}\text{C}$ -PY-label-test substance by combining 50 mg non-radiolabeled test substance and 24 mg radiolabeled test substance (9.970 mL) for a final specific activity of 9.50 mCi/mmol (61,130 dpm/ $\mu\text{g}$ ). The solvent was removed under a gentle stream of nitrogen. The dried test substances were shipped to the contract laboratory.

Aliquots of the dose solution were collected before and after dosing, and shipped to DAS for analysis. HPLC analysis demonstrated that  $^{14}\text{C}$ -PH-XDE-729 methyl averaged 97.7% radiopurity before dosing and 97.6% after dosing, and that the  $^{14}\text{C}$ -PY-XDE-729 methyl averaged 97.7% radiopurity before dosing and 97.8% after dosing.

The target dose rate of 10 mg/kg feed was based on the average feed consumption during the acclimation period, and the amount of radioactivity shipped to the contract lab. The goat dosed with PY-label XDE-729 methyl consumed less than the already restricted amount of feed. The resulting actual dose rates were 10.25 and 11.17 mg/kg dry feed/day for the  $^{14}\text{C}$ -PH-label and  $^{14}\text{C}$ -PY-label dosed animals, respectively. The actual dose rates were 103-112% of target.

Table - B.7.2.2-1

Test Animal Dosing Regime			
Treatment Type	Feeding Level (ppm test material in food on a dry weight basis)	Vehicle	Timing/Duration
Oral	PH: 10.25 ppm PY: 11.17 ppm	Capsules (no absorbent).	A single capsule was administered once a day (at about 9 am) orally by balling gun to each animal for 5 consecutive days.
Test Material Characteristics			
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>		
Common Name	$^{14}\text{C}$ -PH-XDE-729 methyl		
Lot No.	INV031089-0003		
Purity	97.4% (18 Jun 2009), FAPC-G-09-23		
Specific activity	45.3 mCi/mmol, adjusted to 9.63 mCi/mmol		
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>		
Common Name	$^{14}\text{C}$ -PY-XDE-729 methyl		
Lot No.	INV027098-0002		
Purity	97.8% (18 Jun 2009), FAPC-G-09--22		
Specific activity	29.6 mCi/mmol, adjusted to 9.50 mCi/mmol		

Milk was collected twice daily, once in the morning and once in the afternoon. Afternoon samples weighed 616-818 g, while morning samples weighed 1091-1334 g. Urine and faeces were collected at 24-hour intervals immediately prior to dose administration. Cage washes were collected after necropsy. Within 6-8 hours of the administration of the final dose the animals were sacrificed and samples of muscle (loin), muscle (flank), liver, kidney, fat (subcutaneous), fat (omental), fat (renal), GI tract and contents (for mass balance only) were collected and prepared for analysis. Samples were stored at  $\leq -10$  °C pending analysis and shipment to the sponsor.

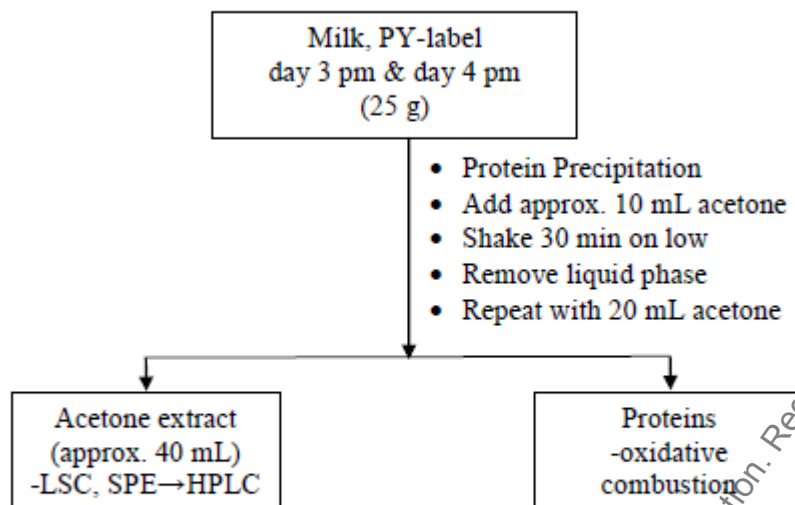
The feed consumption, milk production, animal weights and observations by veterinary personnel were made on the animals during the course of the study. Animal 4976 (dosed with  $^{14}\text{C}$ -PY-labeled XDE-729 methyl) was stated in the study report to be in good health according to the daily observations, however at necropsy the kidneys were noted as being mottled, discoloured, and enlarged. The kidneys were working sufficiently to eat and produce milk, and the observations at necropsy were presumed to be incidental and consistent with normal production dairy goats and therefore without effect on the study. Animal 4977 (dosed with  $^{14}\text{C}$ -PY-labeled XDE-729 methyl) was noted to have blood in milk on study days 4 and 5. At necropsy, no visible pathological evidence was found to explain the presence of blood. Although it is considered a shortcoming of the study that the health of the animals was not better, given that the results of the study reflect a similar metabolic pathway and distribution of residues as observed in the rat study (where animal health was not in question) it would suggest that the health of the goats did not impact on the performance of the study. Furthermore, evaluation of the first and second season's trial data (see section 7.6 *Residues arising from supervised trials*) showed that animal intakes are not significant - the highest dietary burden was 0.035 mg/kg DM basis for beef cattle. Therefore, for the purpose of this authorisation for the representative use on cereal at the proposed GAP, the metabolism study will not be relied on further.

#### Milk

PY milk samples collected on the afternoons (pm) of days 3 and 4 were extracted. The proteins were precipitated from duplicate aliquots of each (approximately 25 g) by the addition of acetone (10 mL). The mixture was shaken for 30 minutes on low on a horizontal shaker, and the liquid phase removed. The solids were extracted one more time with 20 mL acetone, the liquid pooled and the volume measured. Aliquots of the extract were analyzed by LSC. The precipitated proteins were weighed and aliquots analyzed by oxidative combustion. The remainder of the acetone extracts were cleaned-up using the Strata-X SPE method in preparation for HPLC analysis.

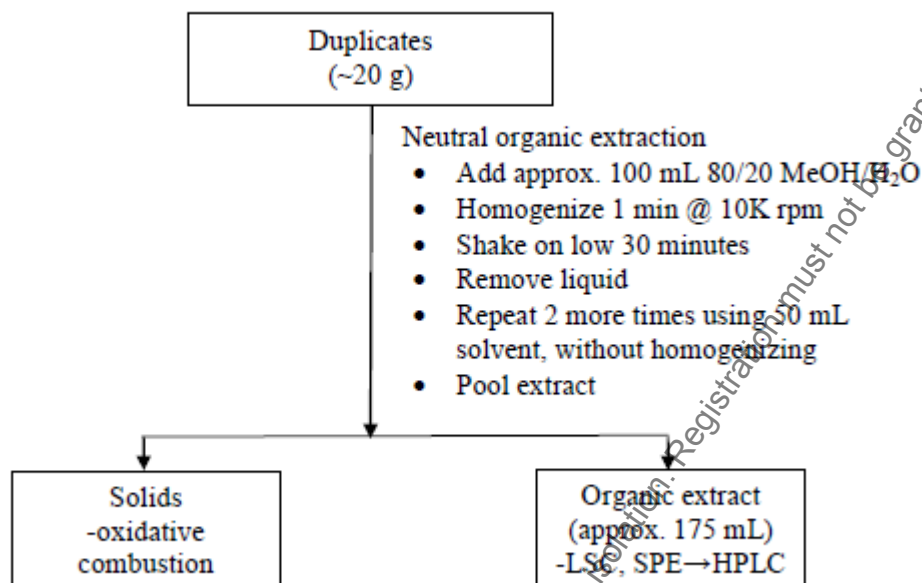
Figure B.7.2.2-1

Figure 4. Schematic Flowchart for the Analysis of Milk

Liver, Kidney, and Faeces:

Duplicates of liver, kidney, and days 1, 3, and 5 faeces (approximately 20 g) were extracted with methanol/water (80/20, v/v). Approximately 100 mL solvent was added and the mixture was homogenized for approximately 2 minutes at 10,000 rpm. After shaking on low on a horizontal shaker for 30 minutes, the liquid phase was separated by centrifugation, and the process repeated two more times (not including homogenization) using 50 mL solvent. The extracts were pooled per sample replicate. The volume of each extract was measured and recorded, and aliquots were analyzed by LSC. The remaining post-extracted solids were weighed and aliquots analyzed by oxidative combustion.

Duplicate aliquots of the neutral organic extracts (40 mL, except 10 or 20 mL of PY-labelled faeces) were cleaned-up using the Strata-X SPE method in preparation for HPLC analysis.

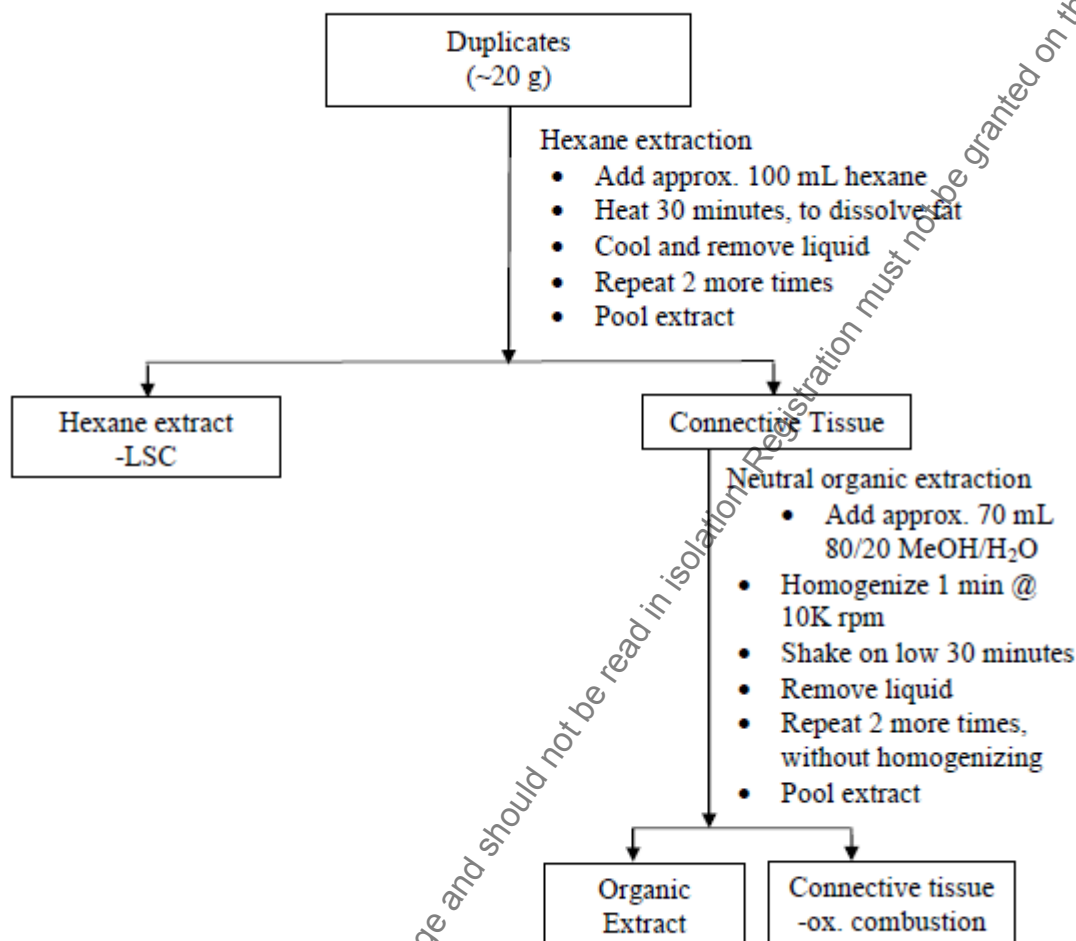
**Figure B.7.2.2-2****Figure 5. Schematic Flowchart for the Analysis of Liver, Kidney, and Feces****Fat:**

The analysis procedure for PH renal fat is described below. The other PH-labelled fat samples and all PY-labelled fat samples contained <0.01 mg/kg XDE-729 methyl equivalents, and were therefore not analyzed further.

Duplicate aliquots of PH-labeled renal fat (approximately 20 g) were first extracted with hexane (approximately 100 mL), heating at 70-75 °C in water bath with an orbital shaker for 30 minutes to dissolve the fat. The process was repeated with 60 mL hexane. The hexane extracts were pooled and the volume recorded and triplicate aliquots were removed for LSC.

The connective tissue remaining after the hexane extraction was further extracted with methanol/water (80/20, v/v). Approximately 70 mL neutral organic solvent was added and the mixture was homogenized for approximately 1 minute at 10,000 rpm. After shaking on a horizontal shaker (low speed) for 30 minutes, the liquid phase was separated, and the process repeated two more times (not including homogenization). The extracts were pooled and the volume recorded and triplicate aliquots were removed for LSC. The remaining connective tissue samples were weighed and aliquots analyzed by oxidative combustion.

Duplicate aliquots of the neutral organic extracts (75 mL) were cleaned-up using the Strata-X SPE method in preparation for HPLC analysis.

**Figure B.7.2.2-3****Figure 6. Schematic Flowchart for the Analysis of Fat****Urine:**

Aliquots of each urine sample were analyzed directly by LSC and HPLC. Additional aliquots of urine (300 µL) were acidified with formic acid (15 µL) in an attempt to lower all samples to a similar pH, then analyzed by HPLC.

**Bound Residue**

Since neutral organic extraction quantitatively removed all of the radioactivity, bound residue determination procedures were not necessary.

### Analytical Methodology

**TRR:** Aliquots (5 x approximately 0.2 g) of the homogenized tissue samples were placed in combustion cones, air-dried at room temperature overnight, and analyzed by oxidative combustion to determine the total radioactive residues in the samples. Milk and urine were analyzed by direct LSC of 0.4-g or 0.2-g aliquots, respectively. The TRR in fat was determined by heated solubilization (approximately 60 minutes at 60-80 °C) of the fat (5 x 0.2-g aliquots) and subsequent LSC. Aliquots (5 x approximately 0.5 g) of the homogenized faeces samples were placed in combustion cones, air-dried at room temperature overnight, and analyzed by oxidative combustion.

**SPE:** The general clean-up procedure for the extracts was with a Strata-X SPE (500 mg, 8B-S100-HDG, Phenomenex Inc., Torrance, California, USA). The samples were prepared by concentrating in a Turbovap (40 °C water bath and 10 psi nitrogen) to remove the majority of the organic solvent then adding 0.1% H<sub>3</sub>PO<sub>4</sub> in water (8 mL). The SPE cartridges were conditioned with methanol (5 mL) followed by 0.1% H<sub>3</sub>PO<sub>4</sub> in water (2 x 5 mL). The concentrated sample was diluted then applied to the conditioned SPE, and eluted at approx. 2 mL/min, collecting the eluate. The SPE was dried for 10 seconds after the SPE had eluted. The sample vial was rinsed with 0.1% H<sub>3</sub>PO<sub>4</sub> in water (5 mL), transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. The SPE cartridge was dried under full vacuum for 20 seconds. The Strata-X SPE was eluted with methanol: 0.1% H<sub>3</sub>PO<sub>4</sub> in water (95:5, v/v) in two aliquots (5 mL each), pooling the elution aliquots.

A glycerol “keeper” was added to the elution samples (0.1 mL 80/20 methanol/glycerol) then the elution samples were concentrated to near dryness (approximately 0.1 mL) in a Turbovap (30 °C water bath and 10 psi nitrogen). The elution samples were reconstituted in 200 µL of acetonitrile, sonicated, then diluted with 700 µL water, and sonicated and mixed well. The volume of each reconstituted elution sample was calculated by weight and density. Triplicate aliquots of each load and reconstituted elution sample were analyzed by LSC. The concentrated elution sample was also analyzed by HPLC.

### Storage Stability

The study report states that samples and extracts were stored at approximately -20 °C when not in use (SBL reported this as -10 °C), see Table B.7.2.2-2.



Table B.7.2.2-2

Summary of Storage Conditions			
Matrix	Storage Temp.(°C)	Actual Storage Duration (Days)	Interval of Demonstrated Storage Stability (Days)
Milk and Edible Tissues	-20	52-172	119
Extracts	-20	102-304	304
Excreta (Urine and Feces)	-20	60-292	292

Storage stability from the study report (A Nature of the Residue Study in the Ruminant with [14C]-XDE-729 Methyl Ester, ID 101389) shows that milk and edible tissues are stored frozen for up to 172 days. Since this is approximately 6 months storage whilst frozen, storage stability does not need to be addressed further. However, for the extracts and excreta, the report states that storage at -20°C took place over 304 and 292 days respectively. The notifier was therefore requested to address storage stability over this storage interval. The following paragraph was provided in response:

*“At DAS, samples and extracts were stored at approximately -20 °C when not in use (SBL reported this as ≤-10 °C). Initial extraction of tissues was within 58-63 days after sacrifice. These analyses were used to determine metabolite levels (% TRR and mg eq/kg). Later analyses were for qualitative mass spectral metabolite identification only. Stability of the extracts is demonstrated by comparison of the figure used for determine metabolite levels with the corresponding radioactive monitoring in the mass spectral report. Feces was analyzed within 6 months, and not re-analyzed by mass spectrometry. Re-analysis of matrices after extended storage demonstrated stability during storage under conditions used. For those samples that were re-analyzed, storage stability data was also provided in the study report. The intervals of storage stability were calculated as follows:*

*Tissue: date of final extraction – date of initial extraction*

*example, milk: 24 NOV 2010 – 28 JUL 2010 = 119 days*

*Extract: date of final analysis (HPLC or LC/MS) – date extracted*

*example, milk: 26 MAR 2011 – 24 NOV 2010 = 122 days”.*

The RMS considers the above response to be acceptable, and storage stability has been addressed.

#### Metabolite isolation:

Larger aliquots (approximately 150 g) of Day 3 pm milk were extracted in duplicate using procedures similar to those described above. SPE of the concentrated acetone extract was hindered, presumably by high levels of fat in the milk, therefore the aqueous phase of the acetone extracts were partitioned against hexane, using acetonitrile to aide breaking the emulsions which formed. The aqueous phase was concentrated to remove organic solvent and clean-up *via* fresh Strata-X SPE was resumed. The hexane phase was analyzed by LSC and discarded due to low radioactivity. The elution samples were combined, concentrated, centrifuged to remove precipitated solids, and ultimately submitted for mass spectral analysis.

Aliquots (100 mL) of both replicates of the kidney extracts were purified by Strata-X SPE after partitioning with hexane to remove fats. The eluents were combined and concentrated under a gentle stream of nitrogen (no heat) and submitted for mass spectral analysis.

Aliquots (1.5 mL) of both labels Day 5 urine were centrifuged (5 minutes at 10,000 rpm) to remove solids, and the supernatants acidified with formic acid (75 µL). The acidified urine samples were submitted for mass spectral analysis.

Metabolites were identified based upon relative retention time and mass spectral matching with the reference standard. There was no difference in metabolites identified from the PH- or PY-labelled groups. There was no evidence of bridge cleavage.

Reference standards were not available for the sulphate conjugate of X11406790 and the N-glucuronic acid conjugate of XDE-729 methyl; however, structural assignments have been proposed through interpretation of the fragmentation pattern in mass spectra in figure 6, figure 31 and figure 32 of the study report ID 101389. However, there were a number of peaks that were prominent in the spectra that had not been identified to a structure. The notifier was requested to provide further information to address the additional peaks. The notifiers response is shown below:

*“Additional spectral peaks are co-extracted natural components, not related to the XDE-729 Methyl test material (ref. figure 6, 31 and 32 of report ID 101389). At the retention time of radioactivity, relevant peaks were determined using chlorine and/or <sup>14</sup>C isotopic patterns and the mass defect of chlorine, to eliminate endogenous components from metabolites of the test substance”.*

This response addresses the concerns raised by the RMS over the additional peaks present in the mass spectral analysis.

#### Milk, Tissue and Excreta TRR Levels

As summarized in Table B.7.2.2-3, 67% and 70% of the dose was recovered from the <sup>14</sup>C-PH-XDE-729 methyl and <sup>14</sup>C-PY-XDE-729 methyl dosed animal, respectively. The majority of the dose was excreted, 32.9% and 33.9% in the faeces, and 20.4% and 28.9% in the urine from the PH- and PY-labelled groups, respectively, accounting for more than 50% of the dosed radioactivity. Additionally, 13.0% and 7.0% of the dose was recovered in the gastrointestinal tract and contents of the PH- and PY-labelled groups, respectively. The majority of this recovered radioactivity was found in the contents of the GI tract, indicating that the radioactivity had not been absorbed. Had the GI contents been allowed to be completely digested, more radioactivity would presumably have been absorbed. Blood was found to contain less than 0.03% of the dosed radioactivity for both dose groups. The remaining carcasses were not evaluated. Overall, absorption and elimination of the <sup>14</sup>C-XDE-729 methyl were rapid.

Milk contained less than 0.1% of the dose. During the dosing period the residue levels in milk reached a plateau of approximately 0.003-0.006 mg/kg XDE-729 methyl equivalents by the day 3 pm sample (Table B.7.2.2-3. and Figure B.7.2.2-4.). In general, the concentration was slightly higher in the samples collected in the afternoon, yet less milk was collected than in the morning samples.

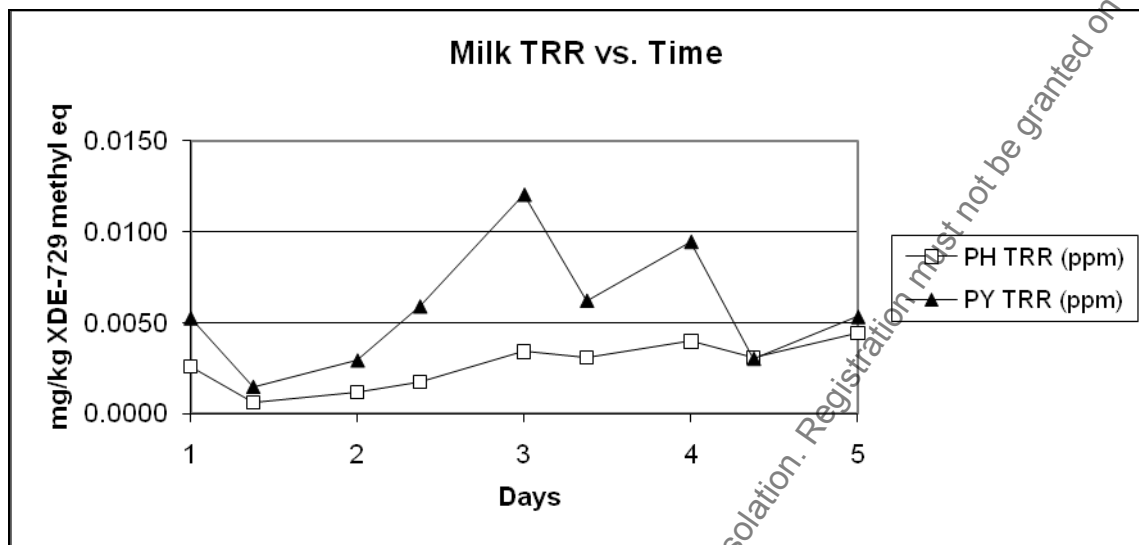
Less than 0.2% of the dose was recovered in the edible tissues. Residue levels are summarized in Table B.7.2.2-3. Residues in the PH-label group kidney, liver, and renal fat were 0.121, 0.077, and 0.016 mg/kg XDE-729 methyl equivalents and 0.041, 0.032, and 0.002 mg/kg XDE-729 methyl equivalents in the PY-labelled group, respectively. Residues in loin muscle, flank muscle, subcutaneous fat, and omental fat were near or below the limit of quantification.

Overall, the residue levels were similar between the two radiolabels, although the FRR levels in the PH-labelled group tissues were slightly higher. The study report claims this may be due to this animal being sacrificed almost an hour earlier than the PY-dosed animal, giving the PY-dosed animal slightly more time to absorb and eliminate the XDE-729 methyl and metabolites.

Table B.7.2.2-3

Total Radioactive Residues (TRRs) in the Excreta, Milk and Edible Tissues of Lactating Goats Dosed with <sup>14</sup> C XDE-729 Methyl					
Matrix	Collection Timing	<sup>14</sup> C-PH-XDE-729 Methyl		<sup>14</sup> C-PY-XDE-729 Methyl	
		(mg/kg)	(% dose)	(mg/kg)	(% dose)
Milk	Day 1 pm	0.003	0.002	0.005	0.005
	Day 1 am	(0.001)	0.001	(0.001)	0.002
	Day 2 pm	(0.001)	0.001	0.003	0.003
	Day 2 am	(0.002)	0.003	0.006	0.009
	Day 3 pm	0.003	0.003	0.012	0.012
	Day 3 am	0.003	0.005	0.006	0.010
	Day 4 pm	0.004	0.005	0.009	0.010
	Day 4 am	0.003	0.005	0.003	0.005
	Day 5 pm	0.004	0.004	0.005	0.004
	total	Not applicable	0.03	Not applicable	0.06
Urine	Day 1	0.807	3.9	1.726	4.3
	Day 2	0.331	2.5	1.571	5.7
	Day 3	0.926	6.6	2.698	8.6
	Day 4	0.688	4.5	2.404	7.6
	Day 5	1.175	2.9	3.385	2.7
	total	Not applicable	20.4	Not applicable	28.9
Faeces	Day 1	1.417	6.4	1.169	6.8
	Day 2	0.694	3.5	0.394	1.9
	Day 3	1.806	6.6	1.444	8.0
	Day 4	1.944	7.6	2.639	14.1
	Day 5	2.412	8.8	1.111	3.1
	total	Not applicable	32.9	Not applicable	33.9
Cage rinse	sacrifice	0.361	0.10	1.385	0.39
Muscle-flank	sacrifice	(0.002)	0.001	(0.001)	0.001
Muscle-loin	sacrifice	ND	0.00	ND	0.000
Liver	sacrifice	0.077	0.11	0.032	0.034
Fat-omental	sacrifice	0.005	0.001	(0.001)	0.001
Fat-subcutan.	sacrifice	(0.003)	0.0001	(0.002)	0.0001
Fat-renal	sacrifice	0.016	0.002	(0.002)	0.0001
Kidney	sacrifice	0.121	0.039	0.041	0.008
Edible tissue	total	Not applicable	0.16	Not applicable	0.05
GI Tract	sacrifice	0.265	1.4	0.219	0.55
GI contents	sacrifice	0.858	11.6	0.876	6.42
Blood	sacrifice	0.010	0.027	0.006	0.013
Total		Not applicable	66.7	Not applicable	70.3

**Pharmacokinetics of  $^{14}\text{C}$  XDE-729 Methyl in the Milk of Lactating Goats**  
**Figure B.7.2.2-4**



### Characterization of Residues

**Milk:** The Day 3 and Day 4 afternoon milk samples collected from the PY-labelled group were extracted as described above; these were the only samples containing near or above 0.01 mg/kg XDE-729 methyl equivalents. The majority of the radioactivity remained in solution after protein precipitation with acetone, approximately 91% of the TRR (Table B.7.2.2-4.). An average of 0.001 mg/kg XDE-729 methyl equivalents was unextractable. The milk solids were noted as slightly pink, due to blood in the original milk samples. The blood did not appear to be extracted. The acetone extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 81-96% in the eluent of the Strata-X SPE, however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the milk contained primarily conjugates of X11406790, with lower levels of X11449757, X11393729, and other free and conjugated metabolites, as shown in Table B.7.2.2-4. Overall, an average of 81% and 68% of the day 3 pm and day 4 pm milk was identified, while an average of  $\leq 0.002$  mg/kg XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites). Given the level of unextractable residue and characterised residue (i.e. not identified) is less than the trigger value 0.01 mg/kg further characterisation is not required.

**Characterization of Residues in Liver:** Aliquots of both the PH- and PY-labelled liver were extracted as described above. The majority of the radioactivity was extracted with neutral organic solvent, approximately 88% and 74% of the TRR from the PH- and PY-labelled groups, respectively (Table B.7.2.2-4.). An average of 0.006-0.007 mg/kg XDE-729 methyl equivalents

was unextractable. The extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 75-105% in the eluent of the Strata-X SPE, however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the liver contained primarily free X11449757 and X11393729, as shown in Table B.7.2.2-4. The two radiolabels were qualitatively similar except that X11406790 and glucuronic acid conjugated X11406790 were only detected in the PY-label. Overall, an average of 74% and 48% of the PH- and PY-labelled liver was identified by one chromatographic system only, while an average of 0.011 and 0.008 mg/kg XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites); the characterized radioactivity was multi-component.

Characterization of Residues in Kidney: Aliquots of both the PH- and PY-labelled kidneys were extracted as described above. The majority of the radioactivity was extracted with neutral organic solvent, approximately 100% and 102% of the TRR from the PH- and PY-labelled groups, respectively (Table B.7.2.2-4.). An average of 0.001-0.002 mg/kg XDE-729 methyl equivalents was unextractable. The extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 91-100% in the eluent of the Strata-X SPE; however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the kidney contained primarily free X11393729 plus lower levels of the sulfate conjugate of X11449757, X11449757, and the glucuronic acid conjugate of X11406790, and the sulfate conjugate of X11406790 (PH-label only), as shown in Table B.7.2.2-4. There was no qualitative difference in metabolites between the two radiolabels. Overall, an average of 78% and 62% of the PH- and PY-labelled kidney was identified, while an average of 0.027 and 0.017 mg/kg XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites) in the PH- and PY-labelled kidneys, respectively; the characterized radioactivity was multi-component.

Characterization of Residues in Fat: Aliquots of the PH-labelled renal fat were extracted as described above; this was the only fat sample that contained above 0.01 mg/kg XDE-729 methyl equivalents. Essentially none of the radioactivity was extracted with hexane. The majority of the radioactivity was extracted with neutral organic solvent, approximately 85% of the TRR (Table B.7.2.2-4.). An average of <0.001 mg/kg XDE-729 methyl equivalents was unextractable. The extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 80-85% in the eluent of the Strata-X SPE, however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the PH-labelled renal fat contained primarily free X11393729 plus lower levels of the sulfate conjugate of X11449757, and X11449757, as shown in Table B.7.2.2-4. Overall, an average of 72% of the TRR was identified by one chromatographic system, while an average of 0.002 mg/kg XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites); the characterized radioactivity was multi-component.

Table B.7.2.2-4.

**Distribution and Characterization of the Parent and the Metabolites in the Milk, Edible Tissues and Excreta from a Lactating Goat Dosed with  $^{14}\text{C}$  XDE729 Methyl.**

	$^{14}\text{C}$ -PH Renal Fat TRR 0.016 mg/kg		$^{14}\text{C}$ -PH Liver TRR 0.077 mg/kg		$^{14}\text{C}$ -PH Kidney TRR 0.121 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable <sup>b</sup>	85.2	0.014	87.9	0.068	99.9	0.121
Parent XDE-729 ME	--	--	--	--	--	--
Polar radioactivity	7.7	0.001	--	--	5.6	0.007
Sulfate conjugate of X11449757	9.5	0.002	--	--	18.3	0.022
X11449757	17.4	0.003	62.0	0.048	14.7	0.018
X11393729	44.8	0.007	12.1	0.009	36.7	0.044
N- or O-glucuronic acid conjugate of X11406790	--	--	--	--	5.9	0.007
N-glucuronic acid conjugate of XDE-729 ME	--	--	--	--	--	--
Sulfate conjugate of X11406790	--	--	--	--	0.8	0.001
X11406790	--	--	--	--	1.5	0.002
<b>Total Identified</b>	71.8	0.012	74.1	0.057	77.9	0.094
Total characterized <sup>c</sup>	13.4	0.002	13.8	0.011	22.0	0.027
Total unextractable	1.2	<0.001	7.2	0.006	1.6	0.002
Accountability <sup>d</sup>	86.9	0.014	95.1	0.073	102	0.123

-- Not observed

<sup>a</sup> mg/kg XDE-729 methyl equivalents

<sup>b</sup> Natural organic extractable. Hexane removed 0.4% of the TRR, <0.001 mg/kg, from the renal fat.

<sup>c</sup> Extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate.

<sup>d</sup>  $\text{Accountability (\% TRR)} = \frac{\text{Total extractable} + \text{Total unextractable}}{\text{TRR}} \times 100$ , where TRR is shown in Table B.7.2.2-3.

3.

Table B.7.2.2-4. (Cont.)

**Distribution and Characterization of the Parent and the Metabolites in the Milk, Edible Tissues and Excreta from a Lactating Goat Dosed with  $^{14}\text{C}$  XDE729 Methyl.**

	$^{14}\text{C}$ -PY D3 pm Milk TRR 0.012 mg/kg		$^{14}\text{C}$ -PY D4 pm Milk TRR 0.009 mg/kg		$^{14}\text{C}$ -PY Liver TRR 0.032 mg/kg		$^{14}\text{C}$ -PY Kidney TRR 0.041 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable	91.5	0.011	90.5	0.009	73.8	0.023	102	0.042
Parent XDE-729 ME	0.4	<0.001	0.5	<0.001	--	--	0.6	<0.001
Polar radioactivity	1.3	<0.001	1.3	<0.001	1.0	<0.001	6.8	0.003
Sulfate conjugate of X11449757	--	--	--	--	--	--	10.4	0.004
X11449757	10.1	0.001	21.9	0.002	31.9	0.010	14.4	0.006
X11393729	2.0	<0.001	3.6	<0.001	5.8	0.002	34.4	0.014
N- or O-glucuronic acid conjugate of X11406790	40.7	0.005	24.5	0.002	1.1	<0.001	1.4	0.001
N-glucuronic acid conjugate of XDE-729 ME	3.5	<0.001	4.2	<0.001	--	--	--	--
Sulfate conjugate of X11406790	21.8	0.003	12.5	0.001	--	--	--	--
X11406790	2.5	<0.001	0.3	<0.001	8.8	0.003	0.3	<0.001
<b>Total Identified</b>	81.0	0.010	67.5	0.006	47.6	0.015	61.5	0.025
Total characterized <sup>b</sup>	10.5	0.001	23.0	0.002	26.1	0.008	40.5	0.017
Total unextractable	10.7	0.001	12.2	0.001	21.8	0.007	2.9	0.001
Accountability <sup>c</sup>	102	0.012	103	0.010	95.6	0.030	105	0.043

-- Not observed

<sup>a</sup> mg/kg XDE-729 methyl equivalents

<sup>b</sup> Extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate.

<sup>c</sup>  $\text{Accountability (\% TRR)} = \frac{\text{Total extractable} + \text{Total unextractable}}{\text{TRR}}$ , where TRR is shown in Table B.7.2.2-

3.

**Characterization of Residues in Urine and Faeces:** Aliquots of both the PH- and PY-labelled days 1, 3, and 5 faeces were extracted as described above. The majority of the radioactivity was extracted with neutral organic solvent, as shown in Table B.7.2.2-5. Levels of radioactivity that were unextractable were at a maximum level on day 3. The maximum level recorded was 0.075 mg/kg; however, levels were never greater than 5% of the TRR therefore no efforts were made to extract and characterise the radioactivity further.

The extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 92-107% in the eluent of the Strata-X SPE; however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the faeces contained primarily free XDE-729 methyl plus lower levels of X11449757, X11406790, N- or O-



Urine was analyzed directly, both with and without the addition of formic acid. Results were similar, with the exception of a sharper peak for the sulfate conjugate of X11449757 when acid was added. Results of the analyses with formic acid are reported in Table B.7.2.2.6. HPLC analysis showed that the urine contained primarily free X11393729 plus lower levels of X11449757, the sulfate conjugate of X11449757, and X11406790, as shown in Table B.7.2.2-5. Because XDE-729 methyl was the primary component in the faeces, it appears that XDE-729 methyl is absorbed then hydrolyzed to the acid X11393729. Lower levels of the sulphate conjugate of X11406790 and N-glucuronic acid conjugate of XDE-729 ME and N- or O-glucuronic acid conjugate of X11406790 were also observed. There was no qualitative difference in metabolites between the two radiolabels.

**Table B.7.2.2-5**

## Summary of Characterization and Identification of Radioactive Residues in the Urine and Faeces from a Ruminant Dosed with $^{14}\text{C}$ XDE-729 Methyl at a Target Level Equivalent to 10 ppm in the Diet.

	<sup>14</sup> C-PH D1 Feces		<sup>14</sup> C-PH D3 Feces		<sup>14</sup> C-PH D5 Feces		<sup>14</sup> C-PY D1 Feces		<sup>14</sup> C-PY D3 Feces		<sup>14</sup> C-PY D5 Feces	
	TRR 1.417 mg/kg		TRR 1.806 mg/kg		TRR 2.412 mg/kg		TRR 1.169 mg/kg		TRR 1.444 mg/kg		TRR 1.111 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable	132	1.869	88.8	1.603	98.7	2.380	138	1.616	132	1.904	118	1.314
Parent XDE-729 ME	105	1.493	43.1	0.778	45.9	1.108	110	1.291	42.1	0.608	82.4	0.915
Polar radioactivity	--	--	--	--	--	--	--	--	0.3	0.004	--	--
Sulfate conjugate of X11449757	--	--	--	--	--	--	--	--	--	--	--	--
X11449757	12.0	0.170	17.1	0.309	21.6	0.521	7.8	0.092	28.8	0.416	12.2	0.135
X11393729	3.5	0.050	4.7	0.030	1.6	0.039	4.7	0.055	6.6	0.095	6.0	0.067
N- or O-glucuronic acid conjugate of X11406790	0.5	0.007	0.2	0.003	0.7	0.016	--	--	--	--	0.3	0.003
N-glucuronic acid conjugate of XDE-729 ME	--	--	--	--	--	--	--	--	--	--	--	--
Sulfate conjugate of X11406790	--	--	--	--	--	--	--	--	--	--	--	--
X11406790	10.5	0.149	22.4	0.405	28.3	0.682	10.9	0.128	46.5	0.671	15.0	0.166
<b>Total Identified</b>	131.9	1.869	84.4	1.525	98.1	2.366	133.9	1.566	124.0	1.790	115.8	1.286
Total characterized <sup>b</sup>	--	--	4.3	0.078	0.6	0.046	4.3	0.050	7.9	0.114	2.5	0.028
Total unextractable	2.5	0.035	3.3	0.060	3.6	0.014	2.5	0.029	5.2	0.075	2.3	0.026
Accountability <sup>c</sup>	134	1.904	92.1	1.663	102	2.467	141	1.645	137	1.979	121	1.340

Table B.7.2.2-5 (Cont)

	<sup>14</sup> C-PH D1 Feces TRR 1.417 mg/kg		<sup>14</sup> C-PH D3 Feces TRR 1.806 mg/kg		<sup>14</sup> C-PH D5 Feces TRR 2.412 mg/kg		<sup>14</sup> C-PY D1 Feces TRR 1.169 mg/kg		<sup>14</sup> C-PY D3 Feces TRR 1.444 mg/kg		<sup>14</sup> C-PY D5 Feces TRR 1.111 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable	132	1.869	88.8	1.603	98.7	2.380	138	1.616	132	1.904	118	1.314
Parent XDE-729 ME	105	1.493	43.1	0.778	45.9	1.108	110	1.291	42.1	0.608	82.4	0.915
Polar radioactivity	--	--	--	--	--	--	--	--	0.3	0.004	--	--
Sulfate conjugate of X11449757	--	--	--	--	--	--	--	--	--	--	--	--
X11449757	12.0	0.170	17.1	0.309	21.6	0.521	7.8	0.092	28.8	0.416	12.2	0.135
X11393729	3.5	0.050	1.7	0.030	1.6	0.039	4.7	0.055	6.6	0.095	6.0	0.067
N- or O-glucuronic acid conjugate of X11406790	0.5	0.007	0.2	0.003	0.7	0.016	--	--	--	--	0.3	0.003
N-glucuronic acid conjugate of XDE-729 ME	--	--	--	--	--	--	--	--	--	--	--	--
Sulfate conjugate of X11406790	--	--	--	--	--	--	--	--	--	--	--	--
X11406790	10.5	0.149	22.4	0.405	28.3	0.682	10.9	0.128	46.5	0.671	15.0	0.166
<b>Total Identified</b>	131.9	1.869	84.4	1.525	98.1	2.366	133.9	1.566	124.0	1.790	115.8	1.286
Total characterized <sup>b</sup>	--	--	4.3	0.078	0.6	0.046	4.3	0.050	7.9	0.114	2.5	0.028
Total unextractable	2.5	0.035	3.3	0.060	3.6	0.014	2.5	0.029	5.2	0.075	2.3	0.026
Accountability <sup>c</sup>	134	1.904	92.1	1.663	102	2.467	141	1.645	137	1.979	121	1.340

Table B.7.2.2-5. (Cont)

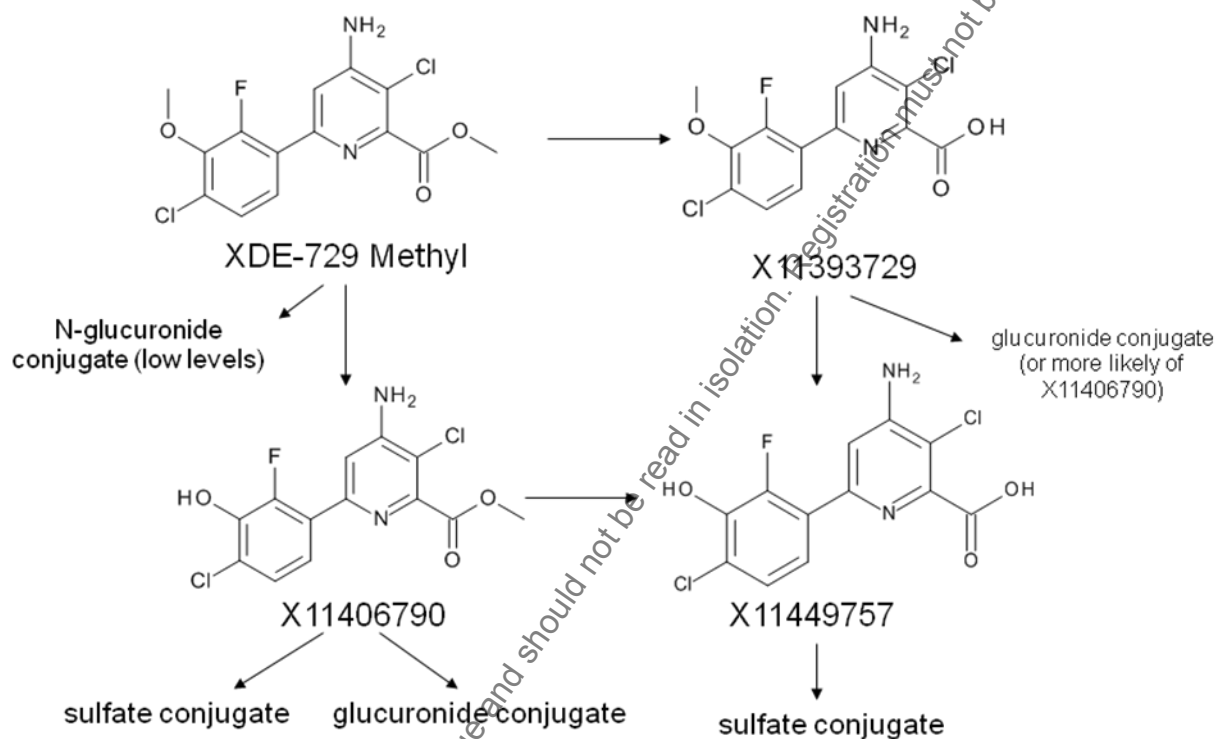
	<sup>14</sup> C-PH D1 Urine (w/FA) TRR 0.807 mg/kg		<sup>14</sup> C-PH D2 Urine (w/FA) TRR 0.331 mg/kg		<sup>14</sup> C-PH D3 Urine (w/FA) TRR 0.926 mg/kg		<sup>14</sup> C-PH D4 Urine (w/FA) TRR 0.688 mg/kg		<sup>14</sup> C-PH D5 Urine (w/FA) TRR 1.175 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable	--	--	--	--	--	--	--	--	--	--
Parent XDE-729 ME	--	--	--	--	--	--	--	--	--	--
Polar radioactivity	--	--	0.8	0.003	--	--	0.4	0.002	1.5	0.018
Sulfate conjugate of X11449757	21.5	0.173	15.3	0.051	19.4	0.180	13.2	0.090	16.5	0.194
X11449757	23.0	0.186	20.5	0.068	28.6	0.265	34.9	0.240	33.3	0.391
X11393729	47.1	0.380	38.9	0.129	32.7	0.302	36.7	0.252	31.5	0.370
N- or O-glucuronic acid conjugate of X11406790	--	--	--	--	--	--	--	--	--	--
N-glucuronic acid conjugate of XDE-729 ME	--	--	--	--	--	--	1.3	0.009	--	--
Sulfate conjugate of X11406790	--	--	0.8	0.003	3.3	0.031	0.5	0.003	0.7	0.008
X11406790	2.4	0.019	6.4	0.021	11.7	0.108	10.2	0.070	9.2	0.108
<b>Total Identified</b>	93.9	0.758	81.8	0.270	95.8	0.887	96.7	0.666	91.2	1.072
Total characterized <sup>b</sup>	--	--	--	--	--	--	--	--	--	--
Total unextractable	--	--	--	--	--	--	--	--	--	--
Accountability <sup>c</sup>	93.9	0.758	81.8	0.270	95.8	0.887	96.7	0.666	91.2	1.072

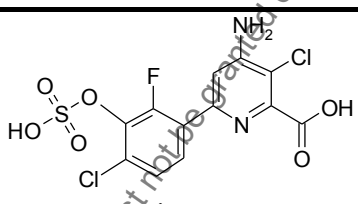
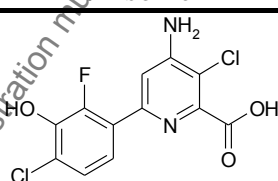
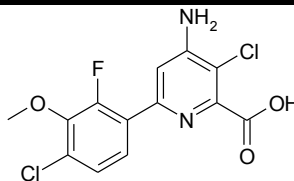
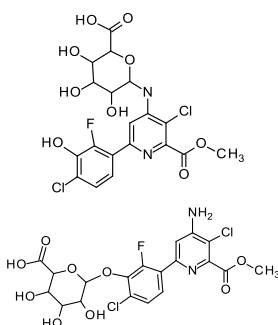
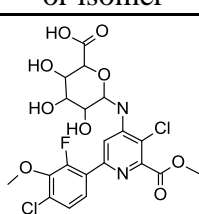
Table B.7.2.2-5. (Cont)

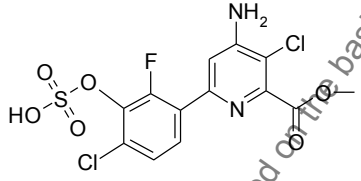
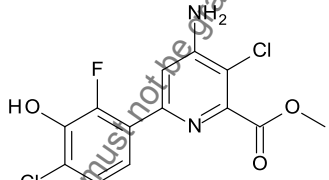
Compound	<sup>14</sup> C-PY D1 Urine (w/FA) TRR 1.726 mg/kg		<sup>14</sup> C-PY D2 Urine (w/FA) TRR 1.571 mg/kg		<sup>14</sup> C-PY D3 Urine (w/FA) TRR 2.698 mg/kg		<sup>14</sup> C-PY D4 Urine (w/FA) TRR 2.404 mg/kg		<sup>14</sup> C-PY D5 Urine (w/FA) TRR 3.385 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable	--	--	--	--	--	--	--	--	--	--
Parent XDE-729 ME	--	--	--	--	--	--	--	--	--	--
Polar radioactivity	--	--	--	--	--	--	--	--	--	--
Sulfate conjugate of X11449757	12.8	0.220	6.8	0.107	2.0	0.054	--	--	5.0	0.168
X11449757	26.4	0.456	32.7	0.514	39.5	1.065	46.7	1.122	37.7	1.276
X11393729	56.3	0.971	49.2	0.773	42.4	1.144	43.8	1.053	53.9	1.824
N- or O-glucuronic acid conjugate of X11406790	--	--	--	--	--	--	--	--	0.3	0.011
N-glucuronic acid conjugate of XDE-729 ME	--	--	0.5	0.008	--	--	--	--	--	--
Sulfate conjugate of X11406790	--	--	0.4	0.006	--	--	--	--	--	--
X11406790	2.2	0.039	8.1	0.127	14.8	0.400	7.7	0.184	2.8	0.095
<b>Total Identified</b>	<b>97.7</b>	<b>1.687</b>	<b>97.8</b>	<b>1.536</b>	<b>98.7</b>	<b>2.663</b>	<b>98.1</b>	<b>2.358</b>	<b>99.7</b>	<b>3.374</b>
Total characterized <sup>b</sup>	--	--	--	--	--	--	--	--	--	--
Total unextractable	--	--	--	--	--	--	--	--	--	--
Accountability <sup>c</sup>	97.7	1.687	97.8	1.536	98.7	2.663	98.1	2.358	99.7	3.374

-- Not observed

<sup>a</sup> mg/kg XDE-729 methyl equivalents<sup>b</sup> Extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate.<sup>c</sup> Accountability (% TRR) =  $\frac{\text{Total extractable} + \text{Total unextractable}}{\text{TRR}}$ , where TRR is shown in Table B.7.2.2-3.

Metabolic Pathway**Figure B.7.2.2-5****Proposed Metabolic Profile of XDE-729 Methyl in a Lactating Goat**

Identification of Residue Components from the <sup>14</sup> C XDE-729 Methyl Ruminant Metabolism Study		
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
sulfate conjugate of X11449757	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-sulfooxy-phenyl)pyridine-2-carboxylic acid	
X11449757	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxyphenyl)-pyridine-2-carboxylic acid	
X11393729	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-pyridine-2-carboxylic acid	
N- or O-glucuronic acid conjugate of X11406790	6-[[3-chloro-6-(4-chloro-2-fluoro-3-hydroxy-phenyl)-2-methoxycarbonyl-4-pyridyl]amino]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid or 6-[3-(4-amino-5-chloro-6-methoxycarbonyl-2-pyridyl)-6-chloro-2-fluoro-phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid	
N-glucuronic acid conjugate of XDE-729 methyl	6-[[3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-2-methoxycarbonyl-4-pyridyl]amino]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid	

sulfate conjugate of X11406790	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-sulfooxy-phenyl)pyridine-2-carboxylate	 or isomer
X11406790	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxyphenyl)pyridine-2-carboxylate	

## CONCLUSIONS

- When dosed at approximately 476 times the maximum theoretical dietary burden to dairy cattle (10 mg/kg dry feed/d vs dietary burden of 0.021 mg/kg DM basis), XDE-729 methyl was rapidly eliminated in the faeces (40.9 and 45.9% of the dose, includes GI contents). Approximately 25% of the dose (20.4% and 28.9%) was rapidly absorbed and eliminated in the urine. Less than 0.1% of the dose was recovered in the combined milk samples, and only one milk sample (PY-labelled day 3 pm) contained greater than 0.01 mg/kg XDE-729 methyl equivalents. Analyses of milk showed the residue levels reached a plateau during the dosing phase. Less than 0.2% of the dose was recovered in the combined edible matrices. Muscle and most fats (with the exception of renal fat) contained less than 0.01 mg/kg XDE-729 methyl equivalents. Kidney and liver contained higher amounts (max 0.121 mg/kg and max 0.077 mg/kg for kidney and liver respectively).
- Residues in milk and tissues were readily extractable. The sulfate conjugate of X11449757 (or isomer), X11449757, X11393729, the N- or O-glucuronic acid conjugate of X11406790 (or isomer), the N-glucuronic acid conjugate of XDE-729 methyl (or isomer), the sulfate conjugate of X11406790 (or isomer), and X11406790 were all detected in edible tissues and/or milk. Less than 0.001 mg/kg XDE-729 methyl was detected in milk or any edible tissue. Generally, greater than 61% (with the exception of <sup>14</sup>C-PY Liver, which was 47.6%) of the residues in milk and tissues were identified as one of the above components, with the remaining residue characterized as multi-component.
- Metabolism in goats proceeds through demethylation to either the carboxylic acid (X11393729) or phenol (X11406790), or both (X11449757). Parent XDE-729 methyl or metabolites may then conjugate with sulfate or glucuronic acid. The metabolic pathway of XDE-729 methyl is similar in goats, hens and rats.
- In the edible matrices, metabolite X11449757 was observed at the highest level, 0.048 mg/kg XDE-729 methyl equivalents, in the PH-labelled liver. Therefore, when normalized to reflect the dietary burden (estimated as 0.021 mg/kg dry feed weight), neither parent or metabolites would be predicted at levels greater than the analytical method proposed limit of quantification, typically 0.01 mg/kg.

- Neither parent nor metabolites (free plus conjugated) would be predicted at levels greater than the analytical method proposed limit of quantification, typically 0.01 mg/kg. DAS proposes that XDE-729 methyl and XDE-729 acid be included in the residue definitions for Risk Assessment and Enforcement/Monitoring purposes. As discussed above for the plant residue definition (Section B.7.1), the applicant has addressed the relative toxicity of X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. Furthermore, the inclusion of the conjugates has been considered in terms of the behavior of conjugated residues in mammalian systems and their impact on human health assessments. The conclusions drawn for the  $\beta$ -D-glucoside conjugates of phenols above (see further discussion of residue definition under Section B.7.1.1 Metabolism of Wheat) are also applicable to sulphate conjugates and glucuronide conjugates.

**To conclude, the opinion of the RMS is that the notifier has provided sufficient evidence to support non-inclusion of the metabolites X11406790 and X11449757 and their conjugates in the residue definition. The proposed residue definition XDE-729 methyl and XDE-729 acid is acceptable.**

### B.7.2.3 Poultry

**Report:** [REDACTED] *A Nature of the Residue Study in the Laying Hen with [<sup>14</sup>C]-XDE-729 Methyl Ester, Unpublished report of [REDACTED] study ID 101390, 27 October 2011.*

**Guidelines:** *OECD Guidance Document 503 for Metabolism in Livestock (Issued 8 January 2007)*

**GLP:** *Yes (certified laboratory)*

In a metabolism study performed in 2011 laying hens were orally dosed (a single gelatine capsule, no absorbent) once a day for seven consecutive days with either <sup>14</sup>C-PH-XDE-729 methyl (radiochemical purity 97.4 %, specific activity 8.31 mCi/mmol) or <sup>14</sup>C-PY-XDE-729 methyl (radiochemical purity 97.8 %, specific activity 8.75 mCi/mmol).

#### Preparation of Test Materials

The <sup>14</sup>C-PH-label-XDE-729 methyl was prepared by combining 77.3 mg non-radiolabeled test substance and 172 mg radiolabeled test substance (9.970 mL) for a final specific activity of 8.31 mCi/mmol (53,457 dpm/ $\mu$ g). The procedure was repeated with the <sup>14</sup>C-PY-label-test substance by combining 69.5 mg non-radiolabeled test substance and 29.1 mg radiolabeled test substance (9.970 mL) for a final specific activity of 8.75 mCi/mmol (56,269 dpm/ $\mu$ g). The solvent was removed under a gentle stream of nitrogen. The dried test substances were shipped to the contract laboratory.

Aliquots of the dose solution were collected before and after dosing, and shipped to DAS for analysis. HPLC analysis demonstrated that the <sup>14</sup>C-PH-XDE-729 methyl averaged 98.0% radiopurity before dosing and 98.2% after dosing. HPLC analysis demonstrated that the <sup>14</sup>C-PY-



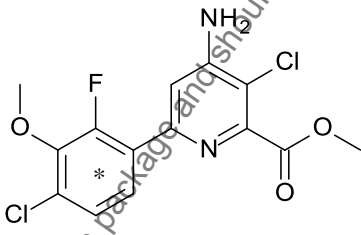
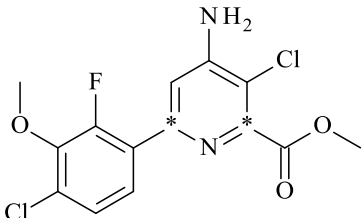
XDE-729 methyl averaged 98.9% radiopurity before dosing and 97.9% after dosing. Therefore, the test solution was stable during the dosing period.

The target dose rate of 10 mg/kg dry feed/day (approximately 625 N the maximum theoretical dietary burden (0.016 mg/kg DM basis)) was based on the average feed consumption during the acclimation period, without adjustment for feed dry matter. The resulting actual dose rates were 11.3 and 11.6 mg/kg dry feed/day for the  $^{14}\text{C}$ -PH-label and  $^{14}\text{C}$ -PY-label dosed groups, respectively.

**Table - B.7.2.3-1**

Test Animal Dosing Regime			
Treatment Type	Feeding Level (ppm test material in food on a dry weight basis)	Vehicle	Timing/Duration
Oral	PH: 11.3 ppm PY: 11.6 ppm	Capsules (no absorbent)	A single capsule was administered once a day (at about 8 am) by oral gavage to a group of 10 animals for 7 consecutive days.

**Table - B.7.2.3-2**

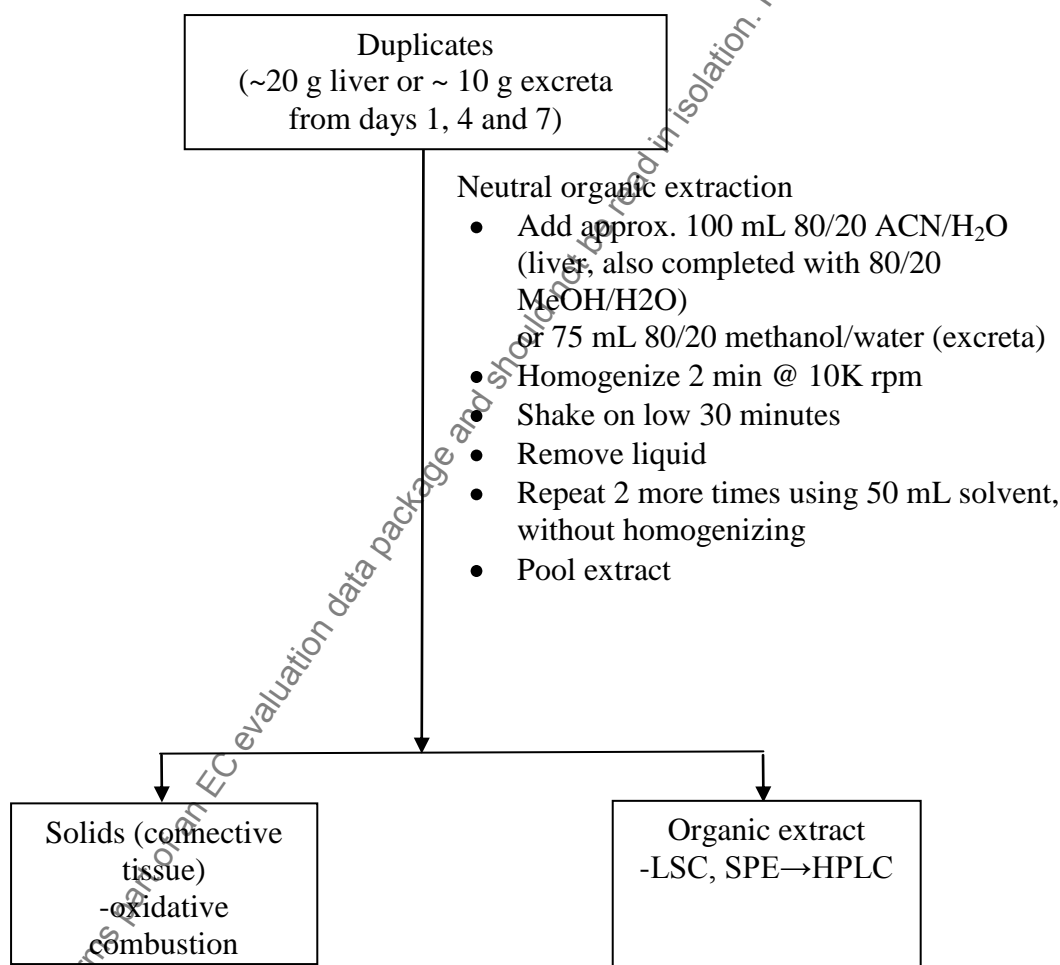
Test Material Characteristics	
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>
Common Name	$^{14}\text{C}$ -PH-XDE-729 methyl
Purity	97.4% (18 Jun 2009), FAPC-G-09-23
Specific activity	45.3 mCi/mmol, adjusted to 8.31 mCi/mmol
Chemical structure	 <p>* indicates position of <math>^{14}\text{C}</math></p>
Common Name	$^{14}\text{C}$ -PY-XDE-729 methyl
Purity	97.8% (18 Jun 2009), FAPC-G-09--22
Specific activity	29.6 mCi/mmol, adjusted to 8.75 mCi/mmol

Eggs were collected twice daily (once in the morning and once in the afternoon, and combined per day per group). Excreta was collected at 24-hour intervals immediately prior to dose administration and pooled per group. Cage washes were collected after necropsy. Within 6-8 hours of the administration of the final dose the animals were sacrificed and samples of liver, fat, muscle (breast), muscle (leg) and skin with fat were collected and prepared for analysis. Muscle, liver, fat, and skin tissue samples were homogenized in the presence of dry ice. All homogenized samples were stored at  $\leq -10^{\circ}\text{C}$  pending analysis and shipment to the sponsor.

#### Liver and Excreta

The flowchart below (Figure-B.7.2.3-1) summarises the methodology for extraction of residues from liver and excreta.

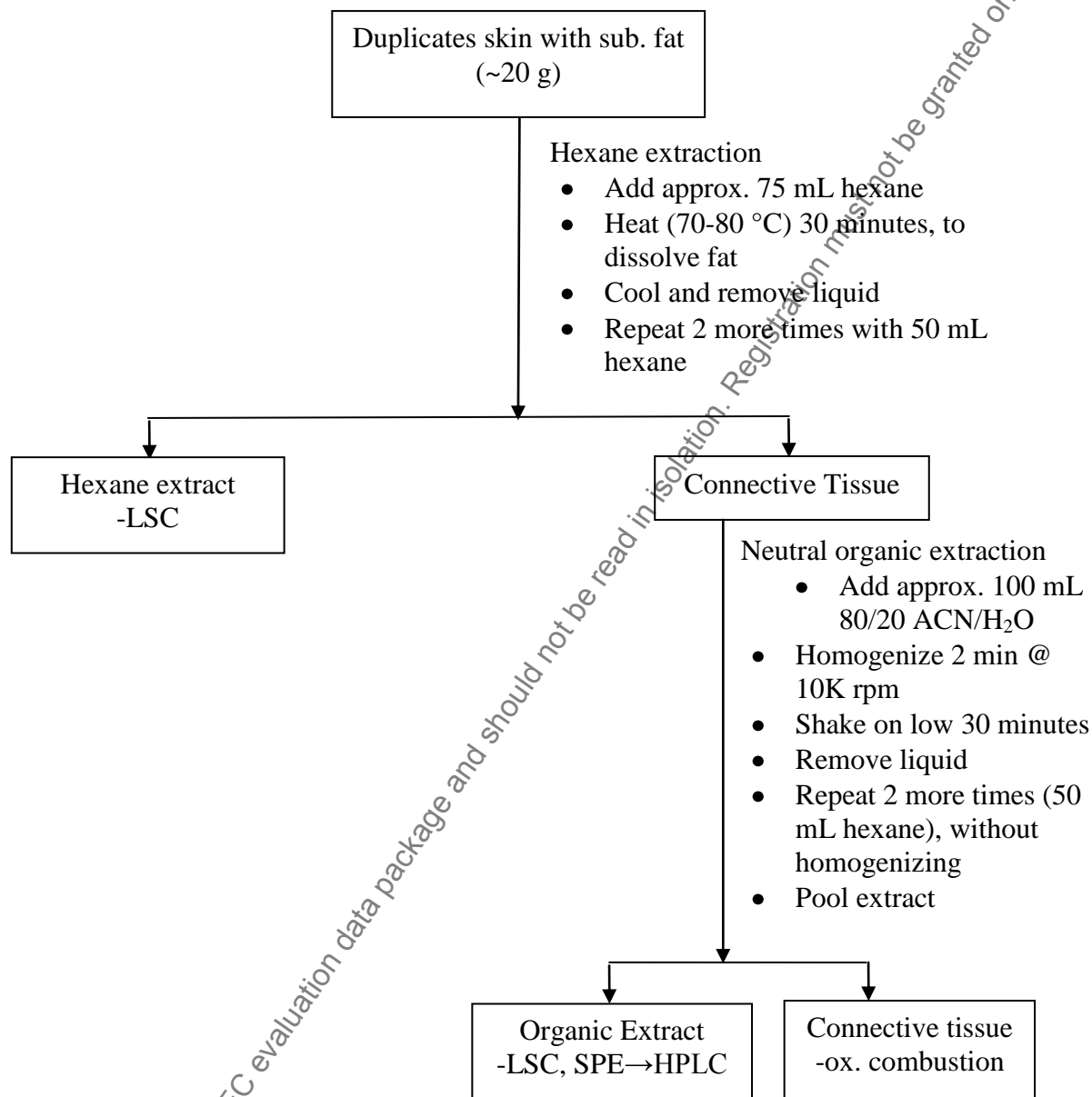
**Figure-B.7.2.3-1:** Schematic flowchart for the analysis of  $^{14}\text{C}$ -XDE-729 Methyl residues in liver, and excreta



#### Skin with Subcutaneous Fat

The flowchart below (Figure-B.7.2.3-2) summarises the methodology for extraction of residues from PH-labelled skin with fat samples. The PY-labelled skin with fat sample contained <0.01 mg/kg XDE-729 methyl equivalents, and was therefore not analyzed further.

**Figure B.7.2.3-2:** Schematic flowchart for the analysis of  $^{14}\text{C}$ -XDE-729 Methyl residues in Skin with Subcutaneous Fat



#### Bound Residue

Since neutral organic extraction quantitatively removed all of the radioactivity, bound residue determination procedures were not necessary.

### Analytical Methodology

Radioactivity in the homogenised samples of eggs, liver, muscle, and skin with fat samples and excreta were analyzed by oxidative combustion of the sample, followed by  $^{14}\text{C}$  activity measured by LSC. Aliquots of fat from the homogenized fat tissue were heated at 60-80 °C to melt, followed by analysis by LSC.

**SPE:** The general clean-up procedure for the extracts was with a Strata-X SPE (500 mg, 8B-S100-HDG, Phenomenex Inc., Torrance, California, USA). The samples were prepared by concentrating in a Turbopap (40 °C water bath and 10 psi nitrogen) to remove the majority of the organic solvent then adding 0.1%  $\text{H}_3\text{PO}_4$  in water (8 mL). The SPE cartridges were conditioned with methanol (5 mL) followed by 0.1%  $\text{H}_3\text{PO}_4$  in water (2 x 5 mL). The concentrated sample was diluted then applied to the conditioned SPE, and eluted at approx. 2 mL/min, collecting the eluate. The SPE was dried for 10 seconds after the SPE had eluted. The sample vial was rinsed with 0.1%  $\text{H}_3\text{PO}_4$  in water (5 mL), transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. The SPE cartridge was dried under full vacuum for 20 seconds. The Strata-X SPE was eluted with methanol: 0.1%  $\text{H}_3\text{PO}_4$  in water (95:5, v/v) in two aliquots (5 mL each), pooling the elution aliquots.

A glycerol “keeper” was added to the elution samples (0.1 mL 80/20 methanol/glycerol) then the elution samples were concentrated to near dryness (approximately 0.1 mL) in a Turbopap (30 °C water bath and 10 psi nitrogen). The elution samples were reconstituted in 200 µL of acetonitrile, sonicated, then diluted with 700 µL water, and sonicated and mixed well. The volume of each reconstituted elution sample was calculated by weight and density. Triplicate aliquots of each load and reconstituted elution sample were analyzed by LSC. The concentrated elution sample was also analyzed by HPLC.

### Storage Stability:

Storage stability from the study report (Rotondaro, S. L. and Adelfinskaya, Y. A. A Nature of the Residue Study in the Laying Hen with  $[^{14}\text{C}]$ -XDE-729 Methyl Ester, Unpublished report of Dow AgroSciences, study ID 101390, 27 October 2011) shows that eggs and edible tissues and excreta are stored frozen for up to 63 and 40 days respectively. Since this is less than 6 months storage whilst frozen, storage stability does not need to be addressed further. However, for the tissue extracts and excreta extracts, the report states that storage at -20°C took place over 417 and 240 days respectively. The notifier was therefore asked to address storage stability over this storage interval.

The following paragraph was submitted by the notifier in response to the above question:

*“Samples were stored at approximately -20 °C when not in use (SBL reported this as  $\leq -10$  °C). Dates of analysis are provided in Table C.1. Initial extraction of liver and skin with fat was 22 days after sacrifice. These analyses were used to determine metabolite levels (% TRR and mg eq/kg). Later analyses were for qualitative mass spectral metabolite identification only. Stability of the extracts is demonstrated by comparison of the figure used for determine metabolite levels with the corresponding radioactive monitoring in the mass spectral report. Re-analysis of matrices after storage demonstrated stability during storage under conditions used. For those samples that were re-analyzed, storage stability data is also provided in Table C.1. The intervals of storage stability were calculated as follows:*

*Tissue: date of final extraction – date of initial extraction*

*example, liver: 28 JUL 2010 – 17 JUN 2010 = 41 days*

*Extract: date of final analysis (HPLC or LC/MS) – date extracted*  
*example, day 4 excreta: 18 FEB 2011 – 23 JUN 2010 = 240 days”*

This response is acceptable, storage stability has been addressed.

#### Metabolite Isolation

Metabolites were isolated from the Day 4 excreta, purified by Strata-X SPE and analyzed by mass spectrometry. Metabolites were identified based upon relative retention time and mass spectral matching with the reference standard. The sulfate conjugate of X11449757 (or isomer), X11449757, X11393729, the sulfate conjugate of X11406790 (or isomer), X11406790, and XDE-729 methyl were identified. There was no difference in metabolites identified from the PH- or PY-labelled groups. There was no evidence of bridge cleavage.

Reference standards were not available for the sulphate conjugate of X11449757 and the sulphate conjugate of X11406790; however, structural assignments have been proposed through interpretation of the fragmentation pattern in mass spectra. However, a number of peaks were noted that were prominent in the spectra, which had not been identified to a structure. The notifier submitted that following case to address this concern:

*“Additional spectral peaks are co-extracted natural components, not related to the XDE-729 Methyl test material. At the retention time of radioactivity, relevant peaks were determined using chlorine and/or <sup>14</sup>C isotopic patterns and the mass defect of chlorine, to eliminate endogenous components from metabolites of the test substance”.*

#### Eggs, Tissue and Excreta TRR Levels

As summarized in Table B.7.2.3-3 below, 94.6% and 93.9% of the dose was recovered from the <sup>14</sup>C-PH-XDE-729 methyl and <sup>14</sup>C-PY-XDE-729 methyl dosed groups, respectively. The majority of the dose was excreted, 94.5% and 93.8% from the PH- and PY-labelled groups, respectively. The remaining carcasses were not evaluated. Overall, elimination of the <sup>14</sup>C-XDE-729 methyl was rapid.

Eggs contained less than 0.01% of the dose. However, during the dosing period the residue levels in eggs did not appear to reach a definite plateau for either the PY label or the PH-label (Figure B.7.2.3-3). However, for both labels, the residue levels remained low, with a maximum of approximately 0.003 mg/kg XDE-729 methyl equivalents. Given that the metabolism study was conducted at approximately 625 times the maximum theoretical dietary burden to hens (0.016 mg/kg DM basis), it is concluded that despite not reaching a plateau, the study is fit for purpose to support the proposed GAP.

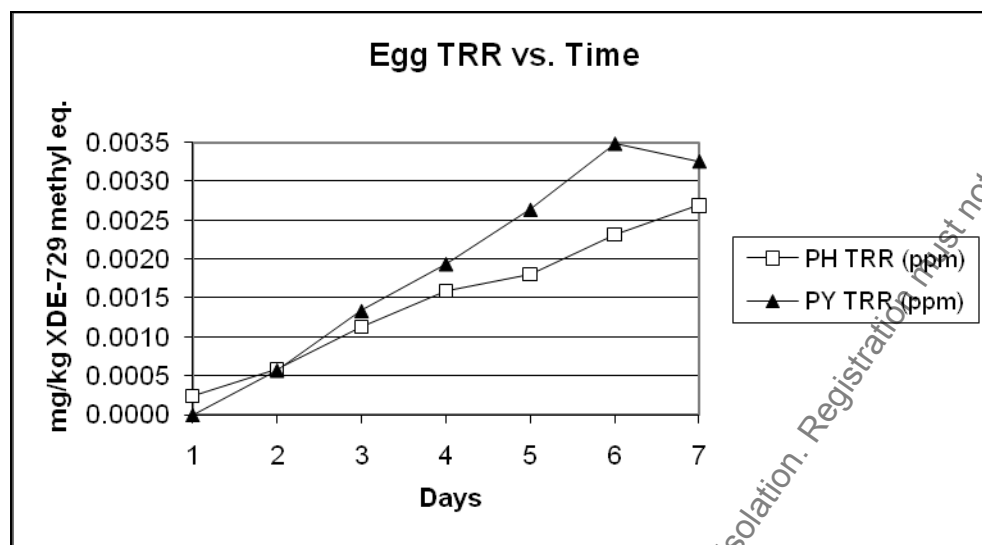
Less than 0.1% of the dose was recovered in the edible tissues. Residue levels are summarized in Table B.7.2.3-3. Residues in the PH-label group liver and skin with fat were 0.046 and 0.016 mg/kg XDE-729 methyl equivalents, and 0.043 and 0.009 mg/kg XDE-729 methyl equivalents in the PY-labelled group, respectively. Residues in the remaining tissues collected contained less than 0.01 mg/kg XDE-729 methyl equivalents (Table B.7.2.3-3).

Table - B.7.2.3-3

**Total Radioactive Residues (TRRs) in the Excreta, Eggs and Edible Tissues of Laying Hens Dosed with  $^{14}\text{C}$  XDE-XDE-729 Methyl**

Matrix	Collection Timing	$^{14}\text{C}$ -PH-XDE-729 Methyl		$^{14}\text{C}$ -PY-XDE-729 Methyl	
		(mg/kg)	(% dose)	(mg/kg)	(% dose)
Eggs	Day 1	ND	0.0002	ND	0.0000
	Day 2	(0.001)	0.0004	(0.001)	0.0004
	Day 3	(0.001)	0.0008	(0.001)	0.0009
	Day 4	(0.002)	0.0011	(0.002)	0.0012
	Day 5	(0.002)	0.0011	0.003	0.0020
	Day 6	0.002	0.0016	0.003	0.0022
	Day 7	0.003	0.0002	0.003	0.0005
	Total	not applicable	0.005	not applicable	0.007
Excreta	Day 1	8.509	12.3	9.152	12.2
	Day 2	9.984	13.9	9.689	14.4
	Day 3	11.901	14.6	10.534	12.5
	Day 4	11.056	14.4	12.180	14.3
	Day 5	10.818	14.0	11.075	14.2
	Day 6	11.027	13.1	11.775	13.4
	Day 7	16.380	12.2	16.721	12.9
	Total	not applicable	94.5	not applicable	93.8
Cage rinse	sacrifice	1.180	0.063	0.468	0.044
Muscle-breast	sacrifice	ND	0.001	ND	0.001
Muscle-leg	sacrifice	(0.003)	0.005	(0.002)	0.006
Liver	sacrifice	0.046	0.028	0.043	0.023
Fat	sacrifice	0.008	0.003	0.005	0.003
Skin with fat	sacrifice	0.016	0.019	0.009	0.012
Edible tissues	Total	not applicable	0.061	not applicable	0.052
Total		not applicable	94.6	not applicable	93.9

Figure B.7.2.3-3

Pharmacokinetics of  $^{14}\text{C}$  XDE-729 Methyl in the Eggs of Laying Hens**Characterisation of Residues**

**Characterization of Residues in Liver:** Aliquots of both the PH- and PY-labelled liver were extracted as described above. The majority of the radioactivity was extracted with neutral organic solvent, approximately 70% when 80/20 acetonitrile/water was used, and approximately 80% when 80/20 methanol/water was used (Table B.7.2.3-4). An average of 0.007-0.008 mg/kg XDE-729 methyl equivalents was unextractable. The extracts were prepared for HPLC *via* the Strata-X SPE clean-up method. The notifier states that recoveries from the methanol/water extract were good, 83-93% in the eluent of the Strata-X SPE, however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the liver contained primarily free X11449757 and the sulfate conjugate of X11406790, plus lower levels of X11406790 and X11393729, as shown in Table B.7.2.3-5. There was no qualitative difference in metabolites between the two radiolabels. Overall, an average of 60% and 41% of the PH- and PY-labelled liver was identified by one chromatographic system only, while an average of 0.011 (23.2%,  $^{14}\text{C}$ -PH) and 0.016 (36.0%  $^{14}\text{C}$ -PY) mg/kg XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites). Given the level of characterised residue (0.011-0.016 mg/kg) and the fact that it was multi-component it is unlikely that any single component would exceed the trigger value 0.01 mg/kg, therefore further consideration is unnecessary.

**Characterization of Residues in Skin with Subcutaneous Fat:** As summarized in Table B.7.2.3-4., Aliquots of the PH-labelled skin with fat were extracted as described above. Approximately 38% of the radioactivity was extracted with hexane, but was not analyzed further because the hexane extract contained an average of only 0.006 mg/kg XDE-729 methyl equivalents. The remainder of the radioactivity was extracted with neutral organic solvent, approximately 63% of the TRR (Table B.7.2.3-4.). An average of 0.001 mg/kg (4.4% TRR) XDE-729 methyl equivalents was unextractable. The extracts were prepared for HPLC *via* the Strata-X SPE clean-

up method. Recoveries were good, 89-107% in the eluent of the Strata-X SPE, however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the PH-labelled skin with fat contained primarily free X11393729 plus lower levels of the sulfate conjugate of X11406790, X11406790, and X11449757, as shown in Table B.7.2.3-5. Overall, an average of 46% was identified by one chromatographic system, while an average of 0.009 mg/kg (54.2% TRR) XDE-729 methyl equivalents was characterized (extracted but did not chromatograph with identified metabolites); the characterized radioactivity was multi-component, a portion of which was hexane extractable. Given that the amount of residue that could not be identified was <0.01 mg/kg, no further consideration is necessary.

Characterization of Residues in Excreta: Aliquots of both the PH- and PY-labelled days 1, 4, and 7 excreta were extracted as described above. The majority of the radioactivity was extracted with neutral organic solvent, as shown in Table B.7.2.3-4. No more than 4% of the TRR was unextractable. The extracts were prepared for HPLC via the Strata-X SPE clean-up method. Recoveries were good, 93-110% in the eluent of the Strata-X SPE; however SPE recovery values were not included in the calculated amounts of individual metabolites. This is acceptable given that the recoveries were within an acceptable range. HPLC analysis showed that the excreta contained primarily free X11393729 plus lower levels of X11449757, X11406790, XDE-729 methyl, the sulfate conjugate of X11406790, and the sulfate conjugate as X11449757, as shown in Table B.7.2.3-5. There was no qualitative difference in metabolites between the two radiolabels.



Table - B.7.2.3-4

**Distribution of the Parent and the Metabolites in the Eggs, Edible Tissues and Excreta from Laying Hens Dosed with  $^{14}\text{C}$  XDE-729 Methyl.**

Fraction	Hexane extraction		Organic Extraction <sup>a</sup>		Post-Extracted Tissue		Recovery %TRR
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
<b>PH-label</b>							
Skin with Fat	38.1	0.006	62.6	0.010	4.4	0.001	105
Liver (A&B)	--	--	72.4	0.034	16.8	0.008	89.2
Liver (C&D)	--	--	82.9	0.038	14.1	0.007	97.1
D1 Excreta	--	--	90.8	7.723	2.0	0.169	92.7
D4 Excreta	--	--	94.3	10.429	2.2	0.246	96.6
D7 Excreta	--	--	88.4	14.487	1.7	0.271	90.1
<b>PY-label</b>							
Liver (A&B)	--	--	70.9	0.031	17.3	0.007	88.1
Liver (C&D)	--	--	76.4	0.033	16.4	0.007	91.0
D1 Excreta	--	--	96.4	8.822	2.4	0.219	98.8
D4 Excreta	--	--	95.1	11.588	3.4	0.413	98.5
D7 Excreta	--	--	94.3	15.744	2.1	0.359	96.5

<sup>a</sup> Neutral extraction solvent was 80/20 acetonitrile/water for liver replicates A & B, 80/20 methanol/water for liver replicates C & D and excreta.

-- Not performed.

Table - B.7.2.3-5

**Summary of Characterization and Identification of Radioactive Residues in the Eggs and Edible Tissues from Hens Dosed with  $^{14}\text{C}$  XDE-729 Methyl at a Target Level Equivalent to 10 ppm in the Diet.**

	$^{14}\text{C}$ -PH Skin with Fat TRR 0.016 mg/kg		$^{14}\text{C}$ -PH Liver TRR 0.046 mg/kg		$^{14}\text{C}$ -PH D1 Excreta TRR 8.509 mg/kg		$^{14}\text{C}$ -PH D4 Excreta TRR 11.059 mg/kg		$^{14}\text{C}$ -PH D7 Excreta TRR 16.380 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total hexane extractable	38.1	0.006	--	--	--	--	--	--	--	--
Total organic extractable <sup>b</sup>	62.6	0.010	82.9	0.038	90.8	7.723	94.3	10.429	88.4	14.487
Parent XDE-729 ME	0.5	<0.001	--	--	7.7	0.653	7.5	0.828	7.3	1.203
Polar radioactivity	0.4	<0.001	2.2	0.001	--	--	--	--	--	--
Sulfate conjugate of X11449757	0.4	<0.001	0.9	<0.001	1.1	0.090	2.0	0.224	0.8	0.133
X11449757	2.9	<0.001	32.3	0.015	16.5	1.403	21.6	2.393	17.8	2.923
X11393729	26.0	0.004	6.3	0.003	50.0	4.254	46.3	5.114	54.7	8.953
Sulfate conjugate of X11406790	12.3	0.002	14.5	0.007	5.1	0.432	4.7	0.520	2.0	0.335
X11406790	4.3	0.001	5.7	0.003	8.3	0.702	9.2	1.018	5.3	0.860
<b>Total Identified</b>	46.4	0.008	59.8	0.028	88.5	7.534	91.3	10.098	88.0	14.407
Total characterized <sup>c</sup>	54.2	0.009	23.2	0.011	2.2	0.189	3.0	0.331	0.5	0.081
Total unextractable	4.4	0.001	14.1	0.007	2.0	0.169	2.2	0.246	1.7	0.271
Accountability <sup>d</sup>	105	0.017	97.1	0.045	92.7	7.892	96.6	10.675	90.1	14.758

	<sup>14</sup> C-PY Liver		<sup>14</sup> C-PY D1 Excreta		<sup>14</sup> C-PY D4 Excreta		<sup>14</sup> C-PY D7 Excreta	
	TRR 0.043 mg/kg		TRR 9.152 mg/kg		TRR 12.180 mg/kg		TRR 16.721 mg/kg	
	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>	% TRR	mg/kg <sup>a</sup>
Total extractable <sup>b</sup>	76.4	0.033	96.4	8.822	95.1	11.588	94.3	15.744
Parent XDE-729 ME	--	--	6.7	0.613	5.2	0.631	5.1	0.850
Polar radioactivity	1.4	0.001	--	--	--	--	--	--
Sulfate conjugate of X11449757	1.7	0.001	3.2	0.290	3.2	0.392	2.1	0.352
X11449757	20.9	0.009	22.7	2.076	20.2	2.463	23.6	3.953
X11393729	5.5	0.002	46.3	4.238	47.8	5.817	52.0	8.698
Sulfate conjugate of X11406790	8.3	0.004	4.9	0.450	7.9	0.968	3.6	0.597
X11406790	4.1	0.002	7.6	0.700	7.8	0.952	6.2	1.029
<b>Total Identified</b>	40.5	0.017	91.4	8.367	92.1	11.222	92.6	15.498
Total characterized <sup>c</sup>	36.0	0.016	5.0	0.455	3.0	0.366	1.8	0.296
Total unextractable	16.4	0.007	2.4	0.219	3.4	0.413	2.1	0.359
Accountability <sup>d</sup>	92.9	0.040	98.8	9.041	98.5	12.001	96.5	16.134

-- Not observed

<sup>a</sup> mg/kg XDE-729 methyl equivalents

<sup>b</sup> Organic solvent was acetonitrile/water (80/20) for skin with fat, and methanol/water (80/20) for liver and excreta.

<sup>c</sup> Extractable radioactivity that was multi-component and did not co-elute with any known reference compound or identified conjugate.

<sup>d</sup> Accountability =  $\frac{\text{Total extractable} + \text{Total unextractable}}{\text{TRR}}$ , where TRR is shown in Table B.7.2.3-3.

Metabolic Pathway

A metabolic pathway is proposed in Figure B.7.2.3-3. and metabolites are identified in Table - B.7.2.3-5. The sulfate conjugate of X11449757 (or isomer), X11449757, X11393729, the sulfate conjugate of X11406790 (or isomer), and X11406790 were all detected in edible tissues. XDE-729 methyl was not detected in any edible tissue at levels  $>0.001$  mg/kg. In the edible matrices, non-conjugated X11449757 was observed at the highest level, except in skin with fat in which X11393729 was observed to be highest. When normalized to a 1X rate, neither parent or metabolites would be predicted at levels greater than 0.001 mg/kg.

The sulfate conjugate of X11449757 (or isomer), X11449757, X11393729, the sulfate conjugate of X11406790 (or isomer), X11406790, and XDE-729 methyl were identified in day 4 excreta.

Metabolism in hens proceeds through demethylation to either the carboxylic acid (X11393729) or phenol (X11406790), or both (X11449757). Metabolites may then conjugate with sulfate. The metabolic pathway of XDE-729 methyl is similar in goats, hens, and rats, although additional conjugates were observed in the goat NOR study (the N- or O-glucuronic acid conjugate of X11406790 (or isomer) and the N-glucuronic acid conjugate of XDE-729 methyl (or isomer))

**Figure B.7.2.3-3. Proposed Metabolic Profile of XDE-729 Methyl in Laying Hens**

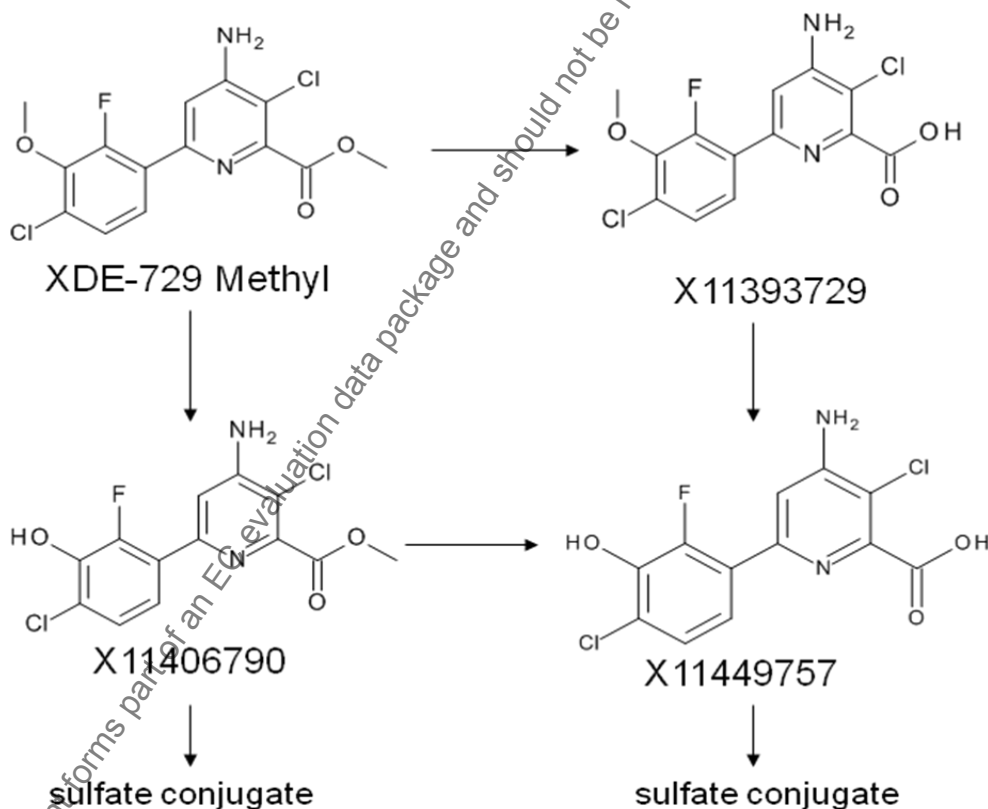
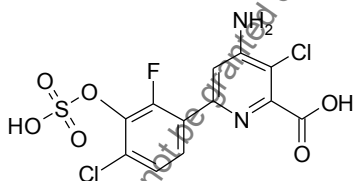
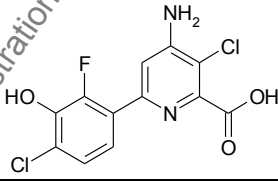
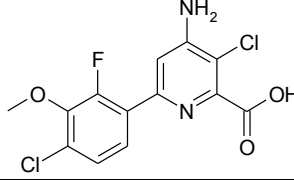
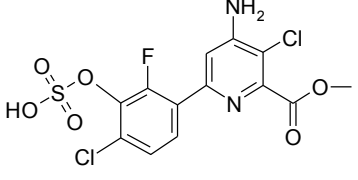
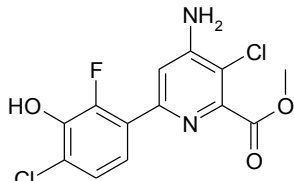
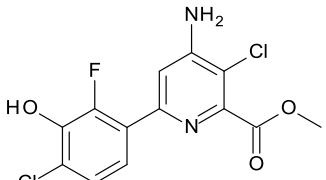


Table - B.7.2.3-6

Identification of Residue Components from the <sup>14</sup> C XDE-729 Methyl Laying Hen Metabolism Study		
Common name/code	Chemical name	Chemical structure
sulfate conjugate of X11449757	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-sulfooxy-phenyl)pyridine-2-carboxylic acid	 or isomer
X11449757	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxyphenyl)-pyridine-2-carboxylic acid	
X11393729	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-pyridine-2-carboxylic acid	
sulfate conjugate of X11406790	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-sulfooxy-phenyl)pyridine-2-carboxylate	 or isomer
X11406790	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxyphenyl)pyridine-2-carboxylate	
XDE-729 methyl	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate	

## Conclusions

- When dosed at approximately 625 times the maximum theoretical dietary burden to hens (0.016 mg/kg DM basis) XDE-729 methyl was rapidly eliminated in the excreta (94.5 and 93.8% of the dose, from the PH- and PY-labelled groups, respectively). Less than 0.1% of the dose was recovered in the combined edible matrices. Muscle and most fats contained less than 0.01 mg/kg XDE-729 methyl equivalents.
- Residues in liver were readily extractable. The sulfate conjugate of X11449757 (or isomer), X11449757, X11393729, the sulfate conjugate of X11406790 (or isomer), and X11406790 were all detected. No XDE-729 methyl was detected. Less than 0.02 mg/kg XDE-729 methyl equivalents was either unextractable or characterized as being multi-component.
- Metabolism proceeds through demethylation to either the carboxylic acid (X11393729) or phenol (X11406790), or both (X11449757). Parent XDE-729 methyl or metabolites may then conjugate with sulfate. The metabolic pathway of XDE-729 methyl is similar in goats, hens, and rats.
- In the edible matrices that were analyzed, metabolite X11449757 was typically observed at the highest level. When normalized to reflect the dietary burden, parent or metabolites would be predicted at levels much less than the analytical method proposed limit of quantification, typically 0.01 mg/kg.
- Neither parent nor metabolites (free plus conjugated) would be predicted at levels greater than the analytical method proposed limit of quantification, typically 0.01 mg/kg. DAS proposes that XDE-729 methyl and XDE-729 acid be included in the residue definitions for Risk Assessment and Enforcement/Monitoring purposes. As discussed above for the plant residue definition (Section B.7.1), the applicant has addressed the relative toxicity of X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. Furthermore, the inclusion of the conjugates has been considered in terms of the behavior of conjugated residues in mammalian systems and their impact on human health assessments. The conclusions drawn for the  $\beta$ -D-glucoside conjugates of phenols above (see further discussion of residue definition under Section B.7.1.1 Metabolism of Wheat) are also applicable to sulphate conjugates and glucuronide conjugates. **To conclude, the opinion of the RMS is that the notifier has provided sufficient evidence to support non-inclusion of the metabolites X11406790 and X11449757 and their conjugates in the residue definition. The proposed residue definition XDE-729 methyl and XDE-729 acid is acceptable.**

#### B.7.2.4 Summary/assessment

Metabolism of XDE-729 has been studied in both lactating goats and laying hens. The results show no difference in behaviour of XDE-729 residue when using the two radiolabelled test items:  $^{14}\text{C}$ -PH-label-XDE-729 methyl and  $^{14}\text{C}$ -PY-label-XDE-729 methyl in the tissues and edible products of lactating goats and laying hens.

Metabolism in lactating goats and laying hens is essentially the same. Similar metabolism is seen in the lactating goat and the rat (see Section B.6, Toxicology and Metabolism) and therefore additional studies in pigs are not required.

In the supervised residues trials (see Section B.7.6) it has been demonstrated that residues  $>0.01$  mg/kg are not expected in cereal grains that form part of the livestock diet, although residues in straw from trials carried out in Southern Europe were significant. Evaluation of the first and second season's data (see below) showed that animal intakes are not significant - the highest dietary burden was 0.041 mg/kg DM basis for beef cattle.

The lactating goat metabolism studies were conducted at a rate equivalent to 476 times the maximum theoretical dietary burden to dairy cattle. In edible matrices, metabolite X11449757 was observed at the highest level, 0.048 mg/kg XDE-729 methyl equivalents, in PH-labelled liver. When normalised to reflect the dietary burden (estimated as 0.021 mg/kg dry feed weight for dairy cattle), neither parent nor metabolites would be predicted at levels greater than the analytical method proposed LOQ (0.01 mg/kg).

The hen metabolism studies were conducted at a rate equivalent to 625 times the maximum theoretical dietary burden to hens. In the edible matrices analysed, metabolite X11449757 was typically observed at the highest level. When normalised to reflect the dietary burden (estimated as 0.016 mg/kg dry feed weight), parent or metabolites would be predicted at levels much less than the analytical method proposed LOQ, (0.01 mg/kg).

#### B.7.3 Definition of the residue (IIA 6.7, IIIA 8.6)

The notifier proposed that XDE-729 methyl and XDE-729 acid be included in the residue definitions for Risk Assessment and Enforcement/Monitoring purposes. As discussed above for the plant residue definition (Section B.7.1), the applicant has addressed the relative toxicity of X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. Furthermore, the inclusion of the conjugates has been considered in terms of the behavior of conjugated residues in mammalian systems and their impact on human health assessments. The conclusions drawn for the  $\beta$ -D-glucoside conjugates of phenols above (see further discussion of residue definition under Section B.7.1 Metabolism of Wheat) are also applicable to sulphate conjugates and glucuronide conjugates. **To conclude, the opinion of the RMS is that the notifier has provided sufficient evidence to support non-inclusion of the metabolites X11406790 and X11449757 and their conjugates in the residue definition. The proposed residue definition XDE-729 methyl and XDE-729 acid is acceptable.**

### B.7.3.1 Definition of the residue in rotational crops

Confined rotational crop metabolism study demonstrated that it is unlikely that crops rotated into wheat fields treated with XDE-729 at 10 g a.s./ha would result in detectable levels of XDE-729 methyl or metabolites in any Raw Agricultural Commodity. Because of the low residue levels in all crops at all plant-back intervals, a metabolic pathway has not been proposed, and a succeeding crop study and tolerance/MRL are not necessary for succeeding crops.

### B.7.3.2 Definition of the residue in animals

The notifier proposed that XDE-729 methyl and XDE-729 acid be included in the residue definitions for Risk Assessment and Enforcement/Monitoring purposes. As discussed above for the animal residue definition, the applicant has addressed the relative toxicity of X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. Furthermore, the inclusion of the conjugates has been considered in terms of the behavior of conjugated residues in mammalian systems and their impact on human health assessments. The conclusions drawn for the  $\beta$ -D-glucoside conjugates of phenols above (see further discussion of residue definition under Section B.7.1.1 Metabolism of Wheat) are also applicable to sulphate conjugates and glucuronide conjugates. **To conclude, the opinion of the RMS is that the notifier has provided sufficient evidence to support non-inclusion of the metabolites X11406790 and X11449757 and their conjugates in the residue definition. The proposed residue definition XDE-729 methyl and XDE-729 acid is acceptable.**

### B.7.4 Use pattern

XDE-729 is a new active substance to the EU and as such there are no registered uses at present within the EU.

### B.7.5 Identification of critical GAPs

The proposed GAP, and representative use, for the use of XDE-729 in the Northern, Central and Southern EU zones is as a post emergence herbicide for broad-leaved weed control in cereals. Intended GAPs were identified as shown in Table B.7.5.



Table B.7.5. Summary of intended uses

Crop and/or situation (a)	Member State or Country	Product Name	F or G (b)	Pests or Group of pests controlled (c)	Formulation		Application			Application rate per treatment			PHI days (k)	Remarks (l)
					Type (d-f)	Conc. of a.s. (i) g/L	Method Kind (f-h)	Growth stage (j)	Number	kg as/ha min max	Water (l/ha) min max	kg as/ha min max		

**Northern Zone**

Winter cereals (soft wheat, barley, rye, triticale)	Northern Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 09 to 29 (Sep 1st- Dec 31st) and BBCH 13 to 45 (March 1 <sup>st</sup> - Jun 20th)	2	0.00196-0.00782 followed by 0.00156 – 0.00625	100-400	0.00782 followed by 0.00625		The applications are made in autumn only, or in spring only or in both autumn and spring. Autumn applications are from BBCH 09 to 29, from Sept 1st to Dec 31st. Spring applications are from BBCH 13 to 45, from March 1st to June 20th.
Spring cereals (wheat, barley)	Northern Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 13 to 45 (March 1 <sup>st</sup> – Jun 20th)	1	0.00156 – 0.00625	100-400	0.00625		The application is made in spring only, from BBCH 13 to 45, from March 1st to June 20th

**XDE 729 Methyl (Halauxifen-methyl)****Volume 3, Annex B.7**

Crop and/or situation (a)	Member State or Country	Product Name	F or G (b)	Pests or Group of pests controlled (c)	Formulation		Application			Application rate per treatment			PHI days (k)	Remarks (l)
					Type (d-f)	Conc. of a.s. (i) <b>g/L</b>	Method Kind (f-h)	Growth stage (j)	Number	kg as/ha min max	Water (l/ha) min max	<b>kg as/ha</b> min max		

**Central Zone**

Winter cereals (soft wheat, durum wheat, barley, spelt, rye, triticale)	Central Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 09 to 29 (Sep 1st-Dec 31st) and BBCH 13 to 45 (Jan 1st - Jun 30th)	2	0.00196-0.00782 followed by 0.00156 – 0.00625	100-400	0.00782 followed by 0.00625		The applications are made in autumn only, or in spring only or in both autumn and spring. Autumn applications are from BBCH 09 to 29, from Sept 1st to Dec 31st. Spring applications are from BBCH 13 to 45, from January 1st to June 30th
Spring cereals (wheat, barley, durum wheat, rye )	Central Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 13 to 45 (Feb 1st-Jun 30th)		0.00156 – 0.00625	100-400	0.00625		The application is made in spring only, from BBCH 13 to 45, from February 1st to June 30th

WARNING: This document forms part of an EC evaluation data package and should not be released in isolation. Registration must not be granted on the basis of this document.

**XDE 729 Methyl (Halauxifen-methyl)****Volume 3, Annex B.7**

Crop and/or situation (a)	Member State or Country	Product Name	F or G (b)	Pests or Group of pests controlled (c)	Formulation		Application			Application rate per treatment			PHI days (k)	Remarks (l)
					Type (d-f)	Conc. of a.s. (i) g/L	Method Kind (f-h)	Growth stage (j)	Number	kg as/ha min max	Water (l/ha) min max	kg as/ha min max		

**Southern Zone**

Winter cereals (soft wheat, durum wheat, barley, spelt, rye, triticale)	Southern Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 09 to 29 (Sep 1st- Dec 31st) and BBCH 13 to 45 (Jan 1st - May 31 <sup>st</sup> )	2	0.00196-0.00782 followed by 0.00156 – 0.00625	100-400	0.00782 followed by 0.00625		The applications are made in autumn only, or in spring only or in both autumn and spring. Autumn applications are from BBCH 09 to 29, from Sept 1st to Dec 31st. Spring applications are from BBCH 13 to 45, from January 1st to May 31 <sup>st</sup>
Spring cereals (wheat, barley, durum wheat, rye )	Southern Zone	GF-2573	F	Broadleaf weeds	EC	XDE-729 methyl 7.817	Overall, Broadcast foliar spray	BBCH 13 to 45 (Feb 1st- May 31 <sup>st</sup> )	1	0.00156 – 0.00625	100-400	0.00625		"The application is made in spring only, from BBCH 13 to 45, from February 1st to May 31 <sup>st</sup>

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)

(c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds

(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated

(i) g/kg or g/l

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) PHI - minimum pre-harvest interval

(m) Remarks may include: Extent of use/economic importance/restrictions

**B.7.6 Residues arising from supervised trials (IIA 6.3; IIIA 8.2)**

A summary of trials conforming to critical GAP are given in Table B.7.6-1. Data which do not reflect the current critical GAP ( $\pm 25\%$ ) for Northern, Central and Southern Member States (as appropriate) have not been included in the summary of residues data. Where data form part of a decline trial, all data have been submitted but the sample which reflects critical GAP is marked by underlining.

Results from trials conforming to GAP, reported in sufficient detail and acceptable analytical information are indicated by underlining. Other trials have been included where the reports lack sufficient detail. Although these reports cannot be directly used for recommending MRLs, they may be useful as supplementary information. Basic criteria for acceptability are given below:

Trials details

crop variety  
location, position and year of trial  
formulation used  
application rate  
maximum number of treatments  
growth stage of crop at treatment  
pre-harvest interval  
residue level (control and treated)

Analytical aspects

method specified and submitted  
storage of samples prior to analysis  
limit of determination  
acceptable recovery (70-110%)

**A summary of supervised residue trials data generated according to critical GAP****Table B.7.6-1 Summary of residues of XDE-729 Methyl and XDE-729 Acid in winter wheat (Northern Zone)**

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ()	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4552A CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mulan	Germany NZ Outdoor (field)	GF-2573	2	7.7	410	--	07-Dec-2009	BBCH 32	97	Grain	<0.01	<0.01	110, 97
					6.3	419	--	05-May-2010		97	Straw	<0.01	<0.01	101, 94
				2	7.5	400	--	07-Dec-2009	BBCH 39	0*	Whole plant	1.00	0.021	99, 95
										0-	Whole plant	<0.01	<0.01	99, 95
					0+	Whole plant	0.126	<0.01		99, 95				
					7	Whole plant	(0.003)	<0.01		99, 95				
					14	Whole plant	<0.01	<0.01		99, 95				
					28	Whole plant	<0.01	<0.01		99, 95				
					56	Whole plant	<0.01	<0.01		99, 95				
					74	Grain	<0.01	<0.01		110, 97				
			74		Straw	<0.01	<0.01	101, 94						
			2		7.6	406	--	07-Dec-2009		BBCH 45	0*	Whole plant	0.937	0.018
				0-					Whole plant		<0.01	<0.01	99, 95	
				0+	Whole plant	0.110	<0.01	99, 95						
				7	Whole plant	<0.01	<0.01	99, 95						
				14	Whole plant	<0.01	<0.01	99, 95						
				28	Whole plant	<0.01	<0.01	99, 95						
				56	Whole plant	<0.01	<0.01	99, 95						
				67	Grain	<0.01	<0.01	110, 97						
				67	Straw	<0.01	<0.01	101, 94						
				1	6.1	404	--	04-Jun-2010	BBCH 45		0+	Whole plant	0.123	<0.01

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										7 14 28 56 67 67	Whole plant Whole plant Whole plant Whole plant Grain Straw	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 99, 95 110, 97 101, 94
CEMS-4552B CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Buzogany	Hungary NZ Outdoor (field)	GF- 2573	2  2	7.4 6.2  7.6 6.1	296 312  303 303	-- --  -- --	10-Dec-2009 19-Apr-2010  10-Dec-2009 30-Apr-2010	BBCH 32	86 86	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.7 6.0	308 298	-- --	10-Dec-2009 07-May-2010	BBCH 39	0* 0- 0+ 7 14 28 56 75 75	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.189 <0.01 0.188 (0.004) <0.01 <0.01 <0.01 <0.01 <0.01	(0.005) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 99, 95 99, 95 99, 95 99, 95 110, 97 101, 94
				2	7.7 6.0	308 298	-- --	10-Dec-2009 07-May-2010	BBCH 45	0* 0- 0+ 7 14 28 56 68 68	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.170 <0.01 0.148 (0.005) <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u>	(0.004) <0.01 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u>	99, 95 99, 95 99, 95 99, 95 99, 95 99, 95 110, 97 101, 94

WARNING: This document forms part of an MRL evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ()	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.0	301	--	07-May-2010	BBCH 45	0+ 7 14 28 56 68 68	Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.144 (0.004) <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 99, 95 99, 95 110, 97 101, 94
CEMS-4552E CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Tarus	Germany NZ Outdoor (field)	GF-2573	2	8.1 6.6	323 330	-- --	09-Dec-2009 20-Apr-2010	BBCH 32	109 109	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.8 6.5	313 327	-- --	09-Dec-2009 25-May-2010	BBCH 39	74 74	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.7 6.6	307 328	-- --	09-Dec-2009 07-Jun-2010	BBCH 58	61 61	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	110, 97 101, 94
				1	5.5	273	--	07-Jun-2010	BBCH 58	61 61	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				CEMS-4552F CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mercato	France NZ Outdoor (field)	GF-2573	2	7.9 6.4	317 320	-- --	31-Dec-2009 23-Apr-2010	BBCH 32	83 83
				2	7.7 5.9	310 293	-- --	31-Dec-2009 14-May-2010	BBCH 39	62 62	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.6 5.7	303 287	-- --	31-Dec-2009 21-May-2010	BBCH 47	55 55	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	110, 97 101, 94

WARNING: This document forms part of a pesticide evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	5.7	287	--	21-May-2010	BBCH 47	55 55	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
CEMS-4889A CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Potenzial	Germany NZ Outdoor (field)	GF- 2573	2	8.8 5.7	118 95	-- --	25-Nov-2010 26-Apr-2011	BBCH 32	91 91	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	6.9 5.1	92 85	-- --	25-Nov-2010 18-May-2011	BBCH 39	0* 0- 0+ 7 13 27 58 69 69	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw	0.946 <0.01 0.245 (0.003) <0.01 <0.01 <0.01 <0.01 <0.01	(0.006) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 100, 97 100, 97 101, 99 103, 98
				2	6.9 5.9	93 98	-- --	25-Nov-2010 23-May-2011	BBCH 45	0* 0- 0+ 8 14 28 53 64 64	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw	0.971 <0.01 0.149 (0.004) <0.01 <0.01 <0.01 <0.01 <0.01	(0.005) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 100, 97 100, 97 101, 99 103, 98
CEMS-4889B CEMS-4889 DAS Ref. ID	Winter Wheat / Magdalena	Hungary NZ Outdoor	GF- 2573	2	7.8 7.9	417 423	-- --	08-Dec-2010 18-Apr-2011	BBCH 32	98 98	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
102082 Y 2010-2011		(field)		2	7.7	409	--	08-Dec-2010	BBCH 39	0*	Whole Plant	0.300	(0.008)	100, 97
					5.7	381	--	06-May-2011		0-	Whole Plant	<0.01	<0.01	100, 97
										0+	Whole Plant	0.214	<0.01	100, 97
										7	Whole Plant	(0.003)	<0.01	100, 97
										14	Whole Plant	<0.01	<0.01	100, 97
										28	Whole Plant	<0.01	<0.01	100, 97
										56	Whole Plant	<0.01	<0.01	100, 97
										80	Grain	<0.01	<0.01	101, 99
										80	Straw	<0.01	<0.01	103, 98
				2	7.8	414	--	08-Dec-2010	BBCH 45-49	0*	Whole Plant	0.242	(0.006)	100, 97
					5.5	365	--	17-May-2011		0-	Whole Plant	<0.01	<0.01	100, 97
										0+	Whole Plant	0.169	<0.01	100, 97
										7	Whole Plant	(0.004)	<0.01	100, 97
										17	Whole Plant	<0.01	<0.01	100, 97
										31	Whole Plant	<0.01	<0.01	100, 97
										55	Whole Plant	<0.01	<0.01	100, 97
										69	Grain	<0.01	<0.01	101, 99
										69	Straw	<0.01	<0.01	103, 98
				1	6.1	408	--	17-May-2011	BBCH 45-49	0+	Whole Plant	0.166	<0.01	100, 97
										7	Whole Plant	(0.005)	<0.01	100, 97
										17	Whole Plant	<0.01	<0.01	100, 97
										28	Whole Plant	<0.01	<0.01	100, 97
										55	Whole Plant	<0.01	<0.01	100, 97
										69	Grain	<0.01	<0.01	101, 99
										69	Straw	<0.01	<0.01	103, 98
CEMS-4889C	Winter	Hungary	GF-	2	7.2	386	--	07-Jan-2011	BBCH 32	77	Grain	<0.01	<0.01	101, 99
CEMS-4889	Wheat /	NZ	2573		8.1	431	--	26-Apr-2011		77	Straw	<0.01	<0.01	103, 98

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
			Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
DAS Ref. ID 102082 Y 2011	Buzogany	Outdoor (field)		2	7.6	406	--	07-Jan-2011	BBCH 39	67	Grain	<0.01	<0.01	101, 99
					6.0	398	--	06-May-2011		67	Straw	<0.01	<0.01	103, 98
				2	7.7	411	--	07-Jan-2011	BBCH 45	56	Grain	<0.01	<0.01	101, 99
					5.9	393	--	17-May-2011		56	Straw	(0.004)	<0.01	103, 98
				1	5.7	382	--	17-May-2011	BBCH 45	56	Grain	<0.01	<0.01	101, 99
										56	Straw	<0.01	<0.01	103, 98
				2	7.6	407	--	05-Jan-2011	BBCH 32	93	Grain	<0.01	<0.01	101, 99
					6.3	422	--	04-Apr-2011		93	Straw	<0.01	<0.01	103, 98
CEMS-4889D CEMS-4889 DAS Ref. ID 102082 Y 2011	Winter Wheat / Boregar	France NZ Outdoor (field)	GF-2573	2	7.7	411	--	05-Jan-2011	BBCH 39	65	Grain	<0.01	<0.01	101, 99
					6.1	404	--	02-May-2011		65	Straw	<0.01	<0.01	103, 98
				2	7.8	418	--	05-Jan-2011	BBCH 45	62	Grain	<0.01	<0.01	101, 99
					6.0	402	--	05-May-2011		62	Straw	<0.01	<0.01	103, 98
				1	6.1	404	--	05-May-2011	BBCH 45	62	Grain	<0.01	<0.01	101, 99
										62	Straw	<0.01	<0.01	103, 98
				2	8.6	115	--	26-Nov-2010	BBCH 32	112	Grain	<0.01	<0.01	101, 99
					6.6	110	--	27-Apr-2011		112	Straw	<0.01	<0.01	103, 98
CEMS-4889E CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Tabasco	Germany NZ Outdoor (field)	GF-2573	2	8.0	106	--	26-Nov-2010	BBCH 39	92	Grain	<0.01	<0.01	101, 99
					4.8	80	--	17-May-2011		92	Straw	<0.01	<0.01	103, 98
				2	9.0	119	--	26-Nov-2010	BBCH 45	84	Grain	<0.01	<0.01	101, 99
					6.8	113	--	25-May-2011		84	Straw	<0.01	<0.01	103, 98
				2	8.0	106	--	26-Nov-2010	BBCH 39	92	Grain	<0.01	<0.01	101, 99
					4.8	80	--	17-May-2011		92	Straw	<0.01	<0.01	103, 98

WARNING: This document forms part of a Pesticide Evaluation data package and should only be used in relation to the Pesticide Registration must not be quoted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.6	110	--	25-May-2011	BBCH 45	84 84	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
CEMS-4889F CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Potencial	Poland NZ Outdoor (field)	GF- 2573	2	7.1 6.1	378 403	-- --	06-Dec-2010 10-May-2011	BBCH 32	92 92	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	7.5 5.8	400 385	-- --	06-Dec-2010 20-May-2011	BBCH 39	82 82	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	6.9 5.9	370 390	-- --	06-Dec-2010 27-May-2011	BBCH 45	75 75	Grain Straw	<u>&lt;0.01</u> <u>(0.003)</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	101, 99 103, 98
				1	6.0	402	--	27-May-2011	BBCH 45	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	8.4 6.2	111 103	-- --	06-Jan-2011 09-May-2011	BBCH 32	85 85	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	8.1 6.4	108 107	-- --	06-Jan-2011 19-May-2011	BBCH 39	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98
				2	8.4 6.8	111 113	-- --	06-Jan-2011 27-May-2011	BBCH 51	67 67	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	101, 99 103, 98
CEMS-4889G CEMS-4889 DAS Ref. ID 102082 Y 2011	Winter Wheat / Oakley	United Kingdom NZ Outdoor (field)	GF- 2573	1	6.0	100	--	27-May-2011	BBCH 51	67 67	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 99 103, 98

WARNING: This document forms part of an EC evaluation package and should not be relied upon for regulatory purposes. Registrants must not be granted on the basis of this document.

Table B.7.6-2 Summary of residues of XDE-729 Methyl and XDE-729 Acid in winter wheat (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4552C CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Isangrain	Spain SZ Outdoor (field)	GF- 2573	2	7.7	308	--	18-Dec-2009	BBCH 32	104	Grain	<0.01	<0.01	110, 97
					6.1	307	--	24-Mar-2010		104	Straw	<0.01	<0.01	101, 94
				2	7.4	296	--	18-Dec-2009	BBCH 39	0*	Whole plant	0.990	(0.004)	99, 95
					5.9	296	--	26-Apr-2010		0-	Whole plant	<0.01	<0.01	99, 95
										0+	Whole plant	0.107	<0.01	99, 95
										7	Whole plant	(0.003)	<0.01	99, 95
										14	Whole plant	<0.01	<0.01	99, 95
										28	Whole plant	<0.01	<0.01	99, 95
										56	Whole plant	<0.01	<0.01	99, 95
										68	Grain	<0.01	<0.01	110, 97
										68	Straw	<0.01	<0.01	101, 94
				2	7.6	302	--	18-Dec-2009	BBCH 45	0*	Whole plant	0.925	(0.006)	99, 95
					5.5	273	--	03-May-2010		0-	Whole plant	<0.01	<0.01	99, 95
										0+	Whole plant	0.094	<0.01	99, 95
										7	Whole plant	(0.004)	<0.01	99, 95
										14	Whole plant	<0.01	<0.01	99, 95
										28	Whole plant	<0.01	<0.01	99, 95
										60	Whole plant	<0.01	<0.01	99, 95
										64	Grain	<0.01	<0.01	110, 97
										64	Straw	<0.01	<0.01	101, 94
					5.7	287	--	03-May-2010	BBCH 45	0+	Whole plant	0.075	<0.01	99, 95
										7	Whole plant	(0.003)	<0.01	99, 95
										14	Whole plant	<0.01	<0.01	99, 95

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										28 60 6464 6464	Whole plant Whole plant Grain Straw	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	99, 95 99, 95 110, 97 101, 94
CEMS-4552D CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Quality	France SZ Outdoor (field)	GF- 2573	2	8.5 5.7	307 284	-- --	22-Dec-2009 06-Apr-2010	BBCH 32	92 92	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	8.1 6.1	291 304	-- --	22-Dec-2009 30-Apr-2010	BBCH 39	0* 0- 0+ 7 14 28 56 68 68	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.721 <0.01 0.059 (0.007) <0.01 <0.01 <0.01 <0.01 <0.01	0.018 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 99, 95 99, 95 99, 95 110, 97 101, 94
				2	8.3 6.2	299 310	-- --	22-Dec-2009 07-May-2010	BBCH 45	0* 0- 0+ 7 14 28 56 61 61	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.774 <0.01 0.067 (0.006) <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u>	0.014 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 99, 95 99, 95 99, 95 110, 97 101, 94
				1	5.7	287	--	07-May-2010	BBCH 45	0+ 7	Whole plant Whole plant	0.135 <0.01	<0.01 <0.01	99, 95 99, 95

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										14 28 56 61 61	Whole plant Whole plant Whole plant Grain Straw	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	99, 95 99, 95 99, 95 110, 97 101, 94
CEMS-4552G CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Botticelli	Spain SZ Outdoor (field)	GF- 2573	2	7.5 6.4	300 322	-- --	27-Dec-2009 05-Apr-2010	BBCH 32	95 95	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.6 6.2	303 308	-- --	27-Dec-2009 28-Apr-2010	BBCH 39	72 72	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				2	7.8 6.0	312 300	-- --	27-Dec-2009 11-May-2010	BBCH 45	59 59	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	110, 97 101, 94
				1	5.9	297	--	11-May-2010	BBCH 45	59 59	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94
				CEMS-4552H CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mieti	Italy SZ Outdoor (field)	GF- 2573	2	7.8 6.1	313 303	-- --	10-Dec-2009 31-Mar-2010	BBCH 32	90 90
2	7.2 6.5	290 323	-- --	10-Dec-2009 29-Apr-2010				BBCH 39	61 61	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94	
2	7.6 5.9	303 330	-- --	10-Dec-2009 04-May-2010				BBCH 45	56 56	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	110, 97 101, 94	
	5.9	330	--	04-May-2010				BBCH 45	56 56	Grain Straw	<0.01 <0.01	<0.01 <0.01	110, 97 101, 94	

WARNING: This document forms part of an MRL evaluation data package and should not be read or used for registration. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>					
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid			
CEMS-4889H CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Enola	Bulgaria SZ Outdoor (field)	GF- 2573	2	8.2	436	--	07-Dec-2010	BBCH 32	93	Grain	<0.01	<0.01	101, 99			
					6.3	418	--	13-Apr-2011		93	Straw	<0.01	<0.01	103, 98			
				2	7.8	413	--	07-Dec-2010		BBCH 39	0*	Whole Plant	0.725	(0.003)	100, 97		
											0-	Whole Plant	<0.01	<0.01	100, 97		
					0+	Whole Plant	0.191	<0.01			100, 97						
					7	Whole Plant	<0.01	<0.01			100, 97						
					14	Whole Plant	<0.01	<0.01			100, 97						
					28	Whole Plant	<0.01	<0.01			100, 97						
					56	Whole Plant	<0.01	<0.01			100, 97						
					62	Grain	<0.01	<0.01			101, 99						
					62	Straw	<0.01	(0.004)			103, 98						
					2	7.9	420	--			07-Dec-2010	BBCH 45	0*	Whole Plant	0.753	(0.004)	100, 97
													0-	Whole Plant	<0.01	<0.01	100, 97
						0+	Whole Plant	0.178			<0.01		100, 97				
			7	Whole Plant		<0.01	<0.01	100, 97									
			13	Whole Plant		<0.01	<0.01	100, 97									
			28	Whole Plant		<0.01	<0.01	100, 97									
			1	6.1	407	--	17-May-2011	BBCH 45	56	Whole Plant	<0.01	<0.01	100, 97				
									59	Grain	<0.01	<0.01	101, 99				
									59	Straw	<0.01	<0.01	103, 98				
									0+	Whole Plant	0.173	<0.01	100, 97				
									7	Whole Plant	<0.01	<0.01	100, 97				
			14	Whole Plant	<0.01	<0.01	100, 97										
			28	Whole Plant	<0.01	<0.01	100, 97										
			56	Whole Plant	<0.01	<0.01	100, 97										
			59	Grain	<0.01	<0.01	101, 99										
			59	Straw	<0.01	<0.01	103, 98										

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4889I CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Nogal	Spain SZ Outdoor (field)	GF- 2573	2	8.5	113	--	28-Dec-2010	BBCH 31- 32	101	Grain	<0.01	<0.01	101, 99
					6.4	107	--	11-Mar-2011		101	Straw	<0.01	<0.01	103, 98
				2	7.5	100	--	28-Dec-2010	BBCH 39	0*	Whole Plant	0.908	0.015	100, 97
					6.0	101	--	06-Apr-2011		0-	Whole Plant	<0.01	<0.01	100, 97
										0+	Whole Plant	0.179	<0.01	100, 97
										7	Whole Plant	(0.004)	<0.01	100, 97
										12	Whole Plant	(0.003)	<0.01	100, 97
										28	Whole Plant	<0.01	<0.01	100, 97
										56	Whole Plant	<0.01	<0.01	100, 97
										75	Grain	<0.01	<0.01	101, 99
										75	Straw	<0.01	<0.01	103, 98
				2	7.4	99	--	28-Dec-2010	BBCH 43- 45	0*	Whole Plant	0.830	0.011	100, 97
					6.3	104	--	18-Apr-2011		0-	Whole Plant	<0.01	<0.01	100, 97
										0+	Whole Plant	0.084	<0.01	100, 97
										7	Whole Plant	(0.007)	<0.01	100, 97
										16	Whole Plant	<0.01	<0.01	100, 97
										29	Whole Plant	<0.01	<0.01	100, 97
										56	Whole Plant	<0.01	<0.01	100, 97
										63	Grain	<0.01	<0.01	101, 99
										63	Straw	<0.01	<0.01	103, 98
				1	6.4	107	--	18-Apr-2011	BBCH 43- 45	0+	Whole Plant	0.170	(0.004)	100, 97
										7	Whole Plant	(0.004)	<0.01	100, 97
										16	Whole Plant	<0.01	<0.01	100, 97
										29	Whole Plant	<0.01	<0.01	100, 97
										56	Whole Plant	<0.01	<0.01	100, 97
										63	Grain	<0.01	<0.01	101, 99
										63	Straw	(0.004)	<0.01	103, 98

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4889J CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Isengrain	Spain SZ Outdoor (field)	GF- 2573	2	8.4	111	--	20-Dec-2010	BBCH 31-	109	Grain	<0.01	<0.01	101, 99
					6.4	107	--	11-Mar-2011	32	109	Straw	<0.01	<0.01	103, 98
				2	8.4	111	--	20-Dec-2010		76	Grain	<0.01	<0.01	101, 99
					5.6	93	--	13-Apr-2011	BBCH 39	76	Straw	<0.01	<0.01	103, 98
				2	8.1	108	--	20-Dec-2010		71	Grain	<0.01	<0.01	101, 99
					5.6	93	--	18-Apr-2011	BBCH 43- 45	71	Straw	<0.01	<0.01	103, 98
				1	5.8	97	--	18-Apr-2011		71	Grain	<0.01	<0.01	101, 99
									BBCH 43- 45	71	Straw	<0.01	<0.01	103, 98
CEMS-4889K CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Paledor	France SZ Outdoor (field)	GF- 2573	2	6.9	91	--	13-Dec-2010	BBCH 32	97	Grain	<0.01	<0.01	101, 99
					6.2	103	--	29-Mar-2011		97	Straw	<0.01	<0.01	103, 98
				2	7.6	101	--	13-Dec-2010	BBCH 45	60	Grain	<0.01	<0.01	101, 99
					6.0	100	--	05-May-2011		60	Straw	(0.006)	(0.004)	103, 98
				2	8.1	108	--	13-Dec-2010	BBCH 45	60	Grain	<0.01	<0.01	101, 99
					6.2	103	--	05-May-2011		60	Straw	(0.004)	<0.01	103, 98
				1	6.2	103	--	05-May-2011	BBCH 45	60	Grain	<0.01	<0.01	101, 99
										60	Straw	(0.003)	<0.01	103, 98

WARNING: This document forms part of an MRL evaluation data package and should not be read or used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
			Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4889L CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Centauro	Greece SZ Outdoor (field)	GF-2573	2	8.0	427	--	27-Dec-2010	BBCH 32	90	Grain	<0.01	<0.01	101, 99
					5.9	396	--	22-Mar-2011		90	Straw	<0.01	<0.01	103, 98
				2	7.3	387	--	27-Dec-2010		73	Grain	<0.01	<0.01	101, 99
					6.0	402	--	08-Apr-2011		73	Straw	(0.003)	<0.01	103, 98
				2	7.1	378	--	27-Dec-2010		63	Grain	<0.01	<0.01	101, 99
					5.9	391	--	18-Apr-2011		63	Straw	<0.01	<0.01	103, 98
				1	6.1	404	--	18-Apr-2011		63	Grain	<0.01	<0.01	101, 99
										63	Straw	(0.004)	<0.01	103, 98
CEMS-4889M CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Blasco	Italy SZ Outdoor (field)	GF-2573	2	7.4	397	--	07-Dec-2010	BBCH 32	90	Grain	<0.01	<0.01	101, 99
					6.5	430	--	24-Mar-2011		90	Straw	<0.01	<0.01	103, 98
				2	7.9	423	--	07-Dec-2010		69	Grain	<0.01	<0.01	101, 99
					6.5	433	--	14-Apr-2011		69	Straw	<0.01	<0.01	103, 98
				2	7.5	400	--	07-Dec-2010		56	Grain	<0.01	<0.01	101, 99
					6.3	420	--	27-Apr-2011		56	Straw	<0.01	<0.01	103, 98
				1	6.3	417	--	27-Apr-2011		56	Grain	<0.01	<0.01	101, 99
										56	Straw	<0.01	<0.01	103, 98
CEMS-4889N CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Aquilante	Italy SZ Outdoor (field)	GF-2573	2	8.1	430	--	06-Dec-2010	BBCH 31-32	91	Grain	<0.01	<0.01	101, 99
					6.4	423	--	23-Mar-2011		91	Straw	<0.01	<0.01	103, 98
				2	7.6	407	--	06-Dec-2010		68	Grain	<0.01	<0.01	101, 99
					6.5	433	--	15-Apr-2011		68	Straw	<0.01	<0.01	103, 98
				2	7.9	420	--	06-Dec-2010		57	Grain	<0.01	<0.01	101, 99

WARNING: This document forms part of an EC evaluation data package and should not be used for any purpose other than the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.0	400	--	26-Apr-2011	BBCH 45	57	Straw	<0.01	<0.01	103, 98
				1	5.8	383	--	26-Apr-2011	BBCH 45	57	Grain	<0.01	<0.01	101, 99
									BBCH 45	57	Straw	<0.01	<0.01	103, 98

\* = Sampled immediately after application no. 1.

0- = Sampled immediately before application no. 2

0+ = Sampled immediately after application no. 2

<sup>a</sup> Limit of Quantitation (LOQ) = 0.01 mg/kg; Limit of Detection (LOD) = 0.003 mg/kg. Residue values equal to or greater than the LOD, but less than the LOQ are displayed within parenthesis.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-3 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in winter wheat (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4552A CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mulan	Germany NZ Outdoor (field)	GF- 2573	2	7.7 6.3	410 419	-- --	07-Dec-2009 05-May-2010	BBCH 32	97 97	Grain Straw	-- --	-- --	-- --
				2	7.5 6.1	400 410	-- --	07-Dec-2009 28-May-2010	BBCH 39	74 74	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				2	7.6 6.0	406 402	-- --	07-Dec-2009 04-Jun-2010	BBCH 45	67 67	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				1	6.1	404	--	04-Jun-2010	BBCH 45	67 67	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
CEMS-4552B CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Buzogany	Hungary NZ Outdoor (field)	GF- 2573	2	7.4 6.2	296 312	-- --	10-Dec-2009 19-Apr-2010	BBCH 32	86 86	Grain Straw	-- --	-- --	-- --
				2	7.6 6.1	303 303	-- --	10-Dec-2009 30-Apr-2010	BBCH 39	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				2	7.7 6.0	308 298	-- --	10-Dec-2009 07-May-2010	BBCH 45	68 68	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				1	6.0	301	--	07-May-2010	BBCH 45	68 68	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4552E CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Tarus	Germany NZ Outdoor (field)	GF- 2573	2	8.1 6.6	323 330	-- --	09-Dec-2009 20-Apr-2010	BBCH 32	109 109	Grain Straw	-- --	-- --	-- --
				2	7.8 6.5	313 327	-- --	09-Dec-2009 25-May-2010	BBCH 39	74 74	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				2	7.7 6.6	307 328	-- --	09-Dec-2009 07-Jun-2010	BBCH 58	61 61	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	100, 98 97, 100
				1	5.5	273	--	07-Jun-2010	BBCH 58	61 61	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
				2	7.9 6.4	317 320	-- --	31-Dec-2009 23-Apr-2010	BBCH 32	83 83	Grain Straw	-- --	-- --	-- --
				2	7.7 5.9	310 293	-- --	31-Dec-2009 14-May-2010	BBCH 39	62 62	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
CEMS-4552F CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mercato	France NZ Outdoor (field)	GF- 2573	2	7.6 5.7	303 287	-- --	31-Dec-2009 21-May-2010	BBCH 47	55 55	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	100, 98 97, 100
				1	5.7	287	--	21-May-2010	BBCH 47	55 55	Grain Straw	<0.01 <0.01	<0.01 <0.01	100, 98 97, 100
CEMS-4889A CEMS-4889 DAS Ref. ID	Winter Wheat / Potenzial	Germany NZ Outdoor	GF- 2573	2	8.8 5.7	118 95	-- --	25-Nov-2010 26-Apr-2011	BBCH 32	91 91	Grain Straw	-- --	-- --	90, 91 87, 83

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
			Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet-mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet-mexyl, Cloquintocet acid
102082 Y 2010-2011		(field)		2	6.9 5.1	92 85	-- --	25-Nov-2010 18-May-2011	BBCH 39	69 69	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				2	6.9 5.9	93 98	-- --	25-Nov-2010 23-May-2011	BBCH 45	64 64	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				2	7.8 7.9	417 423	-- --	08-Dec-2010 18-Apr-2011	BBCH 32	98 98	Grain Straw	-- --	-- --	90, 91 87, 83
				2	7.7 5.7	409 381	-- --	08-Dec-2010 06-May-2011	BBCH 39	80 80	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
CEMS-4889B CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Magdalena	Hungary NZ Outdoor (field)	GF-2573	2	7.8 5.5	414 365	-- --	08-Dec-2010 17-May-2011	BBCH 45-49	69 69	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				1	6.1	408	--	17-May-2011	BBCH 45-49	69 69	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				2	7.2 8.1	386 431	-- --	07-Jan-2011 26-Apr-2011	BBCH 32	77 77	Grain Straw	-- --	-- --	90, 91 87, 83
				2	7.6 6.0	406 398	-- --	07-Jan-2011 06-May-2011	BBCH 39	67 67	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
CEMS-4889C CEMS-4889 DAS Ref. ID 102082 Y 2011	Winter Wheat / Buzogany	Hungary NZ Outdoor (field)	GF-2573	2	7.7 5.9	411 393	-- --	07-Jan-2011 17-May-2011	BBCH 45	56 56	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
					5.7	382	--	17-May-2011	BBCH 45	56	Grain	<0.01	<0.01	90, 91

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
										56	Straw	<0.01	<0.01	87, 83
CEMS-4889D CEMS-4889 DAS Ref. ID 102082 Y 2011	Winter Wheat / Boregar	France NZ Outdoor (field)	GF- 2573	2	7.6	407	--	05-Jan-2011	BBCH 32	93	Grain	--	--	90, 91
					6.3	422	--	04-Apr-2011		93	Straw	--	--	87, 83
				2	7.7	411	--	05-Jan-2011	BBCH 39	65	Grain	<0.01	<0.01	90, 91
					6.1	404	--	02-May-2011		65	Straw	<0.01	<0.01	87, 83
				2	7.8	418	--	05-Jan-2011	BBCH 45	62	Grain	<0.01	<0.01	90, 91
					6.0	402	--	05-May-2011		62	Straw	<0.01	<0.01	87, 83
				1	6.1	404	--	05-May-2011	BBCH 45	62	Grain	<0.01	<0.01	90, 91
										62	Straw	<0.01	<0.01	87, 83
CEMS-4889E CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Tabasco	Germany NZ Outdoor (field)	GF- 2573	2	8.6	115	--	26-Nov-2010	BBCH 32	112	Grain	--	--	90, 91
					6.6	110	--	27-Apr-2011		112	Straw	--	--	87, 83
				2	8.0	106	--	26-Nov-2010	BBCH 39	92	Grain	<0.01	<0.01	90, 91
					4.8	80	--	17-May-2011		92	Straw	<0.01	<0.01	87, 83
				2	9.0	119	--	26-Nov-2010	BBCH 45	84	Grain	<0.01	<0.01	90, 91
					6.8	113	--	25-May-2011		84	Straw	<0.01	<0.01	87, 83
				1	6.6	110	--	25-May-2011	BBCH 45	84	Grain	<0.01	<0.01	90, 91
										84	Straw	<0.01	<0.01	87, 83
CEMS-4889F CEMS-4889 DAS Ref. ID 102082	Winter Wheat / Potencial	Poland NZ Outdoor (field)	GF- 2573	2	7.1	378	--	06-Dec-2010	BBCH 32	92	Grain	--	--	90, 91
					6.1	403	--	10-May-2011		92	Straw	--	--	87, 83
					7.5	400	--	06-Dec-2010	BBCH 39	82	Grain	<0.01	<0.01	90, 91

WARNING: This document forms part of an EC evaluation data package and should not be used for registration purposes. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet-mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet-mexyl, Cloquintocet acid
Y 2010-2011				2	5.8	385	--	20-May-2011	BBCH 45	82	Straw	<0.01	<0.01	87, 83
					6.9	370	--	06-Dec-2010		75	Grain	<0.01	<0.01	90, 91
					5.9	390	--	27-May-2011		75	Straw	<0.01	<0.01	87, 83
				1	6.0	402	--	27-May-2011	BBCH 45	75	Grain	<0.01	<0.01	90, 91
									75	Straw	<0.01	<0.01	87, 83	
CEMS-4889G CEMS-4889 DAS Ref. ID 102082 Y 2011	Winter Wheat / Oakley	United Kingdom NZ Outdoor (field)	GF-2573	2	8.4	111	--	06-Jan-2011	BBCH 32	85	Grain	--	--	90, 91
					6.2	103	--	09-May-2011		85	Straw	--	--	87, 83
				2	8.1	108	--	06-Jan-2011	BBCH 39	75	Grain	<0.01	<0.01	90, 91
					6.4	107	--	19-May-2011		75	Straw	<0.01	<0.01	87, 83
				2	8.4	111	--	06-Jan-2011	BBCH 51	67	Grain	<0.01	<0.01	90, 91
					6.8	113	--	27-May-2011		67	Straw	<0.01	<0.01	87, 83
				1	6.0	106	--	27-May-2011	BBCH 51	67	Grain	<0.01	<0.01	90, 91
										67	Straw	<0.01	<0.01	87, 83

WARNING: This document forms part of an EC evaluation data package and should not be used for any other purpose. Registration must not be granted on the basis of this document.



Table B.7.6-4 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in winter wheat (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet-mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet-mexyl, Cloquintocet acid
CEMS-4552C CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Isangrain	Spain SZ Outdoor (field)	GF-2573	2	7.7	308	--	18-Dec-2009	BBCH 32	104	Grain	--	--	--
					6.1	307	--	24-Mar-2010		104	Straw	--	--	--
				2	7.4	296	--	18-Dec-2009	BBCH 39	71	Grain	<0.01	<0.01	100, 98
					5.9	296	--	26-Apr-2010		71	Straw	<0.01	<0.01	97, 100
				2	7.6	302	--	18-Dec-2009	BBCH 45	64	Grain	<u>&lt;0.01</u>	<u>&lt;0.01</u>	100, 98
					5.5	273	--	03-May-2010		64	Straw	<u>&lt;0.01</u>	<u>&lt;0.01</u>	97, 100
				1	5.7	287	--	03-May-2010	BBCH 45	64	Grain	<0.01	<0.01	100, 98
										64	Straw	<0.01	<0.01	97, 100
CEMS-4552D CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Quality	France SZ Outdoor (field)	GF-2573	2	8.5	307	--	22-Dec-2009	BBCH 32	92	Grain	--	--	--
					5.7	284	--	06-Apr-2010		92	Straw	--	--	--
				2	8.1	291	--	22-Dec-2009	BBCH 39	68	Grain	<0.01	<0.01	100, 98
					6.1	304	--	30-Apr-2010		68	Straw	<0.01	<0.01	97, 100
				2	8.3	299	--	22-Dec-2009	BBCH 45	61	Grain	<u>&lt;0.01</u>	<u>&lt;0.01</u>	100, 98
					6.2	310	--	07-May-2010		61	Straw	<u>&lt;0.01</u>	<u>&lt;0.01</u>	97, 100
				1	5.7	287	--	07-May-2010	BBCH 45	61	Grain	<0.01	<0.01	100, 98
										61	Straw	<0.01	<0.01	97, 100

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4552G CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Botticelli	Spain SZ Outdoor (field)	GF- 2573	2	7.5	300	--	27-Dec-2009	BBCH 32	95	Grain	--	--	--
					6.4	322	--	05-Apr-2010		95	Straw	--	--	--
				2	7.6	303	--	27-Dec-2009	BBCH 39	72	Grain	<0.01	<0.01	100, 98
					6.2	308	--	28-Apr-2010		72	Straw	<0.01	<0.01	97, 100
				2	7.8	312	--	27-Dec-2009	BBCH 45	59	Grain	<0.01	<0.01	100, 98
					6.0	300	--	11-May-2010		59	Straw	<0.01	<0.01	97, 100
				1	5.9	297	--	11-May-2010	BBCH 45	59	Grain	<0.01	<0.01	100, 98
										59	Straw	<0.01	<0.01	97, 100
CEMS-4552H CEMS-4552 DAS Ref. ID 090118 Y 2009-2010	Winter Wheat / Mieti	Italy SZ Outdoor (field)	GF- 2573	2	7.8	313	--	10-Dec-2009	BBCH 32	90	Grain	--	--	--
					6.1	303	--	31-Mar-2010		90	Straw	--	--	--
				2	7.2	290	--	10-Dec-2009	BBCH 39	61	Grain	<0.01	<0.01	100, 98
					6.5	323	--	29-Apr-2010		61	Straw	<0.01	<0.01	97, 100
				2	7.6	303	--	10-Dec-2009	BBCH 45	56	Grain	<0.01	<0.01	100, 98
					5.9	330	--	04-May-2010		56	Straw	<0.01	<0.01	97, 100
				1	5.9	330	--	04-May-2010	BBCH 45	56	Grain	<0.01	<0.01	100, 98
										56	Straw	<0.01	<0.01	97, 100
CEMS-4889H CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Enola	Bulgaria SZ Outdoor (field)	GF- 2573	2	8.2	436	--	07-Dec-2010	BBCH 32	93	Grain	--	--	90, 91
					6.3	418	--	13-Apr-2011		93	Straw	--	--	87, 83
				2	7.8	413	--	07-Dec-2010	BBCH 39	62	Grain	<0.01	<0.01	90, 91
					6.2	411	--	14-May-2011		62	Straw	<0.01	<0.01	87, 83

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
				2	7.9 6.2	420 411	-- --	07-Dec-2010 17-May-2011	BBCH 45 32	59 59	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				1	6.1	407	--	17-May-2011	BBCH 45	59 59	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
CEMS-4889I CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Nogal	Spain SZ Outdoor (field)	GF- 2573	2	8.5 6.4	113 107	-- --	28-Dec-2010 11-Mar-2011	BBCH 31- 32	101 101	Grain Straw	-- --	-- --	90, 91 87, 83
				2	7.5 6.0	100 101	-- --	28-Dec-2010 06-Apr-2011	BBCH 39	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				2	7.4 6.3	99 104	-- --	28-Dec-2010 18-Apr-2011	BBCH 43- 45	63 63	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				1	6.4	107	--	18-Apr-2011	BBCH 43- 45	63 63	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
CEMS-4889J CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Isengrain	Spain SZ Outdoor (field)	GF- 2573	2	8.4 6.4	111 107	-- --	20-Dec-2010 11-Mar-2011	BBCH 31- 32	109 109	Grain Straw	-- --	-- --	90, 91 87, 83
				2	8.4 5.6	111 93	-- --	20-Dec-2010 13-Apr-2011	BBCH 39	76 76	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				2	8.1 5.6	108 93	-- --	20-Dec-2010 18-Apr-2011	BBCH 43- 45	71 71	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83
				1	5.8	97	--	18-Apr-2011	BBCH 43- 45	71 71	Grain Straw	<0.01 <0.01	<0.01 <0.01	90, 91 87, 83

WARNING: This document forms part of an EC evaluation data package and should not be used for any purpose other than the basis of this document. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
									BBCH 43 45					
CEMS-4889K CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Paledor	France SZ Outdoor (field)	GF- 2573	2	6.9	91	--	13-Dec-2010	BBCH 32	97	Grain	--	--	90, 91
					6.2	103	--	29-Mar-2011		97	Straw	--	--	87, 83
				2	7.6	101	--	13-Dec-2010	BBCH 45	60	Grain	<0.01	<0.01	90, 91
					6.0	100	--	05-May-2011		60	Straw	<0.01	<0.01	87, 83
				2	8.1	108	--	13-Dec-2010	BBCH 45	60	Grain	<0.01	<0.01	90, 91
					6.2	103	--	05-May-2011		60	Straw	<0.01	<0.01	87, 83
CEMS-4889L CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Centauro	Greece SZ Outdoor (field)	GF- 2573	2	8.0	427	--	27-Dec-2010	BBCH 32	90	Grain	--	--	90, 91
					5.9	396	--	22-Mar-2011		90	Straw	--	--	87, 83
				2	7.3	387	--	27-Dec-2010	BBCH 39	73	Grain	<0.01	<0.01	90, 91
					6.0	402	--	08-Apr-2011		73	Straw	<0.01	<0.01	87, 83
				2	7.1	378	--	27-Dec-2010	BBCH 45	63	Grain	<0.01	<0.01	90, 91
					5.9	391	--	18-Apr-2011		63	Straw	<0.01	<0.01	87, 83
				1	6.1	404	--	18-Apr-2011	BBCH 45	63	Grain	<0.01	<0.01	90, 91
										63	Straw	<0.01	<0.01	87, 83

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4889M CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Blasco	Italy SZ Outdoor (field)	GF- 2573	2	7.4	397	--	07-Dec-2010	BBCH 32	90	Grain	--	--	90, 91
					6.5	430	--	24-Mar-2011		90	Straw	--	--	87, 83
				2	7.9	423	--	07-Dec-2010	BBCH 39	69	Grain	<0.01	<0.01	90, 91
					6.5	433	--	14-Apr-2011		69	Straw	<0.01	<0.01	87, 83
				2	7.5	400	--	07-Dec-2010	BBCH 45	56	Grain	<0.01	<0.01	90, 91
					6.3	420	--	27-Apr-2011		56	Straw	<0.01	<0.01	87, 83
				1	6.3	417	--	27-Apr-2011	BBCH 45	56	Grain	<0.01	<0.01	90, 91
										56	Straw	<0.01	<0.01	87, 83
CEMS-4889N CEMS-4889 DAS Ref. ID 102082 Y 2010-2011	Winter Wheat / Aquilante	Italy SZ Outdoor (field)	GF- 2573	2	8.1	430	--	06-Dec-2010	BBCH 31-	91	Grain	--	--	90, 91
					6.4	423	--	23-Mar-2011	32	91	Straw	--	--	87, 83
				2	7.6	407	--	06-Dec-2010		68	Grain	<0.01	<0.01	90, 91
					6.5	433	--	15-Apr-2011	BBCH 39	68	Straw	<0.01	<0.01	87, 83
				2	7.9	420	--	06-Dec-2010		57	Grain	<0.01	<0.01	90, 91
					6.0	400	--	26-Apr-2011	BBCH 45	57	Straw	<0.01	<0.01	87, 83
				1	5.8	383	--	26-Apr-2011		57	Grain	<0.01	<0.01	90, 91
									BBCH 45	57	Straw	<0.01	<0.01	87, 83

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-5 Summary of residues of XDE-729 Methyl and XDE-729 Acid in spring wheat (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4719A CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Belvoir	United Kingdom NZ Outdoor (field)	GF- 2573	1	6.3	313	--	22-Jun-2010	BBCH 32	55#	Grain	<0.01	<0.01	99, 81
									55#	Straw	<0.01	<0.01	102, 103	
				1	6.3	314	--	24-Jun-2010	BBCH 39	0	Whole plant	0.103	<0.01	97, 109
									7	Whole plant	<0.01	<0.01	97, 109	
									14	Whole plant	<0.01	<0.01	97, 109	
									28	Whole plant	<0.01	<0.01	97, 109	
									46	Whole plant	<0.01	<0.01	97, 109	
									53#	Grain	<0.01	<0.01	99, 81	
									53#	Straw	<0.01	(0.003)	102, 103	
									64	Grain	<0.01	<0.01	99, 81	
									64	Straw	<0.01	(0.004)	102, 103	
									67	Grain	<0.01	<0.01	99, 81	
									67	Straw	<0.01	(0.003)	102, 103	
				1	6.2	311	--	29-Jun-2010	BBCH 45	0	Whole plant	0.076	<0.01	97, 109
									7	Whole plant	<0.01	<0.01	97, 109	
									14	Whole plant	<0.01	<0.01	97, 109	
									28	Whole plant	<0.01	<0.01	97, 109	
									41	Whole plant	<0.01	<0.01	97, 109	
									48#	Grain	<0.01	<0.01	99, 81	
									48#	Straw	<0.01	<0.01	102, 103	
									59	Grain	<0.01	<0.01	99, 81	
									59	Straw	<0.01	(0.004)	102, 103	
									62	Grain	<0.01	<0.01	99, 81	
									62	Straw	<0.01	(0.003)	102, 103	

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4719B CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Naxos	Germany NZ Outdoor (field)	GF- 2573	1	6.3	83	--	08-Jun-2010	BBCH 32	77#	Grain	<0.01	<0.01	99, 81
										77#	Straw	<0.01	<0.01	102, 103
				1	6.1	82	--	18-Jun-2010	BBCH 39	0	Whole plant	0.258	<0.01	97, 109
										7	Whole plant	(0.005)	<0.01	97, 109
										14	Whole plant	<0.01	<0.01	97, 109
										27	Whole plant	<0.01	<0.01	97, 109
										60	Grain	<0.01	<0.01	99, 81
										60	Straw	<0.01	<0.01	102, 103
										67#	Grain	<0.01	<0.01	99, 81
										67#	Straw	<0.01	<0.01	102, 103
										74	Grain	<0.01	<0.01	99, 81
										74	Straw	(0.003)	<0.01	102, 103
										80	Grain	<0.01	<0.01	99, 81
										80	Straw	<0.01	<0.01	102, 103
				1	6.0	80	--	22-Jun-2010	BBCH 45	0	Whole plant	0.188	<0.01	97, 109
										7	Whole plant	<0.01	<0.01	97, 109
										14	Whole plant	<0.01	<0.01	97, 109
										29	Whole plant	<0.01	<0.01	97, 109
										56	Grain	<0.01	<0.01	99, 81
										56	Straw	(0.003)	<0.01	102, 103
										63#	Grain	<0.01	<0.01	99, 81
										63#	Straw	<0.01	<0.01	102, 103
										70	Grain	<0.01	<0.01	99, 81
										70	Straw	(0.003)	<0.01	102, 103

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										76 76	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
CEMS-4719C CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Triso	Hungary NZ Outdoor (field)	GF- 2573	1	6.6	328	--	13-May-2010	BBCH 32	75# 75#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.4	322	--	24-May-2010	BBCH 39	64# 64#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.3	315	--	03-Jun-2010	BBCH 45	54# 54#	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	99, 81 102, 103
CEMS-4719D CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Triso	Northern France NZ Outdoor (field)	GF- 2573	1	6.4	403	--	27-May-2010	BBCH 32	75# 75#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.6	407	--	08-Jun-2010	BBCH 39	63# 63#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.3	397	--	15-Jun-2010	BBCH 52	56# 56#	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	99, 81 102, 103
CEMS-5001A CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Amaretto	Germany NZ Outdoor (field)	GF- 2573	1	6.4	107	--	20-May-2011	BBCH 32	94# 94#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.3	106	--	25-May-2011	BBCH 39	0 9 15	Whole Plant Whole Plant Whole Plant	0.601 <0.01 <0.01	(0.004) <0.01 <0.01	98, 96 98, 96 98, 96

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details						Residues found <sup>a</sup>					
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.3	106	--	03-Jun-2011	BBCH 45	28	Whole Plant	<0.01	<0.01	98, 96
										82	Grain	<0.01	<0.01	99, 99
										82	Straw	<0.01	<0.01	91, 99
										89#	Grain	<0.01	<0.01	99, 99
										89#	Straw	<0.01	<0.01	91, 99
										96	Grain	<0.01	<0.01	99, 99
										96	Straw	<0.01	<0.01	91, 99
										103	Grain	<0.01	<0.01	99, 99
										103	Straw	<0.01	<0.01	91, 99
										0	Whole Plant	0.132	<0.01	98, 96
										6	Whole Plant	<0.01	<0.01	98, 96
										14	Whole Plant	<0.01	<0.01	98, 96
										28	Whole Plant	<0.01	<0.01	98, 96
										73	Grain	<0.01	<0.01	99, 99
										73	Straw	<0.01	<0.01	91, 99
										80#	Grain	<0.01	<0.01	99, 99
										80#	Straw	<0.01	<0.01	91, 99
										87	Grain	<0.01	<0.01	99, 99
										87	Straw	<0.01	<0.01	91, 99
										94	Grain	<0.01	<0.01	99, 99
										94	Straw	<0.01	<0.01	91, 99

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>			
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid	
CEMS-5001B CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Sponsor	France NZ Outdoor (field)	GF- 2573	1	6.1	410	--	17-May-2011	BBCH 32	98#	Grain	<0.01	<0.01	99, 99	
										98#	Straw	<0.01	<0.01	91, 99	
					1	6.0	398	--	20-May-2011	BBCH 39	0	Whole Plant	0.074	<0.01	98, 96
										6	Whole Plant	(0.007)	<0.01	98, 96	
										12	Whole Plant	(0.003)	<0.01	98, 96	
										27	Whole Plant	<0.01	<0.01	98, 96	
										88	Grain	<0.01	<0.01	99, 99	
										88	Straw	<0.01	<0.01	91, 99	
										95#	Grain	<0.01	<0.01	99, 99	
										95#	Straw	<0.01	<0.01	91, 99	
										101	Grain	<0.01	<0.01	99, 99	
										101	Straw	<0.01	<0.01	91, 99	
										108	Grain	<0.01	<0.01	99, 99	
										108	Straw	<0.01	<0.01	91, 99	
					1	5.5	367	--	25-May-2011	BBCH 45	0	Whole Plant	0.062	<0.01	98, 96
										7	Whole Plant	(0.006)	<0.01	98, 96	
										12	Whole Plant	<0.01	<0.01	98, 96	
										29	Whole Plant	<0.01	<0.01	98, 96	
										83	Grain	<0.01	<0.01	99, 99	
										83	Straw	<0.01	<0.01	91, 99	
										90#	Grain	<0.01	<0.01	99, 99	
										90#	Straw	<0.01	<0.01	91, 99	
										96	Grain	<0.01	<0.01	99, 99	
										96	Straw	<0.01	<0.01	91, 99	
										103	Grain	<0.01	<0.01	99, 99	
										103	Straw	<0.01	<0.01	91, 99	

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-5001C CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Ina	Poland NZ Outdoor (field)	GF- 2573	1	6.1	407	--	25-May-2011	BBCH 32	77#	Grain	<0.01	<0.01	99, 99
										77#	Straw	<0.01	<0.01	91, 99
				1	6.3	420	--	30-May-2011	BBCH 39	72#	Grain	<0.01	<0.01	99, 99
										72#	Straw	(0.004)	<0.01	91, 99
				1	6.3	422	--	07-Jun-2011	BBCH 45	64#	Grain	<0.01	<0.01	99, 99
										64#	Straw	0.012	(0.004)	91, 99
CEMS-5001D CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / AC Barrie	United Kingdom NZ Outdoor (field)	GF- 2573	1	6.3	105	--	13-May-2011	BBCH 32	90#	Grain	<0.01	<0.01	99, 99
										90#	Straw	<0.01	<0.01	91, 99
				1	6.2	103	--	24-May-2011	BBCH 39	79#	Grain	<0.01	<0.01	99, 99
										79#	Straw	<0.01	<0.01	91, 99
				1	6.2	103	--	27-May-2011	BBCH 45	76#	Grain	<0.01	<0.01	99, 99
										76#	Straw	<0.01	<0.01	91, 99
CEMS-5001E CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Korzo	Hungary NZ Outdoor (field)	GF- 2573	1	5.9	393	--	17-May-2011	BBCH 32	69#	Grain	<0.01	<0.01	99, 99
										69#	Straw	<0.01	<0.01	91, 99
				1	5.9	393	--	31-May-2011	BBCH 39	55#	Grain	<0.01	<0.01	99, 99
										55#	Straw	<0.01	<0.01	91, 99
				1	5.6	373	--	03-Jun-2011	BBCH 47	52#	Grain	<0.01	<0.01	99, 99
										52#	Straw	<0.01	<0.01	91, 99

WARNING: This document forms part of an EC evaluation data package and should not be used for registration purposes on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-5001F CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Triso	Germany NZ Outdoor (field)	GF- 2573	1	6.6	110	--	29-Apr-2011	BBCH 32	96#	Grain	<0.01	<0.01	99, 99
										96#	Straw	<0.01	<0.01	91, 99
				1	6.6	110	--	18-May-2011	BBCH 39	77#	Grain	<0.01	<0.01	99, 99
										77#	Straw	<0.01	<0.01	91, 99
				1	6.4	107	--	25-May-2011	BBCH 45	70#	Grain	<0.01	<0.01	99, 99
										70#	Straw	<0.01	<0.01	91, 99

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-6 Summary of residues of XDE-729 Methyl and XDE-729 Acid in spring wheat (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4719F CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Sarina	Spain SZ Outdoor (field)	GF- 2573	1	6.0	379	--	30-Apr-2010	BBCH 32	88#	Grain	<0.01	<0.01	99, 81
									88#	Straw	<0.01	<0.01	102, 103	
				1	5.8	367	--	18-May-2010	BBCH 39	0	Whole plant	0.175	<0.01	97, 109
									7	Whole plant	(0.007)	<0.01	97, 109	
									14	Whole plant	<0.01	<0.01	97, 109	
									28	Whole plant	<0.01	<0.01	97, 109	
									63	Grain	<0.01	<0.01	99, 81	
									63	Straw	<0.01	<0.01	102, 103	
									70#	Grain	<0.01	<0.01	99, 81	
									70#	Straw	<0.01	<0.01	102, 103	
									77	Grain	<0.01	<0.01	99, 81	
									77	Straw	<0.01	<0.01	102, 103	
									84	Grain	<0.01	<0.01	99, 81	
									84	Straw	<0.01	(0.003)	102, 103	
				1	6.1	386	--	21-May-2010	BBCH 45	0	Whole plant	0.181	(0.003)	97, 109
									7	Whole plant	(0.005)	<0.01	97, 109	
									14	Whole plant	<0.01	<0.01	97, 109	
									28	Whole plant	<0.01	<0.01	97, 109	
									60	Grain	<0.01	<0.01	99, 81	
									60	Straw	<0.01	<0.01	102, 103	
									67#	Grain	<0.01	<0.01	99, 81	
									67#	Straw	<0.01	<0.01	102, 103	
									74	Grain	<0.01	<0.01	99, 81	
									74	Straw	<0.01	(0.005)	102, 103	

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										81 81	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
CEMS-4719G CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Cap Horn	Southern France SZ Outdoor (field)	GF- 2573	1	6.5	87	--	10-May-2010	BBCH 32	60# 60#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.3	83	--	21-May-2010	BBCH 39	49# 49#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	5.8	77	--	03-Jun-2010	BBCH 45	36# 36#	Grain Straw	<0.01 0.015	<0.01 (0.005)	99, 81 102, 103
CEMS-4719H CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Amaretto	Greece SZ Outdoor (field)	GF- 2573	1	5.9	297	--	08-Apr-2010	BBCH 32	71# 71#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	6.0	300	--	21-Apr-2010	BBCH 39	58# 58#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
				1	5.9	293	--	30-Apr-2010	BBCH 45	49# 49#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 81 102, 103
CEMS-5001G CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Palesio	Italy SZ Outdoor (field)	GF- 2573	1	6.1	408	--	19-Apr-2011	BBCH 32	66# 66#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.6	440	--	28-Apr-2011	BBCH 39	0 7 14 27 50 57# 57#	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw	0.196 (0.004) <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 98, 96 99, 99 91, 99

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.1	403	--	05-May-2011	BBCH 45	64 64	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.1	403	--	05-May-2011	BBCH 45	0 7 13 27 43 50# 50# 57 57	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw	0.116 (0.006) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 98, 96 99, 99 91, 99 99, 99 91, 99
CEMS-5001H CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Blasco	Italy SZ Outdoor (field)	GF- 2573	1	6.6	439	--	19-Apr-2011	BBCH 32	66# 66#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.0	397	--	28-Apr-2011	BBCH 39	0 7 13 27 50 57# 57# 64 64	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw	0.131 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 98, 96 99, 99 91, 99 99, 99 91, 99
				1	6.1	404	--	05-May-2011	BBCH 45	0 6 12 27 43	Whole Plant Whole Plant Whole Plant Whole Plant Whole Plant	0.106 (0.005) <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 98, 96

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										50# 50# 57 57	Grain Straw Grain Straw	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	99, 99 91, 99 99, 99 91, 99
CEMS-500II CEMS-500I DAS Ref. ID 110411 Y 2011	Spring Wheat / Alcala	Spain SZ Outdoor (field)	GF- 2573	1	6.8	114	--	12-Apr-2011	BBCH 32	78# 78#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.0	100	--	26-Apr-2011	BBCH 39	0 8 15 29 57 57 64# 64# 71 71 78 78	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw Grain Straw Grain Straw	0.178 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 99, 99 91, 99 99, 99 91, 99 99, 99 91, 99 99, 99 91, 99
				1	6.1	101	--	28-Apr-2011	BBCH 45	0 6 13 27 55 55 62# 62# 69 69	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw Grain Straw	0.118 (0.005) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	98, 96 98, 96 98, 96 98, 96 99, 99 91, 99 99, 99 91, 99 99, 99 91, 99 99, 99 91, 99

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 Acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										76 76	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
CEMS-5001J CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Califa	Spain SZ Outdoor (field)	GF- 2573	1	6.4	106	--	07-Apr-2011	BBCH 32	89# 89#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.2	103	--	26-Apr-2011	BBCH 39	70# 70#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.6	110	--	03-May-2011	BBCH 45	63# 63#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
CEMS-5001L CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Claudio	Greece SZ Outdoor (field)	GF- 2573	1	5.7	382	--	06-Apr-2011	BBCH 32	84# 84#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	5.8	389	--	18-Apr-2011	BBCH 39	72# 72#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.1	404	--	29-Apr-2011	BBCH 45	61# 61#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
CEMS-5001M CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Gekora	Greece SZ Outdoor (field)	GF- 2573	1	6.1	404	--	05-Apr-2011	BBCH 32	72# 72#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.2	411	--	20-Apr-2011	BBCH 39	57# 57#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99
				1	6.2	413	--	05-May-2011	BBCH 45	42# 42#	Grain Straw	<0.01 <0.01	<0.01 <0.01	99, 99 91, 99

<sup>a</sup> Limit of Quantitation (LOQ) = 0.01 mg/kg; Limit of Detection (LOD) = 0.003 mg/kg. Residue values equal to or greater than the LOD, but less than the LOQ are displayed within parenthesis.

# = Normal Commercial Harvest

Table B.7.6-7 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in spring wheat (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4719A CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Belvoir	United Kingdom NZ Outdoor (field)	GF- 2573	1	6.3	313	--	22-Jun-2010	BBCH 32	55	Grain	--	--	--
									55	Straw	--	--	--	
				1	6.3	314	--	24-Jun-2010	BBCH 39	53#	Grain	<0.01	<0.01	104, 102
									53#	Straw	<0.01	<0.01	111, 109	
									64	Grain	<0.01	<0.01	104, 102	
									64	Straw	<0.01	<0.01	111, 109	
									67	Grain	<0.01	<0.01	104, 102	
									67	Straw	<0.01	<0.01	111, 109	
				1	6.2	311	--	29-Jun-2010	BBCH 45	48#	Grain	<0.01	<0.01	104, 102
									48#	Straw	<0.01	<0.01	111, 109	
									59	Grain	<0.01	<0.01	104, 102	
									59	Straw	<0.01	<0.01	111, 109	
					62	Grain	<0.01	<0.01	104, 102					
					62	Straw	<0.01	<0.01	111, 109					
CEMS-4719B CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Naxos	Germany NZ Outdoor (field)	GF- 2573	1	6.3	83	--	08-Jun-2010	BBCH 32	77	Grain	--	--	--
									77	Straw	--	--	--	
				1	6.3	82	--	18-Jun-2010	BBCH 39	60	Grain	<0.01	<0.01	104, 102
									60	Straw	<0.01	<0.01	111, 109	
									67#	Grain	<0.01	<0.01	104, 102	
									67#	Straw	<0.01	<0.01	111, 109	
									74	Grain	<0.01	<0.01	104, 102	
									74	Straw	<0.01	<0.01	111, 109	

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
				1	6.0	80	--	22-Jun-2010	BBCH 45	80 80	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
				1	6.0	80	--	22-Jun-2010	BBCH 45	56 56 63# 63# 70 70 76 76	Grain Straw Grain Straw Grain Straw Grain Straw	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	104, 102 111, 109 104, 102 111, 109 104, 102 111, 109 104, 102 111, 109
CEMS-4719C CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Triso	Hungary NZ Outdoor (field)	GF- 2573	1	6.6	328	--	13-May-2010	BBCH 32	75# 75#	Grain Straw	-- --	-- --	-- --
				1	6.4	322	--	24-May-2010	BBCH 39	64# 64#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
				1	6.3	345	--	03-Jun-2010	BBCH 45	54# 54#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
CEMS-4719D CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Triso	Northern France NZ Outdoor (field)	GF- 2573	1	6.4	403	--	27-May-2010	BBCH 32	75# 75#	Grain Straw	-- --	-- --	-- --
				1	6.6	417	--	08-Jun-2010	BBCH 39	63# 63#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
				1	6.3	397	--	15-Jun-2010	BBCH 52	56# 56#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-5001A CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Amaretto	Germany NZ Outdoor (field)	GF- 2573	1	6.4	107	--	20-May-2011	BBCH 32	94# 94#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.3	106	--	25-May-2011	BBCH 39	89# 89#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.3	106	--	03-Jun-2011	BBCH 45	80# 80#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
CEMS-5001B CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Sponsor	France NZ Outdoor (field)	GF- 2573	1	6.1	410	--	17-May-2011	BBCH 32	98# 98#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.0	398	--	20-May-2011	BBCH 39	95# 95#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	5.5	367	--	25-May-2011	BBCH 45	90# 90#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
CEMS-5001C CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Ina	Poland NZ Outdoor (field)	GF- 2573	1	6.1	407	--	25-May-2011	BBCH 32	77# 77#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.3	420	--	30-May-2011	BBCH 39	72# 72#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.3	422	--	07-Jun-2011	BBCH 45	64# 64#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
CEMS-5001D CEMS-5001 DAS Ref. ID	Spring Wheat / AC Barrie	United Kingdom NZ	GF- 2573	1	6.3	105	--	13-May-2011	BBCH 32	90# 90#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
110411 Y 2011		Outdoor (field)		1	6.2	103	--	24-May-2011	BBCH 39	79#	Grain	<0.01	<0.01	93, 94
										79#	Straw	<0.01	<0.01	101, 105
				1	6.2	103	--	27-May-2011	BBCH 45	76#	Grain	<0.01	<0.01	93, 94
										76#	Straw	<0.01	<0.01	101, 105
CEMS-5001E CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Korzo	Hungary NZ Outdoor (field)	GF- 2573	1	5.9	393	--	17-May-2011	BBCH 32	69#	Grain	<0.01	<0.01	93, 94
										69#	Straw	<0.01	<0.01	101, 105
				1	5.9	393	--	31-May-2011	BBCH 39	55#	Grain	<0.01	<0.01	93, 94
										55#	Straw	<0.01	<0.01	101, 105
CEMS-5001F CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Triso	Germany NZ Outdoor (field)	GF- 2573	1	5.6	373	--	03-Jun-2011	BBCH 47	52#	Grain	<0.01	<0.01	93, 94
										52#	Straw	<0.01	<0.01	101, 105
				1	6.6	110	--	29-Apr-2011	BBCH 32	96#	Grain	<0.01	<0.01	93, 94
										96#	Straw	<0.01	<0.01	101, 105
				1	6.6	110	--	18-May-2011	BBCH 39	77#	Grain	<0.01	<0.01	93, 94
										77#	Straw	<0.01	<0.01	101, 105
				1	6.4	107	--	25-May-2011	BBCH 45	70#	Grain	<0.01	<0.01	93, 94
										70#	Straw	<0.01	<0.01	101, 105

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-8 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in spring wheat (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details						Residues found <sup>a</sup>					
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
CEMS-4719F CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Sarina	Spain SZ Outdoor (field)	GF- 2573	1	6.0	379	--	30-Apr-2010	BBCH 32	88	Grain	--	--	--
										88	Straw	--	--	--
				1	5.8	367	--	18-May-2010	BBCH 39	63	Grain	<0.01	<0.01	104, 102
										63	Straw	<0.01	<0.01	111, 109
										70#	Grain	<0.01	<0.01	104, 102
										70#	Straw	<0.01	<0.01	111, 109
										77	Grain	<0.01	<0.01	104, 102
										77	Straw	<0.01	<0.01	111, 109
										84	Grain	<0.01	<0.01	104, 102
										84	Straw	<0.01	<0.01	111, 109
				1	6.1	386	--	21-May-2010	BBCH 45	60	Grain	<0.01	<0.01	104, 102
										60	Straw	<0.01	<0.01	111, 109
										67#	Grain	<0.01	<0.01	104, 102
										67#	Straw	<0.01	<0.01	111, 109
CEMS-4719G CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Cap Horn	Southern France SZ Outdoor (field)	GF- 2573	1	6.5	87	--	10-May-2010	BBCH 32	60#	Grain	--	--	--
										60#	Straw	--	--	--
				1	6.3	83	--	21-May-2010	BBCH 39	49#	Grain	<0.01	<0.01	104, 102
										49#	Straw	<0.01	<0.01	111, 109
				1	5.8	77	--	03-Jun-2010	BBCH 45	36#	Grain	<0.01	<0.01	104, 102

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
										36#	Straw	<0.01	<0.01	111, 109
CEMS-4719H CEMS-4719 DAS Ref. ID 101589 Y 2010	Spring Wheat / Amaretto	Greece SZ Outdoor (field)	GF- 2573	1	5.9	297	--	08-Apr-2010	BBCH 32	71# 71#	Grain Straw	-- --	-- --	-- --
				1	6.0	300	--	21-Apr-2010	BBCH 39	58# 58#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
				1	5.9	293	--	30-Apr-2010	BBCH 45	49# 49#	Grain Straw	<0.01 <0.01	<0.01 <0.01	104, 102 111, 109
CEMS-5001G CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Palesio	Italy SZ Outdoor (field)	GF- 2573	1	6.1	408	--	19-Apr-2011	BBCH 32	66# 66#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.6	440	--	28-Apr-2011	BBCH 39	57# 57#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.1	403	--	05-May-2011	BBCH 45	50# 50#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
CEMS-5001H CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Blasco	Italy SZ Outdoor (field)	GF- 2573	1	6.6	439	--	19-Apr-2011	BBCH 32	66# 66#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.0	397	--	28-Apr-2011	BBCH 39	57# 57#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
				1	6.1	404	--	05-May-2011	BBCH 45	50# 50#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105
CEMS-5001I CEMS-5001 DAS Ref. ID	Spring Wheat / Alcala	Spain SZ Outdoor	GF- 2573	1	6.8	114	--	12-Apr-2011	BBCH 32	78# 78#	Grain Straw	<0.01 <0.01	<0.01 <0.01	93, 94 101, 105

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ai/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl, Cloquintocet acid
110411 Y 2011		(field)		1	6.0	100	--	26-Apr-2011	BBCH 39	64#	Grain	<0.01	<0.01	93, 94
				1	6.1	101	--	28-Apr-2011	BBCH 45	62#	Grain	<0.01	<0.01	93, 94
CEMS-5001J CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Califa	Spain SZ Outdoor (field)	GF- 2573	1	6.4	106	--	07-Apr-2011	BBCH 32	89#	Grain	<0.01	<0.01	93, 94
				1	6.2	103	--	26-Apr-2011	BBCH 39	70#	Grain	<0.01	<0.01	93, 94
CEMS-5001L CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Claudio	Greece SZ Outdoor (field)	GF- 2573	1	5.7	382	--	06-Apr-2011	BBCH 32	84#	Grain	<0.01	<0.01	93, 94
				1	5.8	389	--	18-Apr-2011	BBCH 39	72#	Grain	<0.01	<0.01	93, 94
CEMS-5001M CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Gekora	Greece SZ Outdoor (field)	GF- 2573	1	6.1	404	--	05-Apr-2011	BBCH 32	72#	Grain	<0.01	<0.01	93, 94
				1	6.2	411	--	20-Apr-2011	BBCH 39	57#	Grain	<0.01	<0.01	93, 94
CEMS-5001M CEMS-5001 DAS Ref. ID 110411 Y 2011	Spring Wheat / Gekora	Greece SZ Outdoor (field)	GF- 2573	1	6.2	413	--	05-May-2011	BBCH 45	42#	Grain	<0.01	<0.01	93, 94

# = Normal Commercial Harvest



Table B.7.6-9 Summary of residues of XDE-729 Methyl and XDE-729 Acid in winter barley (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>					
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid			
CEMS-4553A CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Finesse	Germany NZ Outdoor (field)	GF- 2573	2	8.2	327	--	09-Dec-2009	BBCH 32	92	Grain	<0.01	<0.01	101, 95			
					6.3	317	--	20-Apr-2010		92	Straw	<0.01	<0.01	98, 94			
				2	7.4	298	--	09-Dec-2009	BBCH 39	0*	Whole plant	0.405	(0.004)	97, 92			
						5.9	294	--			10-May-2010	0- Whole plant	<0.01	<0.01	97, 92		
					5.9	294	--				0+ Whole plant	0.089	<0.01	97, 92			
											7 Whole plant	(0.006)	<0.01	97, 92			
											15 Whole plant	<0.01	<0.01	97, 92			
											28 Whole plant	<0.01	<0.01	97, 92			
											56 Whole plant	<0.01	<0.01	97, 92			
											72 Grain	<0.01	<0.01	101, 95			
											72 Straw	<0.01	<0.01	98, 94			
					2	7.3	292	--	09-Dec-2009	BBCH 49	0*	Whole plant	0.375	(0.003)	97, 92		
							6.1	304	--			18-May-2010	0- Whole plant	<0.01	<0.01	97, 92	
						6.1	304	--				0+ Whole plant	0.076	<0.01	97, 92		
												7 Whole plant	(0.006)	<0.01	97, 92		
												14 Whole plant	<0.01	<0.01	97, 92		
												28 Whole plant	<0.01	<0.01	97, 92		
												56 Whole plant	<0.01	<0.01	97, 92		
												64 Grain	<0.01	<0.01	101, 95		
												64 Straw	<0.01	<0.01	98, 94		
				1	6.2	309	--	18-May-2010	BBCH 49	0+ 7 14	Whole plant	0.122	<0.01	97, 92			
											Whole plant	(0.006)	<0.01	97, 92			
											Whole plant	<0.01	<0.01	97, 92			

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										28	Whole plant	<0.01	<0.01	97, 92
										56	Whole plant	<0.01	<0.01	97, 92
										64	Grain	<0.01	<0.01	101, 95
										64	Straw	<0.01	<0.01	98, 94
CEMS-4553B	Winter	Hungary	GF-	2	7.5	301	--	10-Dec-2009	BBCH 32	--	Grain	--	--	--
CEMS-4553	Barley /	NZ	2573		6.2	309	--	09-Apr-2010		--	Straw	--	--	--
DAS Ref. ID	Laverda	Outdoor		2	7.5	300	--	10-Dec-2009	BBCH 39	0*	Whole plant	0.457	(0.007)	97, 92
090119		(field)			6.0	301	--	30-Apr-2010		0-	Whole plant	<0.01	<0.01	97, 92
Y										0+	Whole plant	0.148	<0.01	97, 92
2009-2010										7	Whole plant	(0.006)	<0.01	97, 92
										14	Whole plant	<0.01	<0.01	97, 92
										28	Whole plant	<0.01	<0.01	97, 92
										56	Whole plant	<0.01	<0.01	97, 92
										--	Grain	--	--	--
										--	Straw	--	--	--
				2	7.7	308	--	10-Dec-2009	BBCH 45	0*	Whole plant	0.537	(0.008)	97, 92
					6.0	301	--	07-May-2010		0-	Whole plant	<0.01	<0.01	97, 92
										0+	Whole plant	0.075	<0.01	97, 92
										7	Whole plant	(0.004)	<0.01	97, 92
										14	Whole plant	<0.01	<0.01	97, 92
										28	Whole plant	<0.01	<0.01	97, 92
										56	Grain	<0.01	<0.01	101, 95
										56	Straw	<0.01	<0.01	98, 94
				1	6.1	304	--	07-May-2010	BBCH 45	0	Whole plant	0.049	(0.003)	97, 92
										7	Whole plant	(0.006)	<0.01	97, 92

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										14 28 56 56	Whole plant Whole plant Grain Straw	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	97, 92 97, 92 101, 95 98, 94
CEMS-4553E CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Souleyka	Germany NZ Outdoor (field)	GF- 2573	2	8.2 6.7	327 337	-- --	09-Dec-2009 27-Apr-2010	BBCH 32	76 76	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.7 6.5	310 327	-- --	09-Dec-2009 18-May-2010	BBCH 39	62 62	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.7 6.1	307 307	-- --	09-Dec-2009 19-May-2010	BBCH 45	54 54	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				1	6.9	343	--	19-May-2010	BBCH 45	54 54	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
CEMS-4553F CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Hymalaya	France NZ Outdoor (field)	GF- 2573	2	7.7 6.3	307 317	-- --	31-Dec-2009 09-Apr-2010	BBCH 32	90 90	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.4 6.2	297 317	-- --	31-Dec-2009 28-Apr-2010	BBCH 39	71 71	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.7 6.2	310 310	-- --	31-Dec-2009 04-May-2010	BBCH 45	65 65	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
					5.8	290	--	04-May-2010	BBCH 45	65 65	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94

WARNING: This document forms part of an evaluation data package and should not be read or used for registration. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4890A CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Souleyka	Germany NZ Outdoor (field)	GF- 2573	2	8.6	115	--	25-Nov-2010	BBCH 32	87	Grain	<0.01	<0.01	106, 100
					6.6	110	--	15-Apr-2011		87	Straw	<0.01	<0.01	92, 90
				2	8.1	108	--	25-Nov-2010	BBCH 39	0*	Whole Plant	1.305	0.016	100, 96
					6.1	102	--	29-Apr-2011		0-	Whole Plant	<0.01	<0.01	100, 96
										0+	Whole Plant	0.261	(0.004)	100, 96
										7	Whole Plant	0.020	<0.01	100, 96
										14	Whole Plant	(0.004)	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										59	Whole Plant	<0.01	<0.01	100, 96
										73	Grain	<0.01	<0.01	106, 100
										73	Straw	<0.01	<0.01	92, 90
				2	8.0	106	--	25-Nov-2010	BBCH 45	0*	Whole Plant	1.306	0.019	100, 96
					6.1	102	--	03-May-2011		0-	Whole Plant	<0.01	<0.01	100, 96
										0+	Whole Plant	0.206	<0.01	100, 96
										7	Whole Plant	(0.009)	<0.01	100, 96
										14	Whole Plant	(0.004)	<0.01	100, 96
										28	Whole Plant	(0.003)	<0.01	100, 96
										56	Whole Plant	<0.01	<0.01	100, 96
										69	Grain	<0.01	<0.01	106, 100
				1					BBCH 45	69	Straw	<0.01	<0.01	92, 90
					6.1	101	--	03-May-2011		0+	Whole Plant	0.236	<0.01	100, 96
										7	Whole Plant	0.015	<0.01	100, 96
										14	Whole Plant	(0.005)	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										56	Whole Plant	<0.01	<0.01	100, 96
										69	Grain	<0.01	<0.01	106, 100

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registrants must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										69	Straw	<0.01	<0.01	92, 90
CEMS-4890C	Winter	Hungary	GF-	2	7.5	402	--	08-Dec-2010	BBCH 32	99	Grain	<0.01	<0.01	106, 100
CEMS-4890	Barley /	NZ	2573		7.8	415	--	18-Apr-2011		99	Straw	<0.01	<0.01	92, 90
DAS Ref. ID	Nelly	Outdoor		2	7.3	392	--	08-Dec-2010	BBCH 39	81	Grain	<0.01	<0.01	106, 100
102083		(field)			6.1	407	--	06-May-2011		81	Straw	<0.01	<0.01	92, 90
Y				2	7.7	412	--	08-Dec-2010	BBCH 45	70	Grain	<0.01	<0.01	106, 100
2010-2011					5.6	373	--	17-May-2011		70	Straw	<0.01	<0.01	92, 90
				1	5.9	392	--	17-May-2011	BBCH 45	70	Grain	<0.01	<0.01	106, 100
										70	Straw	<0.01	<0.01	92, 90
CEMS-4890D	Winter	France	GF-	2	8.0	429	--	10-Jan-2011	BBCH 32	83	Grain	<0.01	<0.01	106, 100
CEMS-4890	Barley /	NZ	2573		6.5	433	--	06-Apr-2011		83	Straw	<0.01	<0.01	92, 90
DAS Ref. ID	Malicorne	Outdoor		2	8.0	427	--	10-Jan-2011	BBCH 39	61	Grain	<0.01	<0.01	106, 100
102083		(field)			6.0	399	--	28-Apr-2011		61	Straw	<0.01	<0.01	92, 90
Y				2	7.5	398	--	10-Jan-2011	BBCH 57	57	Grain	<0.01	<0.01	106, 100
2011					6.4	427	--	02-May-2011		57	Straw	<0.01	<0.01	92, 90
				1	6.0	400	--	02-May-2011	BBCH 57	57	Grain	<0.01	<0.01	106, 100
										57	Straw	<0.01	<0.01	92, 90
CEMS-4890E	Winter	Germany	GF-	2	8.8	118	--	25-Nov-2010	BBCH 32	71	Grain	<0.01	<0.01	106, 100
CEMS-4890	Barley /	NZ	2573		6.5	108	--	26-Apr-2011		71	Straw	<0.01	<0.01	92, 90
DAS Ref. ID	Highlight	Outdoor		2	8.8	118	--	25-Nov-2010	BBCH 39	61	Grain	<0.01	<0.01	106, 100
102083		(field)			6.3	105	--	06-May-2011		61	Straw	<0.01	<0.01	92, 90
Y														

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
2010-2011				2	8.6 6.0	115 100	-- --	25-Nov-2010 10-May-2011	BBCH 45- 49	57 57	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
CEMS-4890F CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Lomerit	Poland NZ Outdoor (field)	GF- 2573	2	8.1 6.5	433 433	-- --	06-Dec-2010 27-Apr-2011	BBCH 32	70 70	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	7.8 6.5	413 430	-- --	06-Dec-2010 10-May-2011	BBCH 39	57 57	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	7.6 6.4	407 428	-- --	06-Dec-2010 16-May-2011	BBCH 45	51 51	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				1	6.2	413	--	16-May-2011	BBCH 45	51 51	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
CEMS-4890G CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Cassata	United Kingdom NZ Outdoor (field)	GF- 2573	2	8.6 6.4	115 107	-- --	15-Dec-2010 20-Apr-2011	BBCH 32	96 96	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	8.4 5.4	111 90	-- --	15-Dec-2010 04-May-2011	BBCH 39	82 82	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	8.4 6.4	111 107	-- --	15-Dec-2010 11-May-2011	BBCH 45	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				1	6.4	107	--	11-May-2011	BBCH 45	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90

WARNING: This document forms part of an MRL evaluation data package and should not be released for public consultation without the approval of the responsible authority. This document must not be quoted on the basis of this document.

Table B.7.6-10 Summary of residues of XDE-729 Methyl and XDE-729 Acid in winter barley (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4553C CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Demetra	Greece SZ Outdoor (field)	GF- 2573	2	7.6	305	--	30-Dec-2009	BBCH 32	127	Grain	<0.01	<0.01	101, 95
					6.1	307	--	23-Feb-2010		127	Straw	<0.01	<0.01	98, 94
				2	7.2	288	--	30-Dec-2009	BBCH 39	0*	Whole plant	0.394	(0.008)	97, 92
							--	07-Apr-2010		0-	Whole plant	<0.01	<0.01	97, 92
					5.9	296	--			0+	Whole plant	0.185	<0.01	97, 92
							--			7	Whole plant	0.010	<0.01	97, 92
							--			14	Whole plant	(0.005)	<0.01	97, 92
							--			28	Whole plant	(0.004)	<0.01	97, 92
							--			56	Whole plant	<0.01	<0.01	97, 92
							--			84	Grain	<0.01	<0.01	101, 95
							--			84	Straw	<0.01	<0.01	98, 94
				2	7.7	308	--	30-Dec-2009	BBCH 45	0*	Whole plant	0.621	0.012	97, 92
					6.0	299	--	14-Apr-2010		0-	Whole plant	<0.01	<0.01	97, 92
							--			0+	Whole plant	0.153	<0.01	97, 92
							--			7	Whole plant	0.010	<0.01	97, 92
							--			14	Whole plant	(0.007)	<0.01	97, 92
							--			28	Whole plant	(0.006)	(0.003)	97, 92
							--			60	Whole plant	<0.01	<0.01	97, 92
							--			77	Grain	<0.01	<0.01	101, 95
							--			77	Straw	<0.01	<0.01	98, 94
				1	6.0	300	--	14-Apr-2010	BBCH 45	0+	Whole plant	0.163	<0.01	97, 92
							--			7	Whole plant	(0.010)	<0.01	97, 92
							--			14	Whole plant	(0.009)	(0.004)	97, 92
							--			28	Whole plant	(0.007)	(0.007)	97, 92

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										60 77 77	Whole plant Grain Straw	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	97, 92 101, 95 98, 94
CEMS-4553D CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / County	France SZ Outdoor (field)	GF- 2573	2	7.2 6.0	290 299	-- --	17-Dec-2009 02-Apr-2010	BBCH 32	102 102	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.3 6.0	291 299	-- --	17-Dec-2009 11-May-2010	BBCH 45- 51	0* 0- 0+ 7 14 28 56 63 63	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.801 <0.01 0.175 0.049 0.048 0.033 0.019 (0.005) 0.029	(0.005) <0.01 <0.01 (0.007) (0.008) 0.018 0.011 (0.003) 0.021	97, 92 97, 92 97, 92 97, 92 97, 92 97, 92 101, 95 98, 94
				2	6.8 6.1	279 303	-- --	17-Dec-2009 11-May-2010	BBCH 45- 51	0* 0- 0+ 7 14 28 56 63 63	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw	0.888 <0.01 0.206 0.081 0.054 0.077 0.025 (0.005) <u>0.022</u>	(0.006) <0.01 (0.004) 0.014 (0.010) 0.029 0.015 (0.004) <u>0.016</u>	97, 92 97, 92 97, 92 97, 92 97, 92 97, 92 101, 95 98, 94
					6.0	298	--	11-May-2010	BBCH 45- 51	0 7 14	Whole plant Whole plant Whole plant	0.181 0.050 0.041	<0.01 (0.008) (0.006)	97, 92 97, 92 97, 92

WARNING: This document forms part of an EC evaluation package and should not be relied upon for isolation registration must not be quoted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										28 56 63 63	Whole plant Whole plant Grain Straw	0.045 0.015 (0.004) 0.028	0.023 0.012 (0.004) 0.026	97, 92 97, 92 101, 95 98, 94
CEMS-4553G CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Persefoni	Greece SZ Outdoor (field)	GF- 2573	2	7.6 6.1	305 307	-- --	30-Dec-2009 01-Mar-2010	BBCH 32	119 119	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.4 5.9	295 293	-- --	30-Dec-2009 07-Apr-2010	BBCH 39	82 82	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	7.7 6.1	310 307	-- --	30-Dec-2009 14-Apr-2010	BBCH 45	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				1	5.9	293	--	14-Apr-2010	BBCH 45	75 75	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
CEMS-4553H CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Cascador	Bulgaria SZ Outdoor (field)	GF- 2573	2	7.1 6.5	282 324	-- --	24-Nov-2009 10-Apr-2010	BBCH 32	73 73	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94
				2	8.1 6.0	322 298	-- --	24-Nov-2009 29-Apr-2010	BBCH 39	54 54	Grain Straw	<0.01 <0.01	<0.01 (0.005)	101, 95 98, 94
				2	8.2 6.1	327 304	-- --	24-Nov-2009 03-May-2010	BBCH 45	50 50	Grain Straw	<0.01 <0.01	<0.01 (0.005)	101, 95 98, 94
				1	5.8	289	--	03-May-2010	BBCH 45	50 50	Grain Straw	<0.01 <0.01	<0.01 (0.005)	101, 95 98, 94
CEMS-4890H CEMS-4890	Winter Barley /	Bulgaria SZ	GF- 2573	2	7.3 6.3	389 418	-- --	30-Nov-2010 10-Apr-2011	BBCH 32	76 76	Grain Straw	<0.01 <0.01	<0.01 <0.01	101, 95 98, 94

WARNING: This document forms part of the C evaluation data package and should not be used for registration must not be quoted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
DAS Ref. ID 102083 Y 2010-2011	Vanessa	Outdoor (field)		2	7.2	386	--	30- Nov-2010	BBCH 39	0*	Whole Plant	0.338	(0.004)	100, 96
					6.2	410	--	30-Apr-2011		0-	Whole Plant	<0.01	<0.01	100, 96
										0+	Whole Plant	0.134	<0.01	100, 96
										7	Whole Plant	(0.006)	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
				2	7.2	383	--	30- Nov-2010	BBCH 45	0*	Whole Plant	0.295	(0.005)	100, 96
					5.5	368	--	07-May-2011		0-	Whole Plant	<0.01	<0.01	100, 96
										0+	Whole Plant	0.119	<0.01	100, 96
										7	Whole Plant	(0.005)	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
				1	5.8	390	--	07-May-2011	BBCH 45	49	Grain	<0.01	<0.01	101, 95
										49	Straw	<0.01	<0.01	98, 94
										0+	Whole Plant	0.141	<0.01	100, 96
										7	Whole Plant	(0.005)	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										49	Grain	<0.01	<0.01	101, 95
										49	Straw	<0.01	<0.01	98, 94
CEMS-4890I	Winter Barley / Graphic	Spain SZ Outdoor (field)	GF- 2573	2	8.2	109	--	21-Dec-2010	BBCH 32	84	Grain	<0.01	<0.01	101, 95
CEMS-4890					6.4	107	--	09-Mar-2011		84	Straw	<0.01	<0.01	98, 94
DAS Ref. ID 102083				2	7.1	95	--	21-Dec-2010	BBCH 39	0*	Whole Plant	0.993	0.013	100, 96
Y					6.0	100	--	23-Mar-2011		0-	Whole Plant	<0.01	<0.01	100, 96

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registrants must not be quoted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
2010-2011				2	7.1 5.6	95 93	-- --	21-Dec-2010 30-Mar-2011	BBCH 45	0+	Whole Plant	0.217	<0.01	100, 96
										7	Whole Plant	<0.01	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										58	Whole Plant	<0.01	<0.01	100, 96
										70	Grain	<0.01	<0.01	101, 95
										70	Straw	<0.01	<0.01	98, 94
										0*	Whole Plant	0.904	0.012	100, 96
										0-	Whole Plant	<0.01	<0.01	100, 96
										0+	Whole Plant	0.089	<0.01	100, 96
										7	Whole Plant	(0.006)	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										51	Whole Plant	<0.01	<0.01	100, 96
										63	Grain	<0.01	<0.01	101, 95
										63	Straw	(0.003)	<0.01	98, 94
				1	5.6	93	--	30-Mar-2011	BBCH 45	0+	Whole Plant	0.188	<0.01	100, 96
										7	Whole Plant	(0.004)	<0.01	100, 96
										14	Whole Plant	<0.01	<0.01	100, 96
										28	Whole Plant	<0.01	<0.01	100, 96
										51	Whole Plant	<0.01	<0.01	100, 96
										63	Grain	<0.01	<0.01	101, 95
										63	Straw	(0.003)	<0.01	98, 94
CEMS-4890J	Winter	Spain	GF-	2	7.4	98	--	20-Dec-2010	BBCH 31-	109	Grain	<0.01	<0.01	106, 100
CEMS-4890	Barley /	SZ	2573		6.4	107	--	11-Mar-2011	32	109	Straw	<0.01	<0.01	92, 90
DAS Ref. ID	Archipel	Outdoor		2	8.1	108	--	20-Dec-2010		76	Grain	<0.01	<0.01	106, 100
102083		(field)			5.8	97	--	13-Apr-2011	BBCH 39	76	Straw	<0.01	<0.01	92, 90
Y														

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
2010-2011				2	7.6 6.4	101 107	-- --	20-Dec-2010 18-Apr-2011	BBCH 45	71 71	Grain Straw	<0.01 (0.004)	<0.01 <0.01	106, 100 92, 90
				1	5.8	97	--	18-Apr-2011	BBCH 45	71 71	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
CEMS-4890K CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Obzor	Bulgaria SZ Outdoor (field)	GF- 2573	2	8.1 6.3	108 104	-- --	07-Dec-2010 11-Apr-2011	BBCH 32	73 73	Grain Straw	<0.01 (0.004)	<0.01 (0.006)	106, 100 92, 90
				2	8.0 6.1	106 102	-- --	07-Dec-2010 21-Apr-2011	BBCH 39	63 63	Grain Straw	<0.01 (0.009)	<0.01 (0.005)	106, 100 92, 90
				2	7.5 6.1	99 102	-- --	07-Dec-2010 01-May-2011	BBCH 45	53 53	Grain Straw	<0.01 (0.007)	<0.01 (0.003)	106, 100 92, 90
				1	5.7	96	--	01-May-2011	BBCH 45	53 53	Grain Straw	<0.01 (0.006)	<0.01 <0.01	106, 100 92, 90
CEMS-4890L CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Azurel	France SZ Outdoor (field)	GF- 2573	2	7.7 6.5	410 433	-- --	08-Dec-2010 04-Apr-2011	BBCH 32	73 73	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	7.9 6.5	420 430	-- --	08-Dec-2010 14-Apr-2011	BBCH 39	63 63	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				2	7.9 6.1	423 407	-- --	08-Dec-2010 20-Apr-2011	BBCH 45	57 57	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
				1	5.8	387	--	20-Apr-2011	BBCH 45	57 57	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90
CEMS-4890M CEMS-4890	Winter Barley /	Greece SZ	GF- 2573	2	7.6 6.2	404 413	-- --	27-Dec-2010 22-Mar-2011	BBCH 32	97 97	Grain Straw	<0.01 <0.01	<0.01 <0.01	106, 100 92, 90

WARNING: This document forms part of an EC evaluation package and should not be read or used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
DAS Ref. ID 102083 Y 2010-2011	Demetra	Outdoor (field)		2	7.4	393	--	27-Dec-2010	BBCH 39	73	Grain	<0.01	<0.01	106, 100
					5.8	389	--	15-Apr-2011		73	Straw	<0.01	<0.01	92, 90
				2	7.5	402	--	27-Dec-2010	BBCH 45	59	Grain	<0.01	<0.01	106, 100
					5.9	391	--	29-Apr-2011		59	Straw	<0.01	<0.01	92, 90
				1	5.7	382	--	29-Apr-2011	BBCH 45	59	Grain	<0.01	<0.01	106, 100
										59	Straw	(0.005)	<0.01	92, 90
CEMS-4890N CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Atomo	Italy SZ Outdoor (field)	GF- 2573	2	8.2	437	--	06-Dec-2010	BBCH 31-	86	Grain	<0.01	<0.01	106, 100
					6.2	413	--	23-Mar-2011	32	86	Straw	<0.01	<0.01	92, 90
				2	7.6	403	--	06-Dec-2010		63	Grain	<0.01	<0.01	106, 100
					6.3	420	--	15-Apr-2011	BBCH 39	63	Straw	<0.01	<0.01	92, 90
				2	7.9	423	--	06-Dec-2010		56	Grain	<0.01	<0.01	106, 100
					6.3	420	--	22-Apr-2011	BBCH 45	56	Straw	<0.01	<0.01	92, 90
				1	6.3	417	--	22-Apr-2011		56	Grain	<0.01	<0.01	106, 100
									BBCH 45	56	Straw	<0.01	<0.01	92, 90

\* = Sampled immediately after application no. 1.

0- = Sampled immediately before application no. 2

0+ = Sampled immediately after application no. 2

<sup>a</sup> Limit of Quantitation (LOQ) = 0.01 mg/kg; Limit of Detection (LOD) = 0.003 mg/kg. Residue values equal to or greater than the LOD, but less than the LOQ are displayed within parenthesis.

Table B.7.6-11 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in winter barley (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (day s)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4553A CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Finesse	Germany NZ Outdoor (field)	GF- 2573	2	8.2	327	--	09-Dec-2009	BBCH 32	92	Grain	--	--	--
					6.3	317	--	20-Apr-2010		92	Straw	--	--	--
				2	7.4	298	--	09-Dec-2009	BBCH 39	72	Grain	<0.01	<0.01	106, 107
					5.9	294	--	10-May-2010		72	Straw	<0.01	<0.01	104, 99
				2	7.3	292	--	09-Dec-2009	BBCH 49	64	Grain	<0.01	<0.01	106, 107
					6.1	304	--	18-May-2010		64	Straw	<0.01	<0.01	104, 99
				1	6.2	309	--	18-May-2010	BBCH 49	64	Grain	<0.01	<0.01	106, 107
										64	Straw	<0.01	<0.01	104, 99
CEMS-4553B CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Laverda	Hungary NZ Outdoor (field)	GF- 2573	2	7.5	301	--	10-Dec-2009	BBCH 32	--	Grain	--	--	--
					6.2	309	--	09-Apr-2010		--	Straw	--	--	--
				2	7.5	306	--	10-Dec-2009	BBCH 39	--	Grain	--	--	--
					6.0	301	--	30-Apr-2010		--	Straw	--	--	--
				2	7.7	308	--	10-Dec-2009	BBCH 45	56	Grain	<0.01	<0.01	106, 107
					6.0	301	--	07-May-2010		56	Straw	<0.01	<0.01	104, 99
				1	6.1	304	--	07-May-2010	BBCH 45	56	Grain	<0.01	<0.01	106, 107
										56	Straw	<0.01	<0.01	104, 99

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4553E CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Souleyka	Germany NZ Outdoor (field)	GF- 2573	2	8.2	327	--	09-Dec-2009	BBCH 32	76	Grain	--	--	--
					6.7	337	--	27-Apr-2010		76	Straw	--	--	--
				2	7.7	310	--	09-Dec-2009	BBCH 39	62	Grain	<0.01	<0.01	106, 107
					6.5	327	--	11-May 2010		62	Straw	<0.01	<0.01	104, 99
				2	7.7	307	--	09-Dec-2009	BBCH 45	54	Grain	<0.01	<0.01	106, 107
					6.1	307	--	19-May-2010		54	Straw	<0.01	<0.01	104, 99
				1	6.9	343	--	19-May-2010	BBCH 45	54	Grain	<0.01	<0.01	106, 107
										54	Straw	<0.01	<0.01	104, 99
CEMS-4553F CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Hymalaya	France NZ Outdoor (field)	GF- 2573	2	7.7	307	--	31-Dec-2009	BBCH 32	90	Grain	--	--	--
					6.3	317	--	09-Apr-2010		90	Straw	--	--	--
				2	7.4	297	--	31-Dec-2009	BBCH 39	71	Grain	<0.01	<0.01	106, 107
					6.3	317	--	28-Apr-2010		71	Straw	<0.01	<0.01	104, 99
				2	7.7	310	--	31-Dec-2009	BBCH 45	65	Grain	<0.01	<0.01	106, 107
					6.2	310	--	04-May-2010		65	Straw	<0.01	<0.01	104, 99
				1	5.8	290	--	04-May-2010	BBCH 45	65	Grain	<0.01	<0.01	106, 107
										65	Straw	<0.01	<0.01	104, 99

WARNING: This document forms part of an EC evaluation data package and should not be used for isolation/registration, must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4890A CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Souleyka	Germany NZ Outdoor (field)	GF- 2573	2	8.6	115	--	25-Nov-2010	BBCH 32	87	Grain	--	--	76, 74
					6.6	110	--	15-Apr-2011		87	Straw	--	--	77, 75
				2	8.1	108	--	25-Nov-2010	BBCH 39	73	Grain	<0.01	<0.01	76, 74
					6.1	102	--	29-Apr-2011		73	Straw	<0.01	<0.01	77, 75
				2	8.0	106	--	25-Nov-2010	BBCH 45	69	Grain	<0.01	<0.01	76, 74
					6.1	102	--	03-May-2011		69	Straw	<0.01	<0.01	77, 75
				1	6.1	101	--	03-May-2011	BBCH 45	69	Grain	<0.01	<0.01	76, 74
										69	Straw	<0.01	<0.01	77, 75
CEMS-4890C CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Nelly	Hungary NZ Outdoor (field)	GF- 2573	2	7.5	402	--	08-Dec-2010	BBCH 32	99	Grain	--	--	76, 74
					7.8	415	--	18-Apr-2011		99	Straw	--	--	77, 75
				2	7.3	392	--	08-Dec-2010	BBCH 39	81	Grain	<0.01	<0.01	76, 74
					6.1	407	--	06-May-2011		81	Straw	<0.01	<0.01	77, 75
				2	7.7	412	--	08-Dec-2010	BBCH 45	70	Grain	<0.01	<0.01	76, 74
					5.6	375	--	17-May-2011		70	Straw	<0.01	<0.01	77, 75
				1	5.9	392	--	17-May-2011	BBCH 45	70	Grain	<0.01	<0.01	76, 74
										70	Straw	<0.01	<0.01	77, 75

WARNING: This document forms part of an EC evaluation data package and should not be used for registration. No isolation or registration must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4890D CEMS-4890 DAS Ref. ID 102083 Y 2011	Winter Barley / Malicorne	France NZ Outdoor (field)	GF- 2573	2	8.0	429	--	10-Jan-2011	BBCH 32	83	Grain	--	--	76, 74
					6.5	433	--	06-Apr-2011		83	Straw	--	--	77, 75
				2	8.0	427	--	10-Jan-2011	BBCH 39	61	Grain	<0.01	<0.01	76, 74
					6.0	399	--	28-Apr-2011		61	Straw	<0.01	<0.01	77, 75
				2	7.5	398	--	10-Jan-2011	BBCH 57	57	Grain	<0.01	<0.01	76, 74
					6.4	427	--	02-May-2011		57	Straw	<0.01	<0.01	77, 75
				1	6.0	400	--	02-May-2011	BBCH 57	57	Grain	<0.01	<0.01	76, 74
										57	Straw	<0.01	<0.01	77, 75
CEMS-4890E CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Highlight	Germany NZ Outdoor (field)	GF- 2573	2	8.8	118	--	25-Nov-2010	BBCH 32	71	Grain	--	--	76, 74
					6.5	108	--	26-Apr-2011		71	Straw	--	--	77, 75
				2	8.8	118	--	25-Nov-2010	BBCH 39	61	Grain	<0.01	<0.01	76, 74
					6.3	105	--	06-May-2011		61	Straw	<0.01	<0.01	77, 75
				2	8.6	115	--	25-Nov-2010	BBCH 45-	57	Grain	<0.01	<0.01	76, 74
					6.0	100	--	10-May-2011	49	57	Straw	<0.01	<0.01	77, 75

WARNING: This document forms part of an EC evaluation data package and should not be used for isolation or registration. It must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4890F CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Lomerit	Poland NZ Outdoor (field)	GF- 2573	2	8.1	433	--	06-Dec-2010	BBCH 32	70	Grain	--	--	76, 74
					6.5	433	--	27-Apr-2011		70	Straw	--	--	77, 75
				2	7.8	413	--	06-Dec-2010	BBCH 39	57	Grain	<0.01	<0.01	76, 74
					6.5	430	--	10-May-2011		57	Straw	<0.01	<0.01	77, 75
				2	7.6	407	--	06-Dec-2010	BBCH 45	51	Grain	<0.01	<0.01	76, 74
					6.4	428	--	16-May-2011		51	Straw	<0.01	<0.01	77, 75
				1	6.2	413	--	16-May-2011	BBCH 45	51	Grain	<0.01	<0.01	76, 74
										51	Straw	<0.01	<0.01	77, 75
CEMS-4890G CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Cassata	United Kingdom NZ Outdoor (field)	GF- 2573	2	8.6	115	--	15-Dec-2010	BBCH 32	96	Grain	--	--	76, 74
					6.4	107	--	20-Apr-2011		96	Straw	--	--	77, 75
				2	8.4	111	--	15-Dec-2010	BBCH 39	82	Grain	<0.01	<0.01	76, 74
					5.4	90	--	04-May-2011		82	Straw	<0.01	<0.01	77, 75
				2	8.4	111	--	15-Dec-2010	BBCH 45	75	Grain	<0.01	<0.01	76, 74
					6.4	107	--	11-May-2011		75	Straw	<0.01	<0.01	77, 75
				1	6.4	107	--	11-May-2011	BBCH 45	75	Grain	<0.01	<0.01	76, 74
										75	Straw	<0.01	<0.01	77, 75

WARNING: This document forms part of an EC evaluation data package and should not be made available to the public. Registration must not be granted on the basis of this document.

Table B.7.6-12 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in winter barley (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4553C CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Demetra	Greece SZ Outdoor (field)	GF-2573	2	7.6	305	--	30-Dec-2009	BBCH 32	127	Grain	--	--	--
					6.1	307	--	23-Feb-2010		127	Straw	--	--	--
				2	7.2	288	--	30-Dec-2009	BBCH 39	84	Grain	<0.01	<0.01	106, 107
					5.9	296	--	07-Apr-2010		84	Straw	<0.01	<0.01	104, 99
				2	7.7	308	--	30-Dec-2009	BBCH 45	77	Grain	<0.01	<0.01	106, 107
					6.0	299	--	14-Apr-2010		77	Straw	<0.01	<0.01	104, 99
				1	6.0	300	--	14-Apr-2010	BBCH 45	77	Grain	<0.01	<0.01	106, 107
										77	Straw	<0.01	<0.01	104, 99
CEMS-4553D CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / County	France SZ Outdoor (field)	GF-2573	2	7.2	290	--	17-Dec-2009	BBCH 32	102	Grain	--	--	--
					6.0	299	--	02-Apr-2010		102	Straw	--	--	--
				2	7.3	299	--	17-Dec-2009	BBCH 45-51	63	Grain	<0.01	<0.01	106, 107
					6.0	299	--	11-May-2010		63	Straw	<0.01	<0.01	104, 99
				2	6.8	272	--	17-Dec-2009	BBCH 45-51	63	Grain	<0.01	<0.01	106, 107
					6.1	303	--	11-May-2010	BBCH 45-51	63	Straw	<0.01	<0.01	104, 99
				1	6.0	298	--	11-May-2010		63	Grain	<0.01	<0.01	106, 107
										63	Straw	<0.01	<0.01	104, 99

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4553G CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Persefoni	Greece SZ Outdoor (field)	GF- 2573	2	7.6	305	--	30-Dec-2009	BBCH 32	119	Grain	--	--	--
					6.1	307	--	01-Mar-2010		119	Straw	--	--	--
				2	7.4	295	--	30-Dec-2009	BBCH 39	82	Grain	<0.01	<0.01	106, 107
					5.9	293	--	07-Apr-2010		82	Straw	<0.01	<0.01	104, 99
				2	7.7	310	--	30-Dec-2009	BBCH 45	75	Grain	<0.01	<0.01	106, 107
					6.1	307	--	14-Apr-2010		75	Straw	<0.01	<0.01	104, 99
				1	5.9	293	--	14-Apr-2010	BBCH 45	75	Grain	<0.01	<0.01	106, 107
										75	Straw	<0.01	<0.01	104, 99
CEMS-4553H CEMS-4553 DAS Ref. ID 090119 Y 2009-2010	Winter Barley / Cascador	Bulgaria SZ Outdoor (field)	GF- 2573	2	7.1	282	--	24-Nov-2009	BBCH 32	73	Grain	--	--	--
					6.5	324	--	10-Apr-2010		73	Straw	--	--	--
				2	8.1	322	--	24-Nov-2009	BBCH 39	54	Grain	<0.01	<0.01	106, 107
					6.0	298	--	29-Apr-2010		54	Straw	<0.01	<0.01	104, 99
				2	8.2	327	--	24-Nov-2009	BBCH 45	50	Grain	<0.01	<0.01	106, 107
					6.1	304	--	03-May-2010		50	Straw	<0.01	<0.01	104, 99
				1	5.8	289	--	03-May-2010	BBCH 45	50	Grain	<0.01	<0.01	106, 107
										50	Straw	<0.01	<0.01	104, 99

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4890H CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Vanesa	Bulgaria SZ Outdoor (field)	GF- 2573	2	7.3	389	--	30- Nov-2010	BBCH 32	76	Grain	--	--	76, 74
					6.3	418	--	10-Apr-2011		76	Straw	--	--	77, 75
				2	7.2	386	--	30- Nov-2010	BBCH 39	56	Grain	<0.01	<0.01	76, 74
					6.2	410	--	30-Apr-2011		56	Straw	<0.01	<0.01	77, 75
				2	7.2	383	--	30- Nov-2010	BBCH 45	49	Grain	<0.01	<0.01	76, 74
					5.5	368	--	07-May-2011		49	Straw	<0.01	<0.01	77, 75
				1	5.8	390	--	07-May-2011	BBCH 45	49	Grain	<0.01	<0.01	76, 74
										49	Straw	<0.01	<0.01	77, 75
CEMS-4890I CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Graphic	Spain SZ Outdoor (field)	GF- 2573	2	8.2	109	--	21-Dec-2010	BBCH 32	84	Grain	--	--	76, 74
					6.4	107	--	09-Mar-2011		84	Straw	--	--	77, 75
				2	7.1	95	--	21-Dec-2010	BBCH 39	70	Grain	<0.01	<0.01	76, 74
					6.0	100	--	23-Mar-2011		70	Straw	<0.01	<0.01	77, 75
				2	7.1	95	--	21-Dec-2010	BBCH 45	63	Grain	<0.01	<0.01	76, 74
					5.6	93	--	30-Mar-2011		63	Straw	<0.01	<0.01	77, 75
				1	5.6	93	--	30-Mar-2011	BBCH 45	63	Grain	<0.01	<0.01	76, 74
										63	Straw	<0.01	<0.01	77, 75

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4890J CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Archipel	Spain SZ Outdoor (field)	GF- 2573	2	7.4	98	--	20-Dec-2010	BBCH 31	109	Grain	--	--	76, 74
					6.4	107	--	11-Mar-2011		109	Straw	--	--	77, 75
				2	8.1	108	--	20-Dec-2010	BBCH 39	76	Grain	<0.01	<0.01	76, 74
					5.8	97	--	13-Apr-2011		76	Straw	<0.01	<0.01	77, 75
				2	7.6	101	--	20-Dec-2010	BBCH 45	71	Grain	<0.01	<0.01	76, 74
					6.4	107	--	18-Apr-2011		71	Straw	<0.01	<0.01	77, 75
				1	5.8	97	--	18-Apr-2011	BBCH 45	71	Grain	<0.01	<0.01	76, 74
										71	Straw	<0.01	<0.01	77, 75
CEMS-4890K CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Obzor	Bulgaria SZ Outdoor (field)	GF- 2573	2	8.1	108	--	07-Dec-2010	BBCH 32	73	Grain	--	--	76, 74
					6.3	104	--	11-Apr-2011		73	Straw	--	--	77, 75
				2	8.0	106	--	07-Dec-2010	BBCH 39	63	Grain	<0.01	<0.01	76, 74
					6.1	102	--	21-Apr-2011		63	Straw	<0.01	<0.01	77, 75
				2	7.5	99	--	07-Dec-2010	BBCH 45	53	Grain	<0.01	<0.01	76, 74
					6.1	102	--	01-May-2011		53	Straw	<0.01	<0.01	77, 75
				1	5.7	96	--	01-May-2011	BBCH 45	53	Grain	<0.01	<0.01	76, 74
										53	Straw	<0.01	<0.01	77, 75

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be claimed on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4890L CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Azurel	France SZ Outdoor (field)	GF- 2573	2	7.7	410	--	08-Dec-2010	BBCH 32	73	Grain	--	--	76, 74
					6.5	433	--	04-Apr-2011		73	Straw	--	--	77, 75
				2	7.9	420	--	08-Dec-2010	BBCH 39	63	Grain	<0.01	<0.01	76, 74
					6.5	430	--	14-Apr-2011		63	Straw	<0.01	<0.01	77, 75
				2	7.9	423	--	08-Dec-2010	BBCH 45	57	Grain	<0.01	<0.01	76, 74
					6.1	407	--	20-Apr-2011		57	Straw	<0.01	<0.01	77, 75
				1	5.8	387	--	20-Apr-2011	BBCH 45	57	Grain	<0.01	<0.01	76, 74
										57	Straw	<0.01	<0.01	77, 75
CEMS-4890M CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Demetra	Greece SZ Outdoor (field)	GF- 2573	2	7.6	404	--	27-Dec-2010	BBCH 32	97	Grain	--	--	76, 74
					6.2	413	--	22-Mar-2011		97	Straw	--	--	77, 75
				2	7.4	393	--	27-Dec-2010	BBCH 39	73	Grain	<0.01	<0.01	76, 74
					5.8	389	--	15-Apr-2011		73	Straw	<0.01	<0.01	77, 75
				2	7.5	402	--	27-Dec-2010	BBCH 45	59	Grain	<0.01	<0.01	76, 74
					5.9	391	--	29-Apr-2011		59	Straw	<0.01	<0.01	77, 75
				1	5.7	382	--	29-Apr-2011	BBCH 45	59	Grain	<0.01	<0.01	76, 74
										59	Straw	<0.01	<0.01	77, 75

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PH I (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4890N CEMS-4890 DAS Ref. ID 102083 Y 2010-2011	Winter Barley / Atomo	Italy SZ Outdoor (field)	GF- 2573	2	8.2	437	--	06-Dec-2010	BBCH 31-32	86	Grain	--	--	76, 74
					6.2	413	--	23-Mar-2011		86	Straw	--	--	77, 75
				2	7.6	403	--	06-Dec-2010	BBCH 39	63	Grain	<0.01	<0.01	76, 74
					6.3	420	--	15-Apr-2011		63	Straw	<0.01	<0.01	77, 75
				2	7.9	423	--	06-Dec-2010	BBCH 45	56	Grain	<0.01	<0.01	76, 74
					6.3	420	--	22-Apr-2011		56	Straw	<0.01	<0.01	77, 75
				1	6.3	417	--	22-Apr-2011	BBCH 45	56	Grain	<0.01	<0.01	76, 74
										56	Straw	<0.01	<0.01	77, 75

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be claimed on the basis of this document.



Table B.7.6-13 Summary of residues of XDE-729 Methyl and XDE-729 Acid in spring barley (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4720A CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Sebastian	Northern France NZ Outside (field)	GF- 2573	1	5.9	197	--	10-May-2010	BBCH 32	71#	Grain	<0.01	<0.01	108, 104
										71#	Straw	<0.01	<0.01	108, 98
				1	6.1	203	--	25-May-2010	BBCH 39	0	Whole plant	0.169	<0.01	96, 100
										7	Whole plant	<0.01	<0.01	96, 100
										14	Whole plant	<0.01	<0.01	96, 100
										28	Whole plant	<0.01	<0.01	96, 100
										49	Grain	<0.01	<0.01	108, 104
										49	Straw	<0.01	<0.01	108, 98
										56#	Grain	<0.01	<0.01	108, 104
										56#	Straw	<0.01	<0.01	108, 98
										63	Grain	<0.01	<0.01	108, 104
										63	Straw	<0.01	<0.01	108, 98
										70	Grain	<0.01	<0.01	108, 104
										70	Straw	<0.01	<0.01	108, 98
				1	6.1	202	--	01-Jun-2010	BBCH 45-49	0	Whole plant	0.112	<0.01	96, 100
										7	Whole plant	<0.01	<0.01	96, 100
										14	Whole plant	<0.01	<0.01	96, 100
										28	Whole plant	<0.01	<0.01	96, 100
										42	Grain	<0.01	<0.01	108, 104
										42	Straw	<0.01	<0.01	108, 98
										49#	Grain	<0.01	<0.01	108, 104
										49#	Straw	<0.01	<0.01	108, 98
										56	Grain	<0.01	<0.01	108, 104
										56	Straw	<0.01	<0.01	108, 98

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										63	Grain	<0.01	<0.01	108, 104
										63	Straw	<0.01	<0.01	108, 98
CEMS-4720B	Spring	Germany	GF-	1	6.3	83	--	29-May-2010	BBCH 32	63#	Grain	<0.01	<0.01	108, 104
CEMS-4720	Barley /	NZ	2573							63#	Straw	<0.01	<0.01	108, 98
DAS Ref. ID	Quench	Outside		1	5.5	73	--	08-Jun-2010	BBCH 39	4	Whole plant	<0.01	<0.01	96, 100
101590		(field)								7	Whole plant	<0.01	<0.01	96, 100
Y										14	Whole plant	<0.01	<0.01	96, 100
2010										28	Whole plant	<0.01	<0.01	96, 100
										43	Grain	<0.01	<0.01	108, 104
										43	Straw	<0.01	<0.01	108, 98
										53#	Grain	<0.01	<0.01	108, 104
										53#	Straw	<0.01	<0.01	108, 98
										59	Grain	<0.01	<0.01	108, 104
										59	Straw	<0.01	<0.01	108, 98
										66	Grain	<0.01	<0.01	108, 104
										66	Straw	<0.01	<0.01	108, 98
				1	6.0	80	--	15-Jun-2010	BBCH 55	0	Whole plant	0.169	<0.01	96, 100
										7	Whole plant	0.015	(0.003)	96, 100
										14	Whole plant	(0.008)	(0.006)	96, 100
										29	Whole plant	<0.01	<0.01	96, 100
										36	Grain	<0.01	<0.01	108, 104
										36	Straw	<0.01	<0.01	108, 98
										46#	Grain	<0.01	<0.01	108, 104
										46#	Straw	<0.01	<0.01	108, 98
										52	Grain	<0.01	<0.01	108, 104
										52	Straw	<0.01	<0.01	108, 98

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										59 59	Grain Straw	<0.01 <0.01	<0.01 <0.01	108, 104 108, 98
CEMS-4720C CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Jubilant	Hungary NZ Outside (field)	GF- 2573	1	6.2	312	--	07-May-2010	BBCH 32	74# 74#	Grain Straw	<0.01 <0.01	<0.01 <0.01	108, 104 108, 98
				1	6.3	315	--	29-May-2010	BBCH 39	52# 52#	Grain Straw	<0.01 <0.01	<0.01 <0.01	108, 104 108, 98
				1	5.8	291	--	07-Jun-2010	BBCH 45	43# 43#	Grain Straw	<0.01 <0.01	<0.01 (0.003)	108, 104 108, 98
CEMS-4720D CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Belvoir	United Kingdom NZ Outside (field)	GF- 2573	1	6.6	393	--	21-Jun-2010	BBCH 32	59# 59#	Grain Straw	<0.01 <0.01	<0.01 <0.01	108, 104 108, 98
				1	5.8	367	--	25-Jun-2010	BBCH 39	55# 55#	Grain Straw	<0.01 <0.01	<0.01 (0.004)	108, 104 108, 98
				1	6.1	383	--	29-Jun-2010	BBCH 45	51# 51#	Grain Straw	<0.01 (0.004)	<0.01 (0.003)	108, 104 108, 98
CEMS-5002A CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Breamer	Germany NZ Outside (field)	GF- 2573	1	5.8	97	--	20-May-2011	BBCH 32	75# 75#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.0	100	--	23-May-2011	BBCH 39	0 8 15 29 64 64	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw	0.231 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 96, 99 94, 98

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	5.9	99	--	26-May-2011	BBCH 45	72# 72# 78 78 88 88	Grain Straw Grain Straw Grain Straw	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
				1	5.9	99	--	26-May-2011	BBCH 45	0 8 12 26 61 61 69# 69# 75 75 85 85	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw Grain Straw Grain Straw	0.158 <0.01 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
CEMS-5002B CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Sebastian	France NZ Outside (field)	GF- 2573	1  1	6.0  6.0	400  398	--  --	19-Apr-2011  10-May-2011	BBCH 32  BBCH 39	84# 84# 0 7 14 28 56 56 63#	Grain Straw Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain	<0.01 <0.01 0.156 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	96, 99 94, 98 100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99

WARNING: This document forms part of an EC evaluation data package and should not be relied in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.0	398	--	17-May-2011	BBCH 45	63# 69 69 77 77	Straw Grain Straw Grain Straw	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	94, 98 96, 99 94, 98 96, 99 94, 98
				1	6.0	398	--	17-May-2011	BBCH 45	0 7 14 28 49 49 56# 56# 62 62 70 70	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw Grain Straw Grain Straw	0.107 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
CEMS-5002C CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Azit	Poland NZ Outside (field)	GF- 2573	1  1	5.9  6.4	392  410	--  --	23-May-2011  27-May-2011	BBCH 32  BBCH 39	81# 81# 0 7 14 28 70 70 77# 77#	Grain Straw Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw	<0.01 <0.01 0.216 (0.004) <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	96, 99 94, 98 100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	5.6	371	--	31-May-2011	BBCH 45	83 83 91 91	Grain Straw Grain Straw	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	96, 99 94, 98 96, 99 94, 98
				1	5.6	371	--	31-May-2011	BBCH 45	0 7 15 28 66 66 73# 73# 79 79 87 87	Whole Plant Whole Plant Whole Plant Whole Plant Grain Straw Grain Straw Grain Straw Grain Straw	0.197 (0.006) <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
CEMS-5002D CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Wagon	United Kingdom NZ Outside (field)	GF- 2573	1	6.0	100	--	24-May-2011	BBCH 32	83# 83#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.2	103	--	31-May-2011	BBCH 39- 43	76# 76#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.2	103	--	03-Jun-2011	BBCH 45	73# 73#	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	96, 99 94, 98
CEMS-5002E CEMS-5002 DAS Ref. ID 110412	Spring Barley / Jubilant	Hungary NZ Outside (field)	GF- 2573	1	5.8	385	--	17-May-2011	BBCH 32	69# 69#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	5.8	384	--	02-Jun-2011	BBCH 41	53#	Grain	<0.01	<0.01	96, 99

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
Y 2011				1	6.2	413	--	09-Jun-2011	BBCH 45	53#	Straw	<0.01	<0.01	94, 98
										46#	Grain	<0.01	<0.01	96, 99
										46#	Straw	<0.01	<0.01	94, 98
CEMS-5002F CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Ingmar	Germany NZ Outside (field)	GF- 2573	1	6.6	110	--	06-May-2011	BBCH 32	77#	Grain	<0.01	<0.01	96, 99
				1	6.8	113	--	12-May-2011	BBCH 39	71#	Grain	<0.01	<0.01	96, 99
										71#	Straw	<0.01	<0.01	94, 98
				1	6.8	113	--	20-May-2011	BBCH 45	63#	Grain	<0.01	<0.01	96, 99
										63#	Straw	<0.01	<0.01	94, 98
CEMS-5002G CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Prestige	Poland NZ Outside (field)	GF- 2573	1	6.1	408	--	25-May-2011	BBCH 32	77#	Grain	<0.01	<0.01	96, 99
				1	6.4	430	--	02-Jun-2011	BBCH 39	69#	Grain	<0.01	<0.01	96, 99
										69#	Straw	<0.01	<0.01	94, 98
				1	6.3	423	--	07-Jun-2011	BBCH 45	64#	Grain	<0.01	<0.01	96, 99
										64#	Straw	<0.01	<0.01	94, 98

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-14 Summary of residues of XDE-729 Methyl and XDE-729 Acid in spring barley (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4720E CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Otis	Italy SZ Outside (field)	GF- 2573	1	6.3	313	--	28-Apr-2010	BBCH 32	70#	Grain	<0.01	<0.01	108, 104
										70#	Straw	<0.01	<0.01	108, 98
				1	6.1	306	--	12-May-2010	BBCH 39	0	Whole plant	0.324	<0.01	96, 100
										7	Whole plant	<0.01	<0.01	96, 100
										14	Whole plant	<0.01	<0.01	96, 100
										28	Whole plant	<0.01	<0.01	96, 100
										49	Grain	<0.01	<0.01	108, 104
										49	Straw	<0.01	<0.01	108, 98
										56#	Grain	<0.01	<0.01	108, 104
										56#	Straw	<0.01	<0.01	108, 98
										63	Grain	<0.01	<0.01	108, 104
										63	Straw	<0.01	<0.01	108, 98
										70	Grain	<0.01	<0.01	108, 104
										70	Straw	<0.01	<0.01	108, 98
				1	6.1	304	--	21-May-2010	BBCH 45	0	Whole plant	0.222	<0.01	96, 100
										7	Whole plant	(0.009)	<0.01	96, 100
										14	Whole plant	<0.01	<0.01	96, 100
										28	Whole plant	<0.01	<0.01	96, 100
										40	Grain	<0.01	<0.01	108, 104
										40	Straw	<0.01	<0.01	108, 98
										47#	Grain	<0.01	<0.01	108, 104
										47#	Straw	<0.01	<0.01	108, 98
										54	Grain	<0.01	<0.01	108, 104
										54	Straw	<0.01	<0.01	108, 98
										61	Grain	<0.01	<0.01	108, 104



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>			
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid	
										61	Straw	<0.01	<0.01	108, 98	
CEMS-4720F CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Unia	Spain	GF- 2573	1	6.0	350	--	11-May-2010	BBCH 32	57#	Grain	<0.01	<0.01	108, 104	
										57#	Straw	<0.01	<0.01	108, 98	
					1	5.8	338	--	18-May-2010	BBCH 39	0	Whole plant	0.210	(0.004)	96, 100
										7	Whole plant	(0.005)	<0.01	96, 100	
										14	Whole plant	(0.004)	<0.01	96, 100	
										28	Whole plant	<0.01	<0.01	96, 100	
										43	Grain	<0.01	<0.01	108, 104	
										43	Straw	<0.01	<0.01	108, 98	
										50#	Grain	<0.01	<0.01	108, 104	
										50#	Straw	<0.01	<0.01	108, 98	
										57	Grain	<0.01	<0.01	108, 104	
										57	Straw	<0.01	<0.01	108, 98	
										65	Grain	<0.01	<0.01	108, 104	
										65	Straw	<0.01	<0.01	108, 98	
					1	6.0	348	--	20-May-2010	BBCH 45	0	Whole plant	0.143	<0.01	96, 100
										7	Whole plant	(0.003)	<0.01	96, 100	
										14	Whole plant	<0.01	<0.01	96, 100	
										28	Whole plant	<0.01	<0.01	96, 100	
										41	Grain	<0.01	<0.01	108, 104	
										41	Straw	<0.01	<0.01	108, 98	
										48#	Grain	<0.01	<0.01	108, 104	
										48#	Straw	<0.01	<0.01	108, 98	
										55	Grain	<0.01	<0.01	108, 104	
										55	Straw	<0.01	<0.01	108, 98	
										63	Grain	<0.01	<0.01	108, 104	
										63	Straw	<0.01	<0.01	108, 98	

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
CEMS-4720G CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Flavia	Bulgaria SZ Outside (field)	GF- 2573	1	6.2	310	--	08-Jun-2010	BBCH 32	50# 50#	Grain Straw	0.041 0.078	<0.01 (0.007)	108, 104 108, 98
				1	6.3	317	--	20-Jun-2010	BBCH 39	38# 38#	Grain Straw	0.059 0.103	<0.01 0.011	108, 104 108, 98
				1	6.0	300	--	25-Jun-2010	BBCH 45	33# 33#	Grain Straw	0.071 0.124	<0.01 0.013	108, 104 108, 98
CEMS-4720H CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Prestige	Southern France SZ Outside (field)	GF- 2573	1	6.3	83	--	10-May-2010	BBCH 32	67# 67#	Grain Straw	<0.01 (0.005)	<0.01 (0.004)	108, 104 108, 98
				1	6.5	87	--	21-May-2010	BBCH 39	56# 56#	Grain Straw	<0.01 0.014	<0.01 (0.009)	108, 104 108, 98
				1	6.5	87	--	03-Jun-2010	BBCH 45	43# 43#	Grain Straw	<0.01 0.013	<0.01 0.012	108, 104 108, 98
CEMS-5002H CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Rondo	Italy SZ Outside (field)	GF- 2573	1	6.0	402	--	15-Apr-2011	BBCH 32	73# 73#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.3	420	--	27-Apr-2011	BBCH 39	0 7 13 28 55 61# 61# 68 68	Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw Grain Straw	0.147 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.1	406	--	06-May-2011	BBCH 45	0 8 14 31 46 52# 52# 59 59	Whole plant Whole plant Whole plant Whole plant Whole plant Grain Straw Grain Straw	0.127 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98
CEMS-5002I CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Belgrano	Spain SZ Outside (field)	GF- 2573	1	6.6	110	--	15-Apr-2011	BBCH 32	79# 79#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	5.9	99		26-Apr-2011	BBCH 39	0 8 15 29 57 57 64# 64# 71 71 78 78	Whole plant Whole plant Whole plant Whole plant Grain Straw Grain Straw Grain Straw Grain Straw	0.217 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
			1	6.2	103	--	04-May-2011	BBCH 45	0 7 14 27	Whole plant Whole plant Whole plant Whole plant	0.132 (0.004) <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	100, 97 100, 97 100, 97 100, 97	

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registrants must be guided on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
										49 49 56# 56# 63 63 70 70	Grain Straw Grain Straw Grain Straw Grain Straw	<0.01 (0.004) <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 (0.004) <0.01 <0.01	<0.01 <0.01 <u>&lt;0.01</u> <u>&lt;0.01</u> <0.01 <0.01 <0.01 <0.01	96, 99 94, 98 96, 99 94, 98 96, 99 94, 98 96, 99 94, 98
CEMS-5002J CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Atomo	Italy SZ Outside (field)	GF- 2573	1	5.6	93	--	14-Apr-2011	BBCH 32	64# 64#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	5.4	90	--	22-Apr-2011	BBCH 39	56# 56#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.4	107	--	28-Apr-2011	BBCH 45	50# 50#	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	96, 99 94, 98
CEMS-5002K CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Prestige	France SZ Outside (field)	GF- 2573	1	6.4	107	--	04-May-2011	BBCH 32	63# 63#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.4	107	--	10-May-2011	BBCH 39	57# 57#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
				1	6.4	107	--	13-May-2011	BBCH 45	54# 54#	Grain Straw	<u>&lt;0.01</u> <u>&lt;0.01</u>	<u>&lt;0.01</u> <u>&lt;0.01</u>	96, 99 94, 98
CEMS-5002L CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Thessaloni ki	Greece SZ Outside (field)	GF- 2573	1	6.2	411	--	05-Apr-2011	BBCH 32	76# 76#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98
					5.9	392	--	15-Apr-2011	BBCH 39	66# 66#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 99 94, 98

WARNING: This document forms part of an MRL evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	XDE-729 Methyl (mg/Kg)	XDE-729 acid (mg/Kg)	% Recovery XDE-729 Methyl XDE-729 acid
				1	6.5	433	--	27-Apr-2011	BBCH 45	54#	Grain	<0.01	<0.01	96, 99
										54#	Straw	<0.01	<0.01	94, 98
CEMS-5002M CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Violeta	Bulgaria SZ Outside (field)	GF- 2573	1	5.6	373	--	10-May-2011	BBCH 32	71#	Grain	<0.01	<0.01	96, 99
										71#	Straw	<0.01	<0.01	94, 98
				1	6.2	413	--	24-May-2011	BBCH 39	57#	Grain	<0.01	<0.01	96, 99
										57#	Straw	<0.01	<0.01	94, 98
				1	6.5	433	--	27-May-2011	BBCH 45	54#	Grain	<0.01	<0.01	96, 99
										54#	Straw	<0.01	<0.01	94, 98

<sup>a</sup> Limit of Quantitation (LOQ) = 0.01 mg/kg; Limit of Detection (LOD) = 0.003 mg/kg. Residue values equal to or greater than the LOD, but less than the LOQ are displayed within parenthesis.

# = Normal Commercial Harvest

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

Table B.7.6-15 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in spring barley (Northern Zone)

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ()	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet-mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet-mexyl Cloquintocet acid
CEMS-4720A CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Sebastian	Northern France NZ Outside (field)	GF-2573	1	5.9	197	--	10-May-2010	BBCH 32	71	Grain	--	--	--
										71	Straw	--	--	--
				1	6.1	203	--	25-May-2010	BBCH 39	49	Grain	--	--	--
										49	Straw	--	--	--
										56#	Grain	<0.01	<0.01	96, 92
										56#	Straw	<0.01	<0.01	112, 102
										63	Grain	<0.01	<0.01	96, 92
										63	Straw	<0.01	<0.01	112, 102
										70	Grain	<0.01	<0.01	96, 92
										70	Straw	<0.01	<0.01	112, 102
				1	6.1	202	--	01-Jun-2010	BBCH 45-49	42	Grain	--	--	--
										42	Straw	--	--	--
										49#	Grain	<u>&lt;0.01</u>	<u>&lt;0.01</u>	96, 92
										49#	Straw	<u>&lt;0.01</u>	<u>&lt;0.01</u>	112, 102
										56	Grain	<0.01	<0.01	96, 92
										56	Straw	<0.01	<0.01	112, 102
										63	Grain	<0.01	<0.01	96, 92
										63	Straw	<0.01	<0.01	112, 102

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4720B CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Quench	Germany NZ Outside (field)	GF- 2573	1	6.3	83	--	29-May-2010	BBCH 32	63	Grain	--	--	--
										63	Straw	--	--	--
				1	5.5	73	--	08-Jun-2010	BBCH 39	43	Grain	<0.01	<0.01	96, 92
										43	Straw	<0.01	<0.01	112, 102
										53#	Grain	<0.01	<0.01	96, 92
										53#	Straw	<0.01	<0.01	112, 102
										59	Grain	<0.01	<0.01	96, 92
										59	Straw	<0.01	<0.01	112, 102
										66	Grain	<0.01	<0.01	96, 92
										66	Straw	<0.01	<0.01	112, 102
				1	6.0	80	--	15-Jun-2010	BBCH 55	36	Grain	<0.01	<0.01	96, 92
										36	Straw	<0.01	<0.01	112, 102
										46#	Grain	<0.01	<0.01	96, 92
										46#	Straw	<0.01	<0.01	112, 102
										52	Grain	<0.01	<0.01	96, 92
										52	Straw	<0.01	<0.01	112, 102
										59	Grain	<0.01	<0.01	96, 92
										59	Straw	<0.01	<0.01	112, 102

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registrants must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4720C CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Jubilant	Hungary NZ Outside (field)	GF- 2573	1	6.2	312	--	07-May-2010	BBCH 32	74# 74#	Grain Straw	-- --	-- --	-- --
				1	6.3	315	--	29-May-2010	BBCH 39	52# 52#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 92 112, 102
				1	5.8	291	--	07-Jun-2010	BBCH 45	43# 43#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 92 112, 102
				1	6.6	393	--	21-Jun-2010	BBCH 32	59# 59#	Grain Straw	-- --	-- --	-- --
				1	5.8	367	--	25-Jun-2010	BBCH 39	55# 55#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 92 112, 102
				1	6.1	383	--	29-Jun-2010	BBCH 45	51# 51#	Grain Straw	<0.01 <0.01	<0.01 <0.01	96, 92 112, 102
CEMS-5002A CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Breamer	Germany NZ Outside (field)	GF- 2573	1	5.8	99	--	20-May-2011	BBCH 32	75# 75#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85
				1	6.0	100	--	23-May-2011	BBCH 39	72# 72#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85
				1	5.9	99	--	26-May-2011	BBCH 45	69# 69#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85
				1	5.8	99	--	20-May-2011	BBCH 32	75# 75#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85
				1	6.0	100	--	23-May-2011	BBCH 39	72# 72#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85
				1	5.9	99	--	26-May-2011	BBCH 45	69# 69#	Grain Straw	<0.01 <0.01	<0.01 <0.01	86, 86 89, 85

WARNING: This document forms part of an EC evaluation data package and should not be read, isolated, registered, or must not be granted on the basis of this document.



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-5002B CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Sebastian	France NZ Outside (field)	GF- 2573	1	6.0	400	--	19-Apr-2011	BBCH 32	84#	Grain	<0.01	<0.01	86, 86
										84#	Straw	<0.01	<0.01	89, 85
				1	6.0	398	--	10-May-2011	BBCH 39	63#	Grain	<0.01	<0.01	86, 86
										63#	Straw	<0.01	<0.01	89, 85
				1	6.0	398	--	17-May-2011	BBCH 45	56#	Grain	<0.01	<0.01	86, 86
										56#	Straw	<0.01	<0.01	89, 85
CEMS-5002C CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Azit	Poland NZ Outside (field)	GF- 2573	1	5.9	392	--	23-May-2011	BBCH 32	81#	Grain	<0.01	<0.01	86, 86
										81#	Straw	<0.01	<0.01	89, 85
				1	6.1	410	--	27-May-2011	BBCH 39	77#	Grain	<0.01	<0.01	86, 86
										77#	Straw	<0.01	<0.01	89, 85
				1	5.6	371	--	31-May-2011	BBCH 45	73#	Grain	<0.01	<0.01	86, 86
										73#	Straw	<0.01	<0.01	89, 85
CEMS-5002D CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Wagon	United Kingdom NZ Outside (field)	GF- 2573	1	6.0	100	--	24-May-2011	BBCH 32	83#	Grain	<0.01	<0.01	86, 86
										83#	Straw	<0.01	<0.01	89, 85
				1	6.2	103	--	31-May-2011	BBCH 39- 43	76#	Grain	<0.01	<0.01	86, 86
										76#	Straw	<0.01	<0.01	89, 85
				1	6.2	103	--	03-Jun-2011	BBCH 45	73#	Grain	<0.01	<0.01	86, 86
										73#	Straw	<0.01	<0.01	89, 85

WARNING: This document forms part of an EC evaluation data package and should not be used for isolation/registration. Must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-5002E CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Jubilant	Hungary NZ Outside (field)	GF- 2573	1	5.8	385	--	17-May-2011	BBCH 32	69#	Grain	<0.01	<0.01	86, 86
										69#	Straw	<0.01	<0.01	89, 85
				1	5.8	384	--	02-Jun-2011	BBCH 41	53#	Grain	<0.01	<0.01	86, 86
										53#	Straw	<0.01	<0.01	89, 85
				1	6.2	413	--	09-Jun-2011	BBCH 45	46#	Grain	<0.01	<0.01	86, 86
										46#	Straw	<0.01	<0.01	89, 85
CEMS-5002F CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Ingmar	Germany NZ Outside (field)	GF- 2573	1	6.6	110	--	06-May-2011	BBCH 32	77#	Grain	<0.01	<0.01	86, 86
										77#	Straw	<0.01	<0.01	89, 85
				1	6.8	113	--	12-May-2011	BBCH 39	71#	Grain	<0.01	<0.01	86, 86
										71#	Straw	<0.01	<0.01	89, 85
				1	6.8	113	--	20-May-2011	BBCH 45	63#	Grain	<0.01	<0.01	86, 86
										63#	Straw	<0.01	<0.01	89, 85
CEMS-5002G CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Prestige	Poland NZ Outside (field)	GF- 2573	1	6.1	408	--	25-May-2011	BBCH 32	77#	Grain	<0.01	<0.01	86, 86
										77#	Straw	<0.01	<0.01	89, 85
				1	6.4	430	--	02-Jun-2011	BBCH 39	69#	Grain	<0.01	<0.01	86, 86
										69#	Straw	<0.01	<0.01	89, 85
				1	6.3	423	--	07-Jun-2011	BBCH 45	64#	Grain	<0.01	<0.01	86, 86
										64#	Straw	<0.01	<0.01	89, 85

WARNING: This document forms part of an EC evaluation data package and should not be used for isolation/registration. Must not be granted on the basis of this document.

Table B.7.6-16 Summary of residues of Cloquintocet-mexyl and Cloquintocet acid in spring barley (Southern Zone)

GLP and Trial Details	Crop	Country	Application Details						Residues found <sup>a</sup>					
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet-mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet-mexyl Cloquintocet acid
CEMS-4720E CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Otis	Italy SZ Outside (field)	GF-2573	1	6.3	313	--	28-Apr-2010	BBCH 32	70	Grain	--	--	--
										70	Straw	--	--	--
				1	6.1	306	--	12-May-2010	BBCH 39	49	Grain	--	--	--
										49	Straw	--	--	--
										56#	Grain	<0.01	<0.01	96, 92
										56#	Straw	<0.01	<0.01	112, 102
										63	Grain	<0.01	<0.01	96, 92
										63	Straw	<0.01	<0.01	112, 102
										70	Grain	<0.01	<0.01	96, 92
										70	Straw	<0.01	<0.01	112, 102
				1	6.1	304	--	21-May-2010	BBCH 45	40	Grain	--	--	--
										40	Straw	--	--	--
										47#	Grain	<0.01	<0.01	96, 92
										47#	Straw	<0.01	<0.01	112, 102
										54	Grain	<0.01	<0.01	96, 92
										54	Straw	<0.01	<0.01	112, 102
										61	Grain	<0.01	<0.01	96, 92
										61	Straw	<0.01	<0.01	112, 102

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4720F CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Unia	Spain	GF- 2573	1	6.0	350	--	11-May-2010	BBCH 32	57	Grain	--	--	--
										57	Straw	--	--	--
				1	5.8	338	--	18-May-2010	BBCH 39	43	Grain	<0.01	<0.01	96, 92
										43	Straw	<0.01	<0.01	112, 102
										50#	Grain	<0.01	<0.01	96, 92
										50#	Straw	<0.01	<0.01	112, 102
										57	Grain	<0.01	<0.01	96, 92
										57	Straw	<0.01	<0.01	112, 102
										65	Grain	<0.01	<0.01	96, 92
										65	Straw	<0.01	<0.01	112, 102
				1	6.0	348	--	20-May-2010	BBCH 45	41	Grain	<0.01	<0.01	96, 92
										41	Straw	<0.01	<0.01	112, 102
										48#	Grain	<0.01	<0.01	96, 92
										48#	Straw	<0.01	<0.01	112, 102
CEMS-4720G CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Flavia	Bulgaria SZ Outside (field)	GF- 2573	1	6.2	310	--	08-Jun-2010	BBCH 32	50	Grain	--	--	--
										50	Straw	--	--	--
				1	6.0	317	--	20-Jun-2010	BBCH 39	38	Grain	--	--	--
										38	Straw	--	--	--
				1	6.0	300	--	25-Jun-2010	BBCH 45	33	Grain	--	--	--
										33	Straw	--	--	--

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-4720H CEMS-4720 DAS Ref. ID 101590 Y 2010	Spring Barley / Prestige	Southern France SZ Outside (field)	GF- 2573	1	6.3	83	--	10-May-2010	BBCH 32	67	Grain	--	--	--
				1	6.5	87	--	21-May-2010	BBCH 39	56#	Grain	<0.01	<0.01	96, 92
				1	6.5	87	--	03-Jun-2010	BBCH 45	43#	Grain	<0.01	<0.01	112, 102
				1	6.5	87	--	03-Jun-2010	BBCH 45	43#	Grain	<0.01	<0.01	96, 92
				1	6.5	87	--	03-Jun-2010	BBCH 45	43#	Grain	<0.01	<0.01	112, 102
				1	6.5	87	--	03-Jun-2010	BBCH 45	43#	Grain	<0.01	<0.01	96, 92
CEMS-5002H CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Rondo	Italy SZ Outside (field)	GF- 2573	1	6.0	402	--	15-Apr-2011	BBCH 32	73#	Grain	<0.01	<0.01	86, 86
				1	6.3	420	--	27-Apr-2011	BBCH 39	61#	Grain	<0.01	<0.01	89, 85
				1	6.3	420	--	27-Apr-2011	BBCH 39	61#	Grain	<0.01	<0.01	86, 86
				1	6.3	420	--	27-Apr-2011	BBCH 39	61#	Grain	<0.01	<0.01	89, 85
				1	6.1	406	--	06-May-2011	BBCH 45	52#	Grain	<0.01	<0.01	86, 86
				1	6.1	406	--	06-May-2011	BBCH 45	52#	Grain	<0.01	<0.01	89, 85
CEMS-5002I CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Belgrano	Spain SZ Outside (field)	GF- 2573	1	6.6	110	--	11-Apr-2011	BBCH 32	79#	Grain	<0.01	<0.01	86, 86
				1	6.6	110	--	11-Apr-2011	BBCH 32	79#	Grain	<0.01	<0.01	89, 85
				1	5.9	99	--	26-Apr-2011	BBCH 39	64#	Grain	<0.01	<0.01	86, 86
				1	5.9	99	--	26-Apr-2011	BBCH 39	64#	Grain	<0.01	<0.01	89, 85
				1	6.2	103	--	04-May-2011	BBCH 45	56#	Grain	<0.01	<0.01	86, 86
				1	6.2	103	--	04-May-2011	BBCH 45	56#	Grain	<0.01	<0.01	89, 85

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc ( )	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-5002J CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Atomo	Italy SZ Outside (field)	GF- 2573	1	5.6	93	--	14-Apr-2011	BBCH 32	64#	Grain	<0.01	<0.01	86, 86
				1	5.4	90	--	22-Apr-2011	BBCH 39	56#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	28-Apr-2011	BBCH 45	50#	Grain	<0.01	<0.01	89, 85
				1	6.4	107	--	04-May-2011	BBCH 32	63#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	10-May-2011	BBCH 39	57#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	13-May-2011	BBCH 45	54#	Grain	<0.01	<0.01	89, 85
CEMS-5002K CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Prestige	France SZ Outside (field)	GF- 2573	1	6.4	107	--	04-May-2011	BBCH 32	63#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	10-May-2011	BBCH 39	57#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	13-May-2011	BBCH 45	54#	Grain	<0.01	<0.01	89, 85
				1	6.4	107	--	04-May-2011	BBCH 32	63#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	10-May-2011	BBCH 39	57#	Grain	<0.01	<0.01	86, 86
				1	6.4	107	--	13-May-2011	BBCH 45	54#	Grain	<0.01	<0.01	89, 85
CEMS-5002L CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Thessaloni ki	Greece SZ Outside (field)	GF- 2573	1	6.2	411	--	05-Apr-2011	BBCH 32	76#	Grain	<0.01	<0.01	86, 86
				1	5.9	392	--	15-Apr-2011	BBCH 39	66#	Grain	<0.01	<0.01	86, 86
				1	6.5	433	--	27-Apr-2011	BBCH 45	54#	Grain	<0.01	<0.01	86, 86
				1	5.9	392	--	15-Apr-2011	BBCH 39	66#	Grain	<0.01	<0.01	86, 86
				1	6.5	433	--	27-Apr-2011	BBCH 45	54#	Grain	<0.01	<0.01	86, 86
				1	6.5	433	--	27-Apr-2011	BBCH 45	54#	Grain	<0.01	<0.01	86, 86

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

GLP and Trial Details	Crop	Country	Application Details									Residues found <sup>a</sup>		
Trial ID Study ID Report No. GLP(Y/N) Trial Year	Crop Variety	Country Zone Location	Form No.	No. of Appls	Appl Rate (g ae/ha)	Spray Vol (L/ha)	Appl Conc (%)	Appl Date	GS at Last Appl	PHI (days)	Portion Analysed	Cloquintocet- mexyl (mg/Kg)	Cloquintocet acid (mg/Kg)	% Recovery Cloquintocet- mexyl Cloquintocet acid
CEMS-5002M CEMS-5002 DAS Ref. ID 110412 Y 2011	Spring Barley / Violeta	Bulgaria SZ Outside (field)	GF- 2573	1	5.6	373	--	10-May-2011	BBCH 32	71#	Grain	<0.01	<0.01	86, 86
										71#	Straw	<0.01	<0.01	89, 85
				1	6.2	413	--	24-May-2011	BBCH 39	57#	Grain	<0.01	<0.01	86, 86
										57#	Straw	<0.01	<0.01	89, 85
				1	6.5	433	--	27-May-2011	BBCH 45	54#	Grain	<0.01	<0.01	86, 86
										54#	Straw	<0.01	<0.01	89, 85

<sup>a</sup> <0.01 = Not Detected, <0.005 mg/kg

# = Normal Commercial Harvest

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

### B.7.6.1 Summary of residues resulting from supervised trials

Residue trials were conducted in winter wheat, winter barley, spring wheat and spring barley in northern and southern Europe over a two year period. In total there were 83 residue trials conducted with 22 trials in winter wheat (11 in N-EU and 11 in S-EU), 19 trials in spring wheat (10 in N-EU and 9 in S-EU), 21 trials in winter barley (10 in N-EU and 11 in S-EU) and 21 trials in spring barley (11 in N-EU and 10 in S-EU).

The representative formulation applied in these residue trials was GF-2573, an EC formulation containing XDE-729 methyl at a nominal concentration of 7.5 g acid equivalent (a.s) /L. The formulation also contains a herbicide safener, cloquintocet-mexyl, at a nominal concentration of 7.5 g a.s/L.

In the 15 winter wheat and winter barley decline trials where whole plant samples were collected for residue analysis, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection (<0.003 mg/kg) immediately before the second application in the spring, indicating that the preceding autumn application would not be expected to contribute to any residues observed in grain or straw. This conclusion is further confirmed by the finding that residue levels in grain and straw within a given winter wheat or winter barley trial are quite similar when comparing the treatment with an autumn application at 7.5 g ae/ha followed by a spring application at 6.0 g ae/ha at growth stage BBCH 45 to the treatment in which there is only a single spring application at 6.0 g ae/ha at BBCH 45.

Residues of XDE-729 methyl and XDE-729 acid typically decreased rapidly in whole plants following application in the spring, often being non-detectable (<0.003 mg/kg) by approximately 14 to 28 days after application, although in a few trials residues in whole plants remained detectable through a final sample collection at approximately 56 days after application.

Out of 83 trials, residues of XDE-729 methyl or XDE-729 acid in grain were not detected (<0.003 mg/kg) or were <0.01 mg/kg in 82 trials. In one trial in spring barley (Bulgarian trial, CEMS-4720G) residues of XDE-729 methyl significantly exceeded the LOQ of 0.01 mg/kg. The applicant states a number of factors that were unfavourable for normal crop growth and development at this trial site may have contributed to this high residue result. Their analysis of the data indicated that this result was a statistical outlier and therefore the residue value in grain from that trial should not be used for purposes of setting a MRL or for determining potential residue intake in livestock.

Residues of XDE-729 methyl and XDE-729 acid in straw were most frequently not detected (<0.003 mg/kg) or were detected, but below the LOQ (<0.01 mg/kg). However, for the treatment compliant with the critical GAP there were 5 residue trials out of the total of 83 trials in which residues of XDE-729 methyl or XDE-



729 acid were above the LOQ ( $>0.01$  mg/kg). In the same spring barley trial as mentioned previously (Bulgarian trial, CEMS-4720G), residues in straw were substantially greater than observed in any other trial and the applicant's analysis of the data indicated that this result was a statistical outlier. Therefore, the residue value in straw from that trial was not used for the purposes of determining potential residue intake in livestock. Furthermore, it should not be used in future to propose an MRL for animal feed commodities, at such a time when this becomes implemented procedure.

Residues of cloquintocet-mexyl and cloquintocet acid were not detected ( $<0.005$  mg/kg) in the grain or straw from any of the residue trials.

In 2010 winter wheat trials, following application in spring targeted at either BBCH 39 or BBCH 45, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection ( $<0.003$  mg/kg) by 14 to 17 days after application. Residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain or straw in any of the 22 winter wheat trials conducted over the two year period.

The same study design and treatments as described for the winter wheat trials were also used in winter barley trials. In winter barley trials, following application in spring targeted at either BBCH 39 or BBCH 45, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection ( $<0.003$  mg/kg) by 14-15 days after application in 4 of the trials. Residues fell below the limit of detection ( $<0.003$  mg/kg) by 56-60 days after application in two of the trials. However, in one trial in southern France, residues of both XDE-729 methyl and XDE-729 acid remained above the LOQ ( $>0.01$  mg/kg) in whole plant samples through 56 days after application.

Residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain, except in the southern France trial mentioned above (CEMS-4553D), where the level of XDE-729 methyl was  $<0.01$  mg/kg. In straw, residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in the 10 trials conducted in the northern EU climatic zone. However, in the 11 trials conducted in the southern EU climatic zone, 5 trials had residues of XDE-729 methyl or XDE-729 acid in straw that were  $<0.01$  mg/kg and in one trial (CEMS-4553D, southern France) residues of both XDE-729 methyl and XDE-729 acid in straw exceeded the LOQ ( $>0.01$  mg/kg). The applicant states that unfavourable growing conditions along with a slightly late application (BBCH 45-51 rather than BBCH 45) were thought to contribute to the higher residues in the southern France trial. Nonetheless, the residue value in straw from that trial was used for purposes of setting a MRL or for determining potential residue intake in livestock.

In spring wheat, trials in addition to the treatment that was consistent with the critical GAP with a single spring application targeted at BBCH 45, there were also

other treatments included with the spring application at earlier growth stages (BBCH 32 or BBCH 39). Residues of XDE-729 methyl and XDE-729 acid in whole plants were generally below the limit of detection ( $<0.003$  mg/kg) by 12 to 14 days after application, although in one trial residues of XDE-729 methyl were  $<0.01$  mg/kg at 12 days after application. Residues of XDE 729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain in any of the 19 spring wheat trials conducted over the two year period (2010 and 2011). In straw at two trial sites XDE-729 methyl was found at levels  $>0.01$  mg/kg and in these same two trials XDE-729 acid was found at  $<0.01$  mg/kg. Residues of XDE-729 methyl and XDE-729 acid in straw in the remaining trials was typically not detected ( $<0.003$  mg/kg).

The same study design and treatments as described for the spring wheat trials were also used in spring barley trials. In spring barley trials, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection ( $<0.003$  mg/kg) by 28-29 days after application. In 20 out of the 21 trials conducted in 2010 and 2011, residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain. However, in one trial that was conducted in Bulgaria during 2010 (Trial CEMS-4720G), residues of XDE-729 methyl were  $0.071$  mg/kg when the treatment was applied at BBCH 45. Residues of XDE-729 acid were not detected in grain in the trial conducted in Bulgaria. The applicant states that conditions at the Bulgaria trial site were reported to be unfavourable for crop growth and development. These conditions included a late planting date, clay soil which was unfavourable for water availability to the crop, and distribution of rainfall that was not favourable for growing conditions. It was noted that the grain yield was lower than normal with fewer grains per ear and smaller ears than in previous years. The applicant thought that the unfavourable growing conditions that resulted in reduced crop development and yield also were responsible for the abnormal residue value for XDE-729 methyl in grain at this trial site. Also, the conditions at the Bulgaria trial site in 2010 resulted in abnormally rapid maturity and drying of the crop with a PHI of only 33 days from application at growth stage BBCH 45 until harvest. The PHIs from application at BBCH 45 until harvest for the nine other trials conducted in spring barley in southern Europe ranged from 43 to 56 days, with an average of 51 days. So, the 2010 Bulgaria trial (Trial CEMS-4720G) had a PHI for application at BBCH 45 that was 18 days shorter than the average for the other trials and was 10 days shorter than the next shortest PHI among the 10 spring barley trials. Additionally, another trial in spring barley was conducted in Bulgaria during 2011 (Trial CEMS-5002M) and following application at growth stage BBCH 45, residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in both grain and straw. The applicant's further evaluation of the residue data indicated that trial CEMS-4720G is a statistical outlier and is not appropriate for use in setting a MRL in grain. Out of the eight trial sites in 2010, residues of XDE-729 methyl and XDE-729 acid in straw were below the LOQ ( $<0.01$  mg/kg) at six sites. In a trial site in Southern France in 2010 residues of XDE-729 methyl and XDE-729 acid in straw were

0.013 mg/kg and 0.012 mg/kg, respectively, when GF-2573 was applied at BBCH 45. Additionally, at the 2010 trial site in Bulgaria discussed above (Trial CEMS-4720G), residues of XDE-729 methyl and XDE-729 acid in straw were 0.124 mg/kg and 0.013 mg/kg, respectively, when GF-2573 was applied at BBCH 45. As discussed previously, unfavourable conditions for crop growth and development at the 2010 Bulgaria trial site are thought to be responsible for the abnormally high residue levels in this trial. In 2011, residues of XDE-729 methyl and XDE-729 acid were not detected (<0.003 mg/kg) in any of the 13 trials conducted in spring barley, including 6 that were conducted in southern Europe. As with grain, further evaluation of the residue data for straw indicated that trial CEMS-4720G is an outlier and is not appropriate for use in evaluating potential residue intake in livestock or for future use if a MRL is set in straw. The RMS agrees with the reasons given above that the trial CEMS-4720G was an outlier and was therefore not used for the purpose of setting an MRL.

The conditions leading to realistic worst-cases for residues (critical GAP) in cereal crops are summarised in the table below.

**Table B.7.6.1-1**  
**Summary of critical GAPs**

Crop	Rate, g ae/ha (max)	No. of Applications (minimum interval in days)	PHI (days)	Growth Stage at Latest Application (BBCH)
Winter wheat	7.5 (autumn) + 6.0 (spring)	2 (application interval based on growth stage of the crop)	N/A	<u>Late Autumn:</u> Prior to dormancy, but by December 31 <sup>st</sup> , typically BBCH 13-29 <u>Spring:</u> BBCH 45
Spring wheat	6.0	1	N/A	BBCH 45
Winter barley	7.5 (autumn) + 6.0 (spring)	2 (application interval based on growth stage of the crop)	N/A	<u>Late Autumn:</u> Prior to dormancy, but by December 31 <sup>st</sup> , typically BBCH 13-29 <u>Spring:</u> BBCH 45
Spring barley	6.0	1	N/A	BBCH 45

## Winter Wheat

Reference: Rawle, N. W., 2011 "RESIDUES OF XDE-729 IN WINTER WHEAT AT INTERVALS AND HARVEST FOLLOWING MULTIPLE APPLICATIONS OF GF-2573 – NORTHERN AND SOUTHERN EUROPE – 2009 TO 2010", Study No. CEMS-4552, Dow Reference ID 090118

Devine, H. C., 2012 "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN WINTER WHEAT AT INTERVALS AND HARVEST FOLLOWING APPLICATIONS OF GF-2573 OR GF-2685 – NORTHERN AND SOUTHERN EUROPE – 2010 TO 2011", Study No. CEMS-4889, Dow Reference ID 102082

The trials carried out in winter wheat and barley included a total of four treated plots to evaluate residue levels with certain other GAPs in addition to the critical GAP. Three plots per trial had two foliar applications with the first application in late autumn prior to dormancy, but no later than December 31st, and the second application in the spring targeted at either BBCH 32, BBCH 39 or BBCH 45 (with the exception of the German trial CEMS-4552E with application at growth stage BBCH 58 and the Hungary trial CEMS-4889C with application during the first week of January 2011). The fourth plot had a single application in the spring targeted at BBCH 45. Of these four treatments, it was the plot receiving two applications with one in the late autumn and one in the spring targeted at BBCH 45 that is considered the critical GAP treatment for winter cereals. In late autumn, XDE-729 methyl was applied at a target rate of 7.5 g ae/ha (GF-2573 at a nominal rate of 1 L/ha) and in spring applications the target application rate for XDE-729 methyl was 6.0 g ae/ha (GF-2573 at a nominal rate of 0.8 L/ha). Since GF-2573 contains cloquintocet-mexyl at a concentration of 7.5 g ai/L, cloquintocet-mexyl was applied at a target rate of 7.5 g ai/ha in the autumn application and at a target rate of 6.0 g ai/ha in the spring application.

To evaluate decline of XDE-729 methyl and XDE-729 acid residues, samples of whole plants were collected from some of the trials at intervals from the day of application to approximately 8 weeks (56 days) after application in the spring for plots with application timing targeted at growth stage BBCH 39 or BBCH 45. Whole plant samples were not collected from plots receiving a spring application targeted at growth stage BBCH 32. Samples of grain and straw were collected at crop maturity consistent with normal commercial harvest and analyzed for residues of XDE-729 methyl and XDE-729 acid.

Residue trials were conducted over a period of two years (2009-2010 and 2010-2011). In winter wheat, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection ( $<0.003$  mg/kg) immediately before the second application in the spring, indicating that the preceding autumn application would not be expected to contribute to any residues observed in grain or straw. Following application in spring targeted at either BBCH 39 or BBCH 45, residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection ( $<0.003$  mg/kg) by 14 to 17 days after application. Residues of XDE 729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain or straw in any of the twenty two winter wheat trials (11 trials each in the northern and southern EU climatic zones). Residues of cloquintocet-mexyl and cloquintocet were not detected ( $<0.005$  mg/kg) in grain or straw in any of the twenty two winter wheat trials.

For the purposes of the calculation of the STMR/HR and MRL according to the OECD calculator, where the residue summary tables report ND ( $<0.003$  mg/kg), the LOQ value (i.e.  $<0.01$  mg/kg) has been used, since the method of analysis of the residue levels is validated down to the LOQ.

The above summary accurately reflects the results found in both the Southern and Northern zone and the rate/time and number of applications are comparable to the GAP table, no differences were found between the two data sets.

### Winter Barley

Reference: Rawle, N. W., 2011 "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN WINTER BARLEY AT INTERVALS AND HARVEST FOLLOWING MULTIPLE APPLICATIONS OF GF-2573 – NORTHERN AND SOUTHERN EUROPE – 2009 TO 2010", Study No. CEMS-4553, Dow Reference ID 090119

Davine, H. C., 2012 "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN WINTER BARLEY AT INTERVALS AND HARVEST FOLLOWING APPLICATIONS OF GF-2573 OR GF-2685 – NORTHERN AND SOUTHERN EUROPE – 2010 TO 2011", Study No. CEMS-4890, Dow Reference ID 102083

Residue trials were conducted over a period of two years (2010 and 2011). The same study design and treatments as described for the winter wheat trials were also used in winter barley trials.

There were a total of 21 winter barley trials conducted with 10 in the northern EU climatic zone and 11 in the southern EU climatic zone. The first application was made in late autumn prior to dormancy typically at BBCH 20-26, but not later than December 31<sup>st</sup> (with the exception of the Northern French trial CEMS-4690D which was applied on 10th January, however, this was within the +25% limit and therefore acceptable) and the second application in spring targeted at either BBCH 32, BBCH 39 or BBCH 45. As observed with winter wheat, residues of XDE-729 methyl and XDE-729 acid in winter barley whole plants were below the limit of detection (<0.003 mg/kg) immediately before the second application in the spring, indicating that the preceding autumn application would not be expected to contribute to any residues observed in grain or straw.

Following application in spring targeted at either BBCH 39 or BBCH 45, residues of XDE-729 methyl and XDE-729 acid in whole plants were evaluated in a total of 7 decline trials. Of the 7 decline trials, residues were below the limit of detection (<0.003 mg/kg) by 14 – 15 days after application in 4 of the trials. Residues in whole plants fell below the limit of detection (<0.003 mg/kg) by 56 - 60 days after application in two of the trials. However, in one trial in southern France (Trial CEMS-4553D, 1<sup>st</sup> season trial) residues remained above the LOQ in whole plant samples through 56 days after application.

Residues of XDE-729 methyl and XDE-729 acid were not detected (<0.003 mg/kg) in grain and straw, except in the southern France trial mentioned above (CEMS-4553D) where the level of XDE-729 methyl and XDE-729 acid in grain were <0.01 mg/kg. In straw, residues of XDE-729 methyl and XDE-729 acid were

not detected ( $<0.003$  mg/kg) in the 10 trials conducted in the northern EU climatic zone. However, in the 11 trials conducted in the southern EU climatic zone 5 trials had residues of XDE-729 methyl or XDE-729 acid in straw that were  $<0.01$  mg/kg and in one trial (CEMS-4553D, southern France) residues of both XDE-729 methyl and XDE-729 acid in straw exceeded the LOQ (residue at 0.029 and 0.021 mg/kg respectively). In trial CEMS-4553D, the intended application timing for a treatment that was targeted at BBCH 39 was missed and was made instead at the same time as the application targeted at BBCH 45 (made at BBCH 45-51). Since residues in straw were slightly greater in the treatment that was originally targeted for BBCH 39, the residue values from that treatment were selected for use as critical residue values from that trial.

As noted in the study report, the barley in the southern France trial (CEMS-4553D) was shorter than normal and the crop yield was less than normal. The notifier states that this is believed to have been caused by poor plant growth conditions related to high temperatures and low rainfall combined with soil having poor water retention due to high sand content. Additionally, the spring applications targeted at BBCH 39 or BBCH 45 were applied later than planned (at BBCH 45-51) in this trial due to adverse weather conditions. Residues of XDE-729 methyl and XDE-729 acid in grain and straw were not detected ( $<0.003$  mg/kg) in barley in this trial when the spring application took place at BBCH 32. However, in the plots in which the spring application took place when the crop was at growth stage BBCH 45-51, residues of XDE-729 methyl and XDE-729 acid in grain were detected, but were below the LOQ (0.01 mg/kg), but residues in straw were above the LOQ (0.016-0.029 mg/kg). The applicant states that the adverse growing conditions late in the season along with the somewhat late application timing are responsible for the higher residue levels of XDE-729 methyl and XDE-729 acid observed in this trial. Residues of cloquintocet-mexyl and cloquintocet were not detected ( $<0.005$  mg/kg) in grain or straw in any of the 21 winter barley trials.

For the purposes of the calculation of the STMR/HR and MRL according to the OECD calculator, where the residue summary tables report nd ( $<0.003$  mg/kg), the LOQ value (i.e. 0.01 mg/kg) has been used instead, since the method of analysis of the residue levels is validated down to the LOQ. The values in the trials that were above the limit of detection, but below the LOQ, have been reported in parenthesis in the table but again, the LOQ (i.e. 0.01 mg/kg) value will be used for estimation of STMR and MRL.

The above summary accurately reflects the results found in the Southern and Northern zone and the rate/time and number of applications are comparable to the GAP table. However, it is noteworthy that in the Southern zone the degradation time observed in the whole plant samples was longer. Also residues in straw were higher (above the LOQ); however, the higher results came from the French trial (CEMS-4553D), for which adverse weather conditions were reported, and the

second application was made late (BBCH 45-51). The second season's trial results showed residues of XDE-729 methyl and XDE-729 acid in whole plants when applied at BBCH 45 was not detected ( $<0.003$  mg/kg) and therefore provides confirmatory data that the French trial results were attributed to the adverse weather conditions and the late timing of the second application and therefore an outlier.

### Spring Wheat

Reference: Devine, H. C., 2011 "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN SPRING WHEAT AT INTERVALS AND HARVEST FOLLOWING SINGLE APPLICATIONS OF GF-2573 – NORTHERN AND SOUTHERN EUROPE – 2010", Study No. CEMS-4719, Dow Reference ID 101589

Devine, H. C., 2011 "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN SPRING WHEAT AT INTERVALS AND HARVEST FOLLOWING SINGLE APPLICATIONS OF GF-2573 – NORTHERN AND SOUTHERN EUROPE – 2010", Study No. CEMS-4719, Dow Reference ID 101589

Residue trials were conducted over a period of two years (2010 and 2011). In these trials the critical GAP was based on a single application of GF-2573 targeted at a XDE-729 methyl rate of 6.0 g a.s/ha to wheat in the BBCH 45 growth stage. The target nominal application rate of cloquintocet-mexyl included in the application was 6.0 g a/ha. In addition to this treatment, there were two other treatments included in the trials in which a single application of GF-2573 was targeted at either growth stage BBCH 32 or BBCH 39 with the same target application rate, XDE-729 methyl at 6.0 g a.s/ha.

Seven trials (4 in northern Europe and 3 in southern Europe) were completed during 2010 since one of the four planned trials in southern Europe was cancelled. Twelve trials were conducted during 2011 (6 trials each in the northern and southern European climatic zones). Therefore, over the two year period there were a total of 19 trials conducted with 10 trials in the northern EU climatic zone and 9 trials in the southern EU climatic zone.

Whole plant samples were collected in decline trials at approximately 0, 7, 14 and 28 days after application to spring wheat in the treatments where the application was targeted at either growth stage BBCH 39 or BBCH 45. Residues of XDE-729 methyl and XDE-729 acid in whole plants were generally below or at the limit of detection ( $<0.003$  mg/kg) by 12 to 14 days after application although in one trial residues of XDE-729 methyl were  $<0.01$  mg/kg at 12 days after application.



Residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in grain in any of the nineteen spring wheat trials conducted over the two year period. In straw, XDE-729 methyl was below the LOQ ( $<0.01$  mg/kg), except for two trial sites, one in southern France CEMS-4719G and one in Poland (CEMS-5001C), where the residue of XDE-729 methyl was 0.02 mg/kg and 0.016 mg/kg respectively when the treatment was applied at BBCH 45 and in these same two trials XDE-729 acid was found at  $<0.01$  mg/kg. Residues of XDE-729 methyl and XDE-729 acid in straw in the remaining trials was typically not detected ( $<0.003$  mg/kg).

Samples of grain and straw from treatments in which application of GF-2573 was targeted at either BBCH 39 or BBCH 45 were analyzed for residues of cloquintocet-mexyl and cloquintocet acid. However, samples of whole plants and samples of grain and straw from treatments in which GF-2573 application was targeted at BBCH 32 were not analyzed for residues of cloquintocet-mexyl and cloquintocet acid. Residues of cloquintocet-mexyl and cloquintocet were not detected (ND,  $<0.005$  mg/kg) in grain or straw in any of the nineteen spring wheat trials.

For the purposes of the calculation of the STMR/HR and MRL according to the OECD calculator, where the residue summary tables report ND ( $<0.003$  mg/kg), the LOQ value (i.e.  $<0.01$  mg/kg) has been used instead, since the method of analysis of the residue levels is validated down to the LOQ.

The above summary accurately reflects the results found in the Southern and Northern zone and the rate/time and number of applications are comparable to the GAP table.

## Spring Barley

Reference: Devine, H. C., 2011, "RESIDUES OF XDE-729 AND CLOQUINTOCET-MEXYL IN SPRING BARLEY AT INTERVALS AND HARVEST FOLLOWING SINGLE APPLICATIONS OF GF-2573 – NORTHERN AND SOUTHERN EUROPE – 2010", Study No. CEMR-4720, Dow Reference ID 101590

Devine, H. C., 2012 "RESIDUES OF XDE-729, CLOQUINTOCET AND FLORASULAM IN SPRING BARLEY AT INTERVALS AND HARVEST FOLLOWING APPLICATIONS OF GF-2573, GF-2685 OR GF-2644 – NORTHERN AND SOUTHERN EUROPE – 2011", Study No. CEMS-5002, Dow Reference ID 110412

Residue trials were conducted over a period of two years (2010 and 2011). In these trials the critical GAP was based on was a single application of GF-2573 targeted at a XDE-729 methyl rate of 6.0 g a.s/ha to barley in the BBCH 45 growth stage. The corresponding nominal application rate of cloquintocet-mexyl included in GF-2573 was 6.0 g a.s/ha. In addition to this treatment, there were two other treatments included in the trials in which a single application of GF-2573 was targeted at either growth stage BBCH 32 or BBCH 39 with the same target application rate, XDE-729 methyl at 6.0 g a.s/ha.

Eight trials (4 in northern Europe and 4 in southern Europe) were completed during 2010. Thirteen trials were conducted during 2011 (7 trials in northern Europe and 6 trials in southern Europe). Therefore, over the two year period there were a total of 21 trials conducted with 11 in the northern EU climatic zone and 10 in the southern EU climatic zone.

Whole plant samples were collected in decline trials at approximately 0, 7, 14 and 28 days after application to spring barley in the treatments where the application was targeted at either growth stage BBCH 39 or BBCH 45. Residues of XDE-729 methyl and XDE-729 acid in whole plants were below the limit of detection (<0.003 mg/kg) by 28-29 days after application.

In 20 out of the 21 trials conducted in 2010 and 2011, residues of XDE 729 methyl and XDE-729 acid were not detected (<0.003 mg/kg) in grain. However, in one trial that was conducted in Bulgaria during 2010 (Trial CEMS-4720G), residues of XDE-729 methyl were 0.071 mg/kg in grain when the treatment was applied at BBCH 45. Residues in grain at this trial site in the two other treatments applied at earlier growth stages were also above the LOQ of 0.01 mg/kg. Residues of XDE-729 acid were not detected in grain in the trial conducted in Bulgaria. The applicant states that the conditions at the Bulgaria trial site were reported to be unfavorable for crop growth and development. These conditions included a late

planting date, clay soil which was unfavorable for water availability to the crop, and distribution of rainfall that was not favorable for growing conditions. It was noted that the grain yield was lower than normal with fewer grains per ear and smaller ears than in previous years. It is proposed that the unfavorable growing conditions that resulted in reduced crop development and yield also were responsible for the abnormal residue value for XDE-729 methyl in grain at this trial site. Out of the eight trial sites in 2010, residues of XDE-729 methyl and XDE-729 acid in straw were below the LOQ ( $<0.01$  mg/kg) at six sites. In a trial site in Southern France residues of XDE-729 methyl and XDE-729 acid in straw were 0.013 mg/kg and 0.012 mg/kg, respectively, when GF-2573 was applied at BBCH 45. Additionally, at the trial site in Bulgaria, residues of XDE-729 methyl and XDE-729 acid in straw were 0.124 mg/kg and 0.013 mg/kg, respectively, when GF-2573 was applied at BBCH 45. As discussed previously, the applicant states that unfavorable conditions for crop growth and development at the Bulgaria trial site are thought to be responsible for the abnormally high residue levels in this trial site.

The applicant states that the conditions at the Bulgaria trial site in 2010 resulted in abnormally rapid maturity and drying of the crop with a PHI of only 33 days from application at growth stage BBCH 45 until harvest. The PHIs from application at BBCH 45 until harvest for the nine other trials conducted in spring barley in southern Europe ranged from 43 to 56 days, with an average of 51 days. So, the 2010 Bulgaria trial (Trial CEMS-4720G) had a PHI for application at BBCH 45 that was 18 days shorter than the average for the other trials and was 10 days shorter than the next shortest PHI among the 10 spring barley trials. Additionally, another trial in spring barley was conducted in Bulgaria during 2011 (Trial CEMS-5002M) and following application at growth stage BBCH 45, residues of XDE-729 methyl and XDE-729 acid were not detected ( $<0.003$  mg/kg) in both grain and straw. Following full evaluation of the residue data, it is agreed that trial CEMS-4720G is an outlier and is not appropriate for use in setting a MRL in grain. Given all of the other trials in the submission demonstrate residues in grain are  $<LOQ$ , and the study on the metabolism in wheat supports an LOQ situation in grain, CRD agree it is reasonable to assume the data from this trial may be regarded as an outlier.

Samples of grain and straw from treatments in which application of GF-2573 was targeted at either BBCH 39 or BBCH 45 were analyzed for residues of cloquintocet-mexyl and cloquintocet acid. However, samples of whole plants and samples of grain and straw from treatments in which GF-2573 application was targeted at BBCH 32 were not analyzed for residues of cloquintocet-mexyl and cloquintocet acid. Additionally, samples of grain and straw from the 2010 trial conducted in Bulgaria (Trial CEMS-4720G) were not analyzed for residues of cloquintocet-mexyl or cloquintocet since in that trial there was application of a maintenance chemical that contained cloquintocet-mexyl (Axial 50 EC, containing cloquintocet-mexyl at 12.5 g/L) to the treated plots. Residues of cloquintocet-

mexyl and cloquintocet were not detected (ND, <0.005 mg/kg) in grain or straw in any of the twenty spring barley trials from which samples were analyzed.

For the purposes of the calculation of the STMR/HR and MRL according to the OECD calculator, where the residue summary tables report ND (<0.003mg/kg), the LOQ value (i.e. <0.01 mg/kg) has been used instead, since the method of analysis of the residue levels is validated down to the LOQ.

The above summary accurately reflects the results found in the Southern and Northern zone and the rate/time and number of applications are comparable to the GAP table.

The critical values selected from the trials for risk assessment and EU MRL setting purposes are as follows:

**Table B.7.6.1-2**

**XDE-729 Methyl and XDE-729 acid  
Northern Zone**

Crop (situation)	Number of relevant trials	Range of residues* (mg/kg)	STMR (mg/kg)	HR (mg/kg)	Estimated MRL (Grain) (rounded value from OECD calculator)	Estimated MRL† (Straw) (rounded value from OECD calculator)
Winter Wheat	11	Grain: all samples <0.02 Straw: all samples <0.02	0.02 (Grain and Straw)	0.02 (Grain and Straw)	0.02	0.02
Winter Barley	10	Grain: all samples <0.02 Straw: all samples <0.02	0.02 (Grain and Straw)	0.02 (Grain and Straw)	0.02	0.02
Spring Wheat	10	Grain: all samples <0.02 Straw: 9 samples <0.02, one sample 0.026	0.02 (Grain and straw)	0.02 (Grain) 0.026 (straw)	0.02	0.03
Spring Barley	11	Grain: all samples <0.02 Straw: all samples <0.02	0.02 (Grain and Straw)	0.02 (Grain and Straw)	0.02	0.02

\*The residue definition for both risk assessment and enforcement is XDE-729 methyl ester and XDE-729 acid. The residue level is the sum of the two components in the residue definition

†An estimated MRL for straw is shown in the table above; however, at the time of evaluation this information is not required as part of the authorization. It is for information only, with a view to when MRLs will be set for animal feed commodities in future.

**Table B.7.6.1-3**  
**XDE-729 Methyl and XDE-729 acid**  
**Southern Zone**

Crop (situation)	Number of relevant trials	Range of residues* (mg/kg)	STMR (mg/kg)	HR (mg/kg)	Estimated MRL (Grain) (rounded value from OECD calculator)	Estimated MRL† (Straw) (rounded value from OECD calculator)
Winter Wheat	11	Grain: all samples <0.02 Straw: all samples <0.02	0.02 (Grain and Straw)	0.02 (Grain) 0.02 (Straw)	0.02	0.02
Winter Barley	11	Grain: all samples <0.02 Straw: 10 samples <0.02, one sample at 0.05	0.02 (Grain and Straw)	0.02 (Grain) 0.05 (Straw)	0.02	0.06
Spring Wheat	9	Grain: all samples <0.02 Straw: 8 samples <0.02, one sample 0.03	0.02 (Grain and Straw)	0.02 (Grain) 0.03 (Straw)	0.02	0.04
Spring Barley	10	Grain: all samples <0.02 Straw: 8 samples <0.02, one sample 0.025	0.02 (Grain and Straw)	0.02 (Grain) 0.025 (Straw)	0.02	0.03

\*The residue definition for both risk assessment and enforcement is XDE-729 methyl ester and XDE-729 acid. The residue level is the sum of the two components in the residue definition

†An estimated MRL for straw is shown in the table above; however, at the time of evaluation this information is not required as part of the authorization. It is for information only, with a view to when MRLs will be set for animal feed commodities in future.

**B.7.6.2 Analytical method for residues determination**

Olberding, E. L. (2011), Determination of Residues of XDE 729 Methyl Ester and XDE 729 Acid in Agricultural Commodities and Wheat Processed Products using Online Solid-Phase Extraction and Liquid Chromatography with Mass Spectrometry  
Document Number Dow AgroSciences LLC Study Number 140005

Guidelines SANCO/825/00 rev. 8

SANCO/3029/99 rev. 4

Residues of XDE-729 methyl ester and XDE-729 acid are extracted from agricultural commodities by homogenizing and shaking with an acetonitrile/water (80:20) solution. One hundred microliters of a glycerin/methanol solution (10:90) containing 0.025 µg/mL of a mixed stable-isotope internal standard solution are added to a 500-µL aliquot of the extraction solution and the sample is then concentrated to near dryness. The sample extract is then diluted to 1.0 mL with a methanol/water solution (20:80) for analysis. The final solution is purified and analyzed using an online reversed-phase solid-phase extraction (SPE) procedure coupled with liquid chromatography using a Zorbax SB-C8 column (gradient elution: Mobile Phase A – water containing 0.10% formic acid and Mobile Phase B – methanol containing 0.10% formic acid) and positive-ion electrospray tandem mass spectrometry (LC/MS/MS). The MS/MS ion transitions monitored for each analyte are shown below:

XDE-729 methyl  $m/z$  Q1/Q3 345/250 (quantitation)  
 $m/z$  Q1/Q3 345/235 (confirmation 1)  
 $m/z$  Q1/Q3 347/252 (confirmation 2)

XDE-729 acid  $m/z$  Q1/Q3 331/250 (quantitation)  
 $m/z$  Q1/Q3 331/235 (confirmation 1)  
 $m/z$  Q1/Q3 333/252 (confirmation 2)

The method has been validated for a range of crops within the acid, wet, dry, oily and wheat processed products groups including turnip root, wheat forage, barley grain, barley hay, barley straw, wheat grain, wheat hay, wheat straw, apple, orange, canola seed, soybean seed, wheat grain (aspirated grain fractions), wheat grain bran (total), wheat grain bread (whole grain), wheat grain flour (whole meal), wheat grain germ (dry milling), wheat grain gluten, wheat grain shorts and wheat grain starch. A summary of the validation data is presented in Tables B.7.6.2-1 to B.7.6.2-5. Acceptable procedural recoveries were also demonstrated alongside the residue trials data. The method can be considered valid for the determination of the

residues of XDE-729 methyl and XDE-729 acid in the wheat and barley samples from the residues trials and in the storage stability tests.

**Table B.7.6.2-1.**

**Summary of Recovery of XDE-729 Methyl Ester and XDE-729 Acid from Wet Agricultural Commodities (turnip root, wheat forage)**

Analyte	Fortification Level (µg/g)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-729 Ester - Quant	0.010	12	92 - 102	97	2.9	3.0
XDE-729 Ester - Quant	0.100	12	93 - 102	97	2.6	2.6
XDE-729 Ester - Quant	1.00	12	92 - 99	96	2.0	2.1
XDE-729 Ester - Quant	0.010 - 1.00	36	92 - 102	97	2.5	2.6
XDE-729 Acid - Quant	0.010	12	89 - 108	96	6.2	6.5
XDE-729 Acid - Quant	0.100	12	90 - 100	96	3.0	3.1
XDE-729 Acid - Quant	1.00	12	91 - 100	94	2.5	2.6
XDE-729 Acid - Quant	0.010 - 1.00	36	89 - 108	95	4.2	4.4

**Table B.7.6.2-2.**

**Summary of Recovery of XDE-729 Methyl Ester and XDE-729 Acid from Dry Agricultural Commodities (barley grain, barley hay, barley straw, wheat grain, wheat hay, wheat straw)**

Analyte	Fortification Level (µg/g)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-729 Ester - Quant	0.010	36	86 - 107	96	3.9	4.1
XDE-729 Ester - Quant	0.100	36	90 - 109	99	4.4	4.5
XDE-729 Ester - Quant	1.00	36	92 - 111	100	4.3	4.3
XDE-729 Ester - Quant	0.010 - 1.00	108	86 - 111	98	4.4	4.4
XDE-729 Acid - Quant	0.010	36	88 - 111	99	5.6	5.6
XDE-729 Acid - Quant	0.100	36	90 - 108	97	3.7	3.8
XDE-729 Acid - Quant	1.00	36	90 - 102	94	2.6	2.7
XDE-729 Acid - Quant	0.010 - 1.00	108	88 - 111	97	4.5	4.6

**Table B.7.6.2-3.**

**Summary of Recovery of XDE-729 Methyl Ester and XDE-729 Acid from Acidic Agricultural Commodities (apple fruit (whole), orange fruit (whole))**

Analyte	Fortification Level (µg/g)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-729 Ester - Quant	0.010	12	91 - 96	94	1.7	1.8
XDE-729 Ester - Quant	0.100	12	91 - 98	95	2.2	2.3
XDE-729 Ester - Quant	1.00	12	95 - 98	97	0.9	0.9
XDE-729 Ester - Quant	0.010 - 1.00	36	91 - 98	95	2.0	2.1
XDE-729 Acid - Quant	0.010	12	89 - 98	95	2.6	2.7
XDE-729 Acid - Quant	0.100	12	91 - 97	94	2.1	2.2
XDE-729 Acid - Quant	1.00	12	90 - 96	94	1.4	1.5
XDE-729 Acid - Quant	0.010 - 1.00	36	89 - 98	94	2.1	2.2

**Table B.7.6.2-4.**

**Summary of Recovery of XDE-729 Methyl Ester and XDE-729 Acid from Oily Agricultural Commodities (canola seed, soybean seed)**

Analyte	Fortification Level (µg/g)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-729 Ester - Quant	0.010	12	95 - 102	98	2.0	2.1
XDE-729 Ester - Quant	0.100	12	96 - 104	99	2.2	2.2
XDE-729 Ester - Quant	1.00	12	93 - 104	98	3.1	3.1
XDE-729 Ester - Quant	0.010 - 1.00	36	93 - 104	99	2.4	2.5
XDE-729 Acid - Quant	0.010	12	93 - 111	99	4.6	4.6
XDE-729 Acid - Quant	0.100	12	92 - 98	96	1.9	2.0
XDE-729 Acid - Quant	1.00	12	89 - 100	95	2.7	2.9
XDE-729 Acid - Quant	0.010 - 1.00	36	89 - 111	97	3.7	3.8



**Table B.7.6.2-5.**

**Summary of Recovery of XDE-729 Methyl Ester and XDE-729 Acid from Wheat Processed Products (wheat grain + aspirated grain fractions, wheat grain bran (total), wheat grain bread (whole grain), wheat grain flour (whole meal), wheat grain germ (dry milling), wheat grain gluten, wheat grain shorts, wheat grain starch)**

Analyte	Fortification Level (µg/g)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-729 Ester - Quant	0.010	24	93 - 103	98	3.0	3.1
XDE-729 Ester - Quant	0.100	24	94 - 106	99	2.6	2.7
XDE-729 Ester - Quant	1.00	24	94 - 105	99	2.8	2.9
XDE-729 Ester - Quant	0.010 - 1.00	72	93 - 106	99	2.8	2.9
XDE-729 Acid - Quant	0.010	24	80 - 102	91	5.6	6.1
XDE-729 Acid - Quant	0.100	24	77 - 99	91	5.5	6.1
XDE-729 Acid - Quant	1.00	24	75 - 99	91	6.3	6.9
XDE-729 Acid - Quant	0.010 - 1.00	72	75 - 102	91	5.7	6.3

#### Calculated Limits of Detection and Quantitation

The LOD and LOQ for the determination of residues of XDE-729 methyl ester and XDE-729 acid in agricultural commodities were calculated using the standard deviation from the 0.010-µg/g recovery results. The LOD was calculated as three times the standard deviation (3s), and the LOQ was calculated as ten times the standard deviation (10s) of the results.

#### Standard Curve Linearity

Power regression analysis was used to describe the detector response as a function of the calibration standard concentrations (0.075 ng/mL-25.0 ng/mL, equivalent sample concentration 0.003-1.00 µg/g). For the least squares regression equations describing the detector response as a function of the standard calibration curve concentrations, the coefficients of determination ( $r^2$ ) were greater than or equal to 0.999 for all of the calibration curve determinations during the method validation. The results indicate linearity of the detector response as a function of the standard concentration.

#### Recovery Levels and Precision

The method validation study was conducted to determine the recovery levels and the precision of the method for the determination of residues of XDE-729 methyl ester and XDE-729 acid in agricultural commodities. The performance of the analytical method was determined with each set of samples by fortifying aliquots of the appropriate control matrix with a mixed solution of XDE-729 methyl ester and XDE-729 acid and analyzing the set following the procedures described within this evaluation. Samples were fortified at the limit of detection (LOD) of 0.003

µg/g, the limit of quantitation (LOQ) of 0.010 µg/g, and at 0.10 µg/g and 1.00 µg/g. Samples fortified at the LOD were analyzed only to demonstrate observable peaks at the LOD level; the results were not included for average percent recovery calculations. An unfortified control matrix and reagent blank were also included in each set.

For each analyte, the method was validated over the concentration range of 0.01-1.00 mg/kg with a limit of quantitation of 0.01 mg/kg.

The individual recoveries were within the range of 75-111%.

At the 0.01-mg/kg level (LOQ), the mean recoveries were within the range of 91-99%, with relative standard deviations within the range of 1.8-6.5%.

At the 0.10-mg/kg level (10x LOQ), the mean recoveries were within the range of 91-99%, with relative standard deviations within the range of 2.0-6.1%.

At the 1.00-mg/kg level (100x LOQ), the mean recoveries were within the range of 91-100%, with relative standard deviations within the range of 0.9-6.9%.

The above results comply with the acceptance criteria of SANCO/3029/99 rev. 4.

#### Selectivity/Confirmation

The LC/MS/MS method is highly selective for both the quantitation and confirmation of XDE-729 methyl ester and XDE-729 acid. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

XDE-729 ME  $m/z$  345/250 (quantitation)

$m/z$  345/235 (confirmation)

(M+6 ISTD)  $m/z$  351/256 (quantitation)

XDE-729 acid  $m/z$  331/250 (quantitation)

$m/z$  331/285 (confirmation)

(M+6 ISTD)  $m/z$  337/256 (quantitation)

Confirmation was determined according to Commission Decision (2002/657/EC).

The confirmation ratios for each analyte were determined by calculating the peak area ratios of the confirmation transition to the quantitation transition.

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards, and the confirmation ratios of the analytes in the samples were  $\pm 20\%$  of the average confirmation ratios of the standards. The confirmation ratios for each analyte in all sample matrices were

within  $\pm 20\%$  of the average confirmation ratios of the standards, indicating that the method is selective for the determination of XDE-729 methyl ester and XDE-729 acid in agricultural commodities and wheat processed products. This data is contained in the report.

#### Matrix effects

Matrix effects were determined by comparing the peak areas of solvent calibration standards to peak areas of matrix-matched standards at a single concentration level. For XDE-729 methyl ester, matrix effects ranged from -28% to 9% across all crops. For XDE-729 acid, matrix effects ranged from -7% to 10% across all crops. Matrix effects are normalized however through the use of stable-isotope internal standards, resulting in accurate quantitative results.

In this assay, the analytes and internal standards are quantitated using MS/MS transitions characteristic of each compound. When using stable-isotope labelled internal standards, there is a possibility that isotopic contributions will occur between the transitions used for quantitation of the unlabelled and labelled compounds. The degree of isotopic crossover for each analyte and its respective stable isotope internal standard was determined and expressed as the crossover factor. The study report demonstrates that the analyte  $\rightarrow$  ISTD crossover contribution was minimal for the concentration range of the calibration curve and the concentration of the labelled internal standard. As a result, no significant mass spectral isotopic crossover was observed and therefore no correction of the measured quantitation ratio was performed. The study report states however that if through use of the method isotopic crossover is encountered, it should be assessed and the respective quantitation ratios corrected for accurate determination of concentrations.

#### Stability of Solutions and Sample Extracts

Stock solutions of XDE-729 methyl ester and XDE-729 acid prepared in methanol were tested after 295 days of storage at ambient temperature and were found to be stable.

Calibration standard solutions of XDE-729 methyl ester and XDE-729 acid prepared in methanol/water (20:80) were tested after 131 days of storage at approximately 4 °C and were found to be stable.

The stability of the final sample extracts was evaluated as part of the current study. Final sample extracts were evaluated for a storage period of 4 days. For XDE-729 methyl ester, on Day 0 the recoveries ranged from 97-103%, while on Day 4, the recoveries ranged from 96-102%. For XDE-729 acid, on Day 0 the recoveries ranged from 92-105%, while on Day 4, the recoveries ranged from 90-112%. These results comply with the acceptance criteria of SANCO/825/00/rev. 8.1.

### Extraction Efficiency

The extraction efficiency of this method was evaluated using representative wheat matrices from a XDE-729 methyl ester nature of residue study. Samples containing incurred  $^{14}\text{C}$  residues were reanalyzed with the sample analysis procedure described above. Results obtained using the analytical method were equivalent to those obtained in the metabolism study, demonstrating the suitability of this analytical method for the determination of XDE-729 methyl ester and XDE-729 acid in plant matrices.

### **Analytical method for determination of residue levels of the safener.**

Reference: McLean, N. (2006) Method Validation Report for the Determination of Cloquintocet-mexyl and its Acid Metabolite in Wheat using Enviro-Test Laboratories Method M313, Enviro-Test Laboratories Study Number ETL04DOW05  
Enviro-Test Laboratories Method M313  
U.S. EPA MRID 46908309  
PMRA Number 1283350  
PMRA Sub Number 2006-4728

This method has been submitted in support of both pre-registration data requirements and post-registration monitoring, and control for components included in the residue definition for plants and animals. An enforcement method of analysis is not required for determination of the safener in plant matrices in the context of this evaluation for authorisation of the active substance. The method is evaluated therefore as a pre-registration method that has been used to determine residues levels of safener in the submitted residue field trials.

Matrix, limit of quantitation	wheat forage	(wet crops)	0.01 mg/kg
	wheat grain	(dry crops)	0.01 mg/kg
	wheat hay	(dry crops)	0.01 mg/kg
	wheat straw	(dry crops)	0.01 mg/kg
Description	<u>Scope</u>		
	This method is applicable for the quantitative determination of residues of cloquintocet-mexyl and cloquintocet acid in agricultural commodities. The method was validated over the concentration range of 0.01-0.10 mg/kg with a validated limit of quantitation of 0.01 mg/kg.		
	<u>Principle</u>		
	Residues of cloquintocet-mexyl and cloquintocet acid were extracted from a 5.0-gram sample by homogenizing and shaking with two 100-mL portions of an acetone/citrate buffer (80:20) solution. A 1.0-mL aliquot of		

the combined extract was then purified using a Phenomenex Strata-X reversed-phase polymeric solid-phase extraction (SPE) cartridge. After elution from the SPE cartridge with methanol containing 0.10% formic acid, 20 µL of a mixed stable-isotope internal standard solution were added to the eluate yielding a final volume of approximately 2 mL. After preparation, the samples were analyzed by liquid chromatography using a Keystone Aquasil C18 column (gradient elution, Mobile phase A – water and Mobile phase B – 0.1% formic acid in acetonitrile) coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring one MS/MS transition characteristic of each analyte and internal standard.

#### Calibration

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least squares equation which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of five standards over the concentration range of 0.050-2.00 ng/mL (equivalent sample concentration 0.004 µg/g - 0.16 µg/g) demonstrated linearity with correlation coefficients (r) of at least 0.990. It is noted that the concentration range tested does not strictly comply with either SANCO/825/00 rev.8.1 for post enforcement monitoring methods or SANCO/3029/99 rev.4 for guidance in support of pre-registration methods; however, neither of these guidance documents are written specifically for the determination of levels of safener. Given that at the time of evaluation, post enforcement methods of analysis for safener are not required, the RMS consider that given that the calibration range covers the appropriate range for validation of recovery and precision for the method, it may be considered fit for purpose for the pre-registration method for data generation.

#### Validation

For each analyte, the method was validated over the concentration range of 0.01-0.10 mg/kg with a limit of quantitation of 0.01 mg/kg.

The individual recoveries were within the range of 71-112%.

For the validated concentration range of 0.01-0.10 mg/kg, the mean recoveries were within the range of 76-99%, with relative standard deviations within the range of 4.2-8.8%. These results comply with the acceptance criteria of SANCO/825/00/rev. 7 and rev. 8.1.

#### Selectivity/Confirmation

The LC/MS/MS method is highly selective for both the quantitation and confirmation of cloquintocet-mexyl and cloquintocet acid. Analysis of control samples resulted in no significant signals at the expected retention

	<p>times of the analytes. Identification is ensured by monitoring one MS/MS transition for each analyte and internal standard as follows:</p> <table> <tr> <td>cloquintocet-mexyl</td><td><math>m/z</math> 336/238 (quantitation)</td></tr> <tr> <td>(M+5 ISTD)</td><td><math>m/z</math> 341/243 (quantitation)</td></tr> <tr> <td>cloquintocet acid</td><td><math>m/z</math> 238/179 (quantitation)</td></tr> <tr> <td>(M+5 ISTD)</td><td><math>m/z</math> 243/182 (quantitation)</td></tr> </table> <p>The RMS note that the study report contains no chromatograms for the Stable Isotope Internal Standard, this is considered a considerable short coming of the study report. The study report for the ILV of the method (see below Dow AgroSciences LLC Study Number 040096, PTRL Europe Study Number P 798 G) however does contain this information. Therefore, the ILV study report as evaluated below has been used to support the current study (Enviro-Test Laboratories Study Number ETL04DOW05). It is noted that this method is being evaluated as a pre-registration method to support data generation from the submitted field trials, and as such does not require a corresponding ILV study report. Given that in this instance the ILV report addresses the deficiencies in the original study report however, the RMS considers that the ILV study report may be evaluated and relied on to support validation of the method as a method for data generation.</p> <p><u>Stability of Solutions and Sample Extracts</u></p> <p>The stability of the stock solutions, calibration standard solutions, and sample extracts were not evaluated as part of this study.</p> <p><u>Extraction Efficiency</u></p> <p>Extraction efficiency was not addressed for the current validation study. This is not considered to be a data gap however, since the residue trials conducted demonstrate an LOQ situation for the safener.</p> <p><u>Matrix Effects</u></p> <p>Matrix effects were not evaluated as part of this study. However, it is noted that matrix effects are normalized through the use of stable-isotope internal standards.</p>	cloquintocet-mexyl	$m/z$ 336/238 (quantitation)	(M+5 ISTD)	$m/z$ 341/243 (quantitation)	cloquintocet acid	$m/z$ 238/179 (quantitation)	(M+5 ISTD)	$m/z$ 243/182 (quantitation)
cloquintocet-mexyl	$m/z$ 336/238 (quantitation)								
(M+5 ISTD)	$m/z$ 341/243 (quantitation)								
cloquintocet acid	$m/z$ 238/179 (quantitation)								
(M+5 ISTD)	$m/z$ 243/182 (quantitation)								

Table B.7.6.2-6

**Method Validation Results for Analysis of Cloquintocet-Mexyl and Cloquintocet-Acid in Wheat Forage**

Sample I.D.	Dow Agro I.D.	Cloquintocet-acid			Cloquintocet-mexyl		
		Fortification (ng/g)	Result (ng/g)	Result (%)	Fortification (ng/g)	Result (ng/g)	Result (%)
L1341-MB1	Method Blank	-	<5	-	-	<5	-
L1341-1-1	control wheat forage	-	<5	-	-	<5	-
L1341-1+1	control wheat forage	5.00	4.42	88	5.00	3.78	76
L1341-1+2	control wheat forage	10.0	8.82	88	10.0	9.13	91
L1341-1+3	control wheat forage	10.0	7.14	71	10.0	8.32	83
L1341-1+4	control wheat forage	20.0	16.7	84	20.0	17.8	89
L1341-1+5	control wheat forage	20.0	15.0	75	20.0	18.0	90
L1341-1+6	control wheat forage	50.0	40.1	80	50.0	48.6	97
L1341-1+7	control wheat forage	50.0	46.5	93	50.0	53.8	108
L1341-1+8	control wheat forage	100	77.4	77	100	94.7	95
L1341-1+9	control wheat forage	100	80.5	81	100	92.3	92

Average =

81

93

Standard deviation =

7.1

7.3

Relative standard deviation =

8.8

7.8

(n=8)

LOD spike (5.00 ng/g) not included in average and standard deviation.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.6.2-7

**Method Validation Results for Analysis of Cloquintocet-Mexyl and Cloquintocet-Acid in Wheat Hay**

Sample I.D.	Dow Agro I.D.	Cloquintocet-acid			Cloquintocet-mexyl		
		Fortification (ng/g)	Result (ng/g)	Result (%)	Fortification (ng/g)	Result (ng/g)	Result (%)
L1341-MB2	Method Blank	-	<5	-	-	<5	-
L1341-2-1	control wheat hay	-	<5	-	-	<5	-
L1341-2+1	control wheat hay	5.00	3.52	70	5.00	4.05	81
L1341-2+2	control wheat hay	10.0	7.25	73	10.0	9.63	96
L1341-2+3	control wheat hay	10.0	7.58	76	10.0	9.89	99
L1341-2+4	control wheat hay	20.0	16.1	81	20.0	20.5	103
L1341-2+5	control wheat hay	20.0	17.4	87	20.0	21.5	108
L1341-2+6	control wheat hay	50.0	35.5	71	50.0	43.6	87
L1341-2+7	control wheat hay	50.0	45.6	91	50.0	56.1	112
L1341-2+8	control wheat hay	100	78.2	78	100	95.1	95
L1341-2+9	control wheat hay	100	75.8	76	100	91.6	92

Average =

79

99

Standard deviation =

6.9

8.3

Relative standard deviation =

8.7

8.4

(n=8)

LOD spike (5.00 ng/g) not included in average and standard deviation.



**Table B.7.6.2-8. Method Validation Results for Analysis of Cloquintocet-Mexyl and Cloquintocet-Acid in Wheat Grain**

Sample I.D.	Dow Agro I.D.	Cloquintocet-acid			Cloquintocet-mexyl		
		Fortification (ng/g)	Result (ng/g)	Result (%)	Fortification (ng/g)	Result (ng/g)	Result (%)
L1341-MB3	Method Blank	-	<5	-	-	<5	-
L1341-3-1	control wheat grain	-	<5	-	-	<5	-
L1341-3+1	control wheat grain	5.00	3.52	70	5.00	4.43	89
L1341-3+2	control wheat grain	10.0	7.85	79	10.0	8.72	87
L1341-3+3	control wheat grain	10.0	7.61	76	10.0	9.13	91
L1341-3+4	control wheat grain	20.0	16.2	81	20.0	18.9	95
L1341-3+5	control wheat grain	20.0	16.1	81	20.0	20.0	100
L1341-3+6	control wheat grain	50.0	44.7	89	50.0	54.1	108
L1341-3+7	control wheat grain	50.0	39.8	80	50.0	46.6	93
L1341-3+8	control wheat grain	100	88.3	88	100	99.7	100
L1341-3+9	control wheat grain	100	86.9	87	100	99.6	100

Average = 83 97

Standard deviation = 4.7 6.6

Relative standard deviation = 5.7 6.8

(n=8)

LOD spike (5.00 ng/g) not included in average and standard deviation.

**Table B.7.6.2-8. Method Validation Results for Analysis of Cloquintocet-Mexyl and Cloquintocet-Acid in Wheat Straw**

Sample I.D.	Dow Agro I.D.	Cloquintocet-acid			Cloquintocet-mexyl		
		Fortification (ng/g)	Result (ng/g)	Result (%)	Fortification (ng/g)	Result (ng/g)	Result (%)
L1341-MB4	Method Blank	-	<5	-	-	<5	-
L1341-4-1	control wheat straw	-	<5	-	-	<5	-
L1341-4+1	control wheat straw	5.00	3.67	73	5.00	3.81	76
L1341-4+2	control wheat straw	10.0	7.44	74	10.0	8.79	88
L1341-4+3	control wheat straw	10.0	7.68	77	10.0	8.36	84
L1341-4+4	control wheat straw	20.0	15.8	79	20.0	19.0	95
L1341-4+5	control wheat straw	20.0	16.4	82	20.0	19.1	96
L1341-4+6	control wheat straw	50.0	38.6	77	50.0	47.7	95
L1341-4+7	control wheat straw	50.0	36.1	72	50.0	42.7	85
L1341-4+8	control wheat straw	100	74.3	74	100	88.8	89
L1341-4+9	control wheat straw	100	76.0	76	100	94.5	95

Average =

91

Standard deviation =

4.9

Relative standard deviation =

4.2

5.4

(n=8)

LOD spike (5.00 ng/g) not included in average and standard deviation.

**Conclusion**

Overall, there were several areas where problems were encountered with the submitted study report. The study report does not include certificates of analysis, which would be expected to be contained within the study report. As discussed above, the notifier has submitted the method in support of both pre-registration data requirements and post-registration monitoring. The method is not suitable as a monitoring method; however, it is not considered necessary to have a monitoring method for the safener at the time the evaluation was written for the submission of approval of the new active substance XDE-729. As discussed above, there are areas of the validation of the method as written in the current study report that fall short of modern standards; however, the ILV report (see below) contains further data in these areas of validation, which when considered with the validation contained within the current study report as evaluated above, suggest the method is fit for purpose as a pre-registration method for analysis of the levels of safener in the residue trials.

### Independent Laboratory Validation of the Enforcement Method for the Determination of the Safener in Plant Matrices

Reference: Class, T. (2005) Cloquintocet-mexyl: Independent Laboratory Validation of an Analytical Method for the Determination of Cloquintocet-mexyl and its Acid Metabolite in Cereal, Dow AgroSciences LLC Study Number 040096  
 PTRL Europe Study Number P 798 G  
 U.S. EPA MRID 46908312  
 PMRA Number 1283352  
 PMRA Sub Number 2006-4728

This method has been submitted by the notifier in support of both pre-registration data requirements and post-registration monitoring, and control for components included in the residue definition for plants and animals. The method is not suitable as a monitoring method; however, it was not considered necessary to have a monitoring method for the safener at the time the evaluation was written for the submission of authorisation of the new active substance XDE-729. Therefore the method is being evaluated as a pre-registration method to support data generation from the submitted field trials, and as such does not require a corresponding ILV study report. This ILV report addresses the deficiencies in the original study report however, and therefore the RMS considers that the ILV study report may be evaluated and relied on to support validation of the method as a method for data generation.

Matrix, limit of quantitation	wheat shoots (wet crops) 0.01 mg/kg wheat grain (dry crops) 0.01 mg/kg wheat straw (dry crops) 0.01 mg/kg
Description	<p><u>Scope</u></p> <p>The objective of this study was to independently validate Enviro-Test Laboratories method M313, "Determination of Residues of Cloquintocet-mexyl and its Acid Metabolite in Crop Samples by Liquid Chromatography with Tandem Mass Spectrometry Detection."</p> <p>This method is applicable for the quantitative determination of residues of cloquintocet-mexyl and cloquintocet acid in agricultural commodities. The method was validated over the concentration range of 0.01-0.10 mg/kg with a validated limit of quantitation of 0.01 mg/kg.</p> <p><u>Principle</u></p> <p>Residues of cloquintocet-mexyl and cloquintocet acid were extracted from a 5.0-gram sample by homogenizing and shaking with two 100-mL portions of an acetone/citrate buffer (80:20) solution. A 1.0-mL aliquot of the combined extract was then purified using a Phenomenex Strata-X reversed-phase polymeric solid-phase extraction (SPE) cartridge. After</p>

elution from the SPE cartridge with methanol containing 0.10% formic acid, 20 µL of a mixed stable-isotope internal standard solution was added to the eluate, which was subsequently concentrated to remove the acetone. Five-hundred microliters of water were then added to the sample to yield a final volume of approximately 2 mL. After preparation, the samples were analyzed by liquid chromatography using a Keystone Aquasil C18 column coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

#### Calibration

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis without weighting. For the least squares equation which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of six standards over the concentration range of 0.050-2.00 ng/mL demonstrated linearity with correlation coefficients (r) of at least 0.999.

#### Validation

Untreated control wheat grain, straw and shoots were obtained from field trials. The specimens were homogenised frozen with dry ice. One ILV trial of the method was run for each of the 3 cereal types: wheat grain, straw and shoots. Each sample set consisted of the following:

- Two unfortified control samples
- Five control samples fortified at 10 ng/g (LOQ)
- Five control samples fortified at 100 ng/g (10 x LOQ)

For each analyte, the method was validated over the concentration range of 0.01-0.10 mg/kg with a limit of quantitation of 0.01 mg/kg.

The individual recoveries were within the range of 76-119%.

At the 0.01-mg/kg level (LOQ), the mean recoveries were within the range of 79-106%, with relative standard deviations within the range of 2-11%.

At the 0.10-mg/kg level (10x LOQ), the mean recoveries were within the range of 100-109%, with relative standard deviations within the range of 5-6%.

These results comply with the acceptance criteria of SANCO/825/00/rev. 7 and rev. 8.1.

#### Selectivity/Confirmation

The LC/MS/MS method is highly selective for both the quantitation and confirmation of cloquintocet-mexyl and cloquintocet acid. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition

	<p>characteristic of each internal standard as follows:</p> <p>cloquintocet-mexyl <math>m/z</math> 336/238 (quantitation)  <math>m/z</math> 336/179 (confirmation)  (M+5 ISTD) <math>m/z</math> 341/243 (quantitation)</p> <p>cloquintocet acid <math>m/z</math> 238/179 (quantitation)  <math>m/z</math> 238/192 (confirmation)  (M+5 ISTD) <math>m/z</math> 243/182 (quantitation)</p> <p><u>Stability of Solutions and Sample Extracts</u></p> <p>The stability of the stock solutions, calibration standard solutions, and sample extracts was not evaluated as part of this study as it is not a requirement of an independent laboratory validation.</p> <p><u>Matrix Effects</u></p> <p>Matrix effects were not evaluated as part of this study as they are not a requirement of an independent laboratory validation. However, it is noted that matrix effects are normalized through the use of stable-isotope internal standards, resulting in accurate quantitative results irrespective of the magnitude of matrix effects.</p>
--	---

Table B.7.6.2-9.

Validation Data (quantitation)	Matrix	Fortification Level (mg/kg)	Recovery Rate (%)		RSD (%)	n
			mean	range		
cloquintocet- mexyl $m/z$ 336→238	<u>wet crops</u>	0.01	96	89-102	7	5
	wheat shoots	0.10	104	98-112	5	5
		0.01-1.00	100	89-112	7	10
cloquintocet- mexyl $m/z$ 336→238	<u>dry crops</u>	0.01	106	99-119	8	5
	wheat grain	0.10	109	105-118	5	5
		0.01-1.00	108	99-119	6	10
cloquintocet- mexyl $m/z$ 336→238	<u>dry crops</u>	0.01	98	94-100	2	5
	wheat straw	0.10	102	95-111	6	5
		0.01-1.00	100	94-111	5	10

Table B.7.6.2-10.

Validation Data (quantitation)	Matrix	Fortification Level (mg/kg)	Recovery Rate (%)		RSD (%)	n
			mean	range		
cloquintocet- acid <i>m/z</i> 238→179	<u>wet crops</u>	0.01	85	71-94	11	5
	wheat shoots	0.10	101	95-110	6	5
		0.01-1.00	93	71-110	12	10
cloquintocet- acid <i>m/z</i> 238→179	<u>dry crops</u>	0.01	89	80-102	11	5
	wheat grain	0.10	108	103-119	6	5
		0.01-1.00	99	80-119	13	10
cloquintocet- acid <i>m/z</i> 238→179	<u>dry crops</u>	0.01	79	76-85	5	5
	wheat straw	0.10	100	94-108	5	5
		0.01-1.00	89	76-108	13	10

### Conclusions

The method is satisfactorily validated in order to support the use of the method to determine residue levels of safener in residue trials for pre-registration data generation. As a re-registration method, an ILV study is not necessary; however, due to deficiencies in the original method validation report (as discussed above) the ILV study was relied upon as supportive validation data to support the method for data generation. It is noted that the method is slightly modified in the ILV study in that removal of residual acetone in the final SPE extracts was required in order to obtain satisfactory peak shape for the acid metabolite and allow accurate peak area integration. Thus the acetone was evaporated and water (0.5 ml) was added to the remaining methanol/water concentrate to obtain final extracts with an approximate 1/1 methanol/water ratio.

It is noted that there appears to be some modifications to the chromatographic system used in the ILV study (Dow AgroSciences LLC Study Number 040096, PTRL Europe Study Number 798 G) compared to the initial method validation study (McLean, N. (2006) Method Validation Report for the Determination of Cloquintocet-mexyl and its Acid Metabolite in Wheat using Enviro-Test Laboratories Method M313, Enviro-Test Laboratories Study Number ETL04DOW05). In particular, the mobile phase was modified from gradient elution with following solvent system: Mobile Phase A: Water/Mobile Phase B: 0.1% formic acid in acetonitrile to gradient elution using Mobile Phase A: 0.1% formic acid in water/Mobile Phase B: 0.1% formic acid in acetonitrile.

Given that the method as outlined in the primary validation data was the method used to collect the residues data, and the ILV study is being relied on to support this data, rather than being validated as an ILV study fulfilling the requirements of SANCO/825/00/rev. 7 and rev. 8.1, the modification of the solvent system is acceptable.

**B.7.7 Stability of residues prior to analysis****Overall conclusions: Stability of Residues****Plant Matrices**

The frozen storage stability of XDE 729 methyl ester and its major metabolite XDE 729 acid have been determined in crops representing the four European Union crop groupings as part of an ongoing 24 month study. The crops included lettuce (a high-water crop), wheat grain (a dry crop), oilseed rape seed (an oily crop), and oranges (a high-acid crop). Data has been collected to approximately 16 months and indicates that residues of XDE 729 methyl ester and XDE 729 acid are stable, with no observable degradation.

The frozen storage stability of the safener cloquintocet-mexyl and its major metabolite cloquintocet acid have been determined in crops representing the four European Union crop groupings as part of an ongoing 24 month study. The crops included lettuce (a high-water crop), wheat grain (a dry crop), oilseed rape seed (an oily crop), and oranges (a high-acid crop). Data has been collected to 338 days (approximately 11 months) and indicates that residues of cloquintocet-mexyl and cloquintocet acid are stable, with no observable degradation.

**Animal Tissues**

The frozen storage stability of XDE 729 methyl ester and its major metabolites, XDE 729 acid and X11449757, have been determined in ruminant and poultry tissues as part of an ongoing 24 month study.

For XDE 729 methyl ester and XDE 729, data has been collected to approximately 12 months for bovine muscle, bovine milk, poultry liver, and poultry eggs, and indicates that XDE 729 methyl ester and XDE 729 acid are stable, with no observable degradation.

For X11449757, data has been collected to approximately 6 months for bovine muscle, bovine milk, poultry liver, and poultry eggs, and indicates that X11449757 is stable, with no observable degradation.

**Soil**

The frozen storage stability of XDE 729 methyl ester and its major metabolites, XDE 729 acid and X11449757, have been determined in soil (LUFA 2.2, loamy sand) as part of an ongoing 24 month study. Data has been collected to 12 months and indicates that XDE 729 methyl ester, XDE 729 acid, and X11449757 are stable, with no observable degradation.

**B.7.7.1 Plant Matrices – Lettuce, Wheat Grain, Oilseed Rape Seed and Whole Orange (XDE-729 Methyl Ester and XDE-729 Acid)**

*Report:* Devine, H. C. (2012)

*Title:* X11393728 (XDE 729 Methyl) and X11393729 (XDE 729): Residue Stability Study in Crops under Frozen Storage Conditions.

***Interim Report 2: Sixteen Months Stability Data***

*Document Number:* Dow AgroSciences LLC Study Number 110563, CEMAS Study Number CEMS-4957

*Guidelines:* EC Guideline 1607/VI/97 rev.2, Appendix H 7032/VI/95 rev.5

*Good Laboratory Practices:* Yes

**Summary**

Separate samples of agricultural commodities (lettuce, wheat grain, oilseed rape seed, and whole orange) were fortified with XDE-729 methyl ester and XDE-729 acid at 0.10 mg/kg and were stored in polyethylene containers at  $\leq -18^{\circ}\text{C}$ . The crop selection for frozen storage stability residues was chosen to represent the four European Union crop groupings (high-water content, dry, high-fat content, and high-acid content). These conditions are consistent with the storage of actual field samples. The results of this study indicate that XDE-729 methyl ester and XDE-729 acid in crop samples from field studies can be stored frozen for at least 12 months with no observable degradation of residues.

**Test Procedure**

Five-gram aliquots of the specimens were placed in separate, labelled, polypropylene screw-top bottles. The recovery samples for storage stability analysis were fortified at the beginning of the study with a mixed fortification solution containing both XDE-729 methyl ester and XDE-729 acid to achieve the fortification level of 0.10 mg/kg for each analyte. An additional six spare sets of fortified specimens for each matrix were prepared at the start of the study to allow for any required repeat analyses.

The stored fortified samples were stored in a freezer set to maintain a specimen temperature of  $\leq -18^{\circ}\text{C}$ . The bulk unfortified control specimens were also stored at  $\leq -18^{\circ}\text{C}$ .



### Analytical Method

#### Scope

The analytical method used for the determination of XDE-729 methyl ester and XDE-729 acid was Dow AgroSciences Method 110005, "Determination of Residues of XDE-729 Methyl Ester and XDE-729 Acid in Agricultural Commodities and Wheat Processed Products using Online Solid-Phase Extraction and Liquid Chromatography with Mass Spectrometry". This method is applicable for the quantitative determination of residues of XDE-729 methyl ester and XDE-729 acid in agricultural commodities representative of the four European crop groupings and wheat processed products. The method was validated over the concentration range of 0.01-1.00 mg/kg with a validated limit of quantitation of 0.01 mg/kg.

#### Principle

Residues of XDE-729 methyl ester and XDE-729 acid were extracted from a 5.0-gram sample by homogenizing and shaking with 100.0 mL of an acetonitrile/water (80:20) solution. One-hundred microliters of a glycerin/methanol solution (10:90 w/v) containing a mixed stable-isotope internal standard were added to a 500-µL aliquot of the acetonitrile/water extraction solution and the sample was concentrated to near dryness. The sample extract was then diluted to 1.0 mL with a methanol/water (20:80) solution for analysis. After preparation, the solution was purified using a reversed-phase online solid-phase extraction procedure and analyzed by liquid chromatography using a Zorbax SB-C8 column (gradient elution: Mobile Phase A – water containing 0.10% formic acid and Mobile Phase B – methanol containing 0.10% formic acid) coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

#### Calibration

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting.

#### Method Performance

The efficiency of the analytical method was determined at the time of analysis for each sampling event by creating two procedural recovery (freshly fortified) samples at the initial time point and at each of the following time points; 97 days, 120 days, 174 days, and 366 days, and analysing them according to the above method.

For XDE-729 methyl ester, the mean recoveries were within the range of 87-111% with standard deviations within the range of 4.2-7.2%.

For XDE-729 acid, the mean recoveries were within the range 88-110% with standard deviations within the range of 3.3-6.7%.

The storage stability sample concentrations were corrected for the mean recovery values of the procedural samples.

Table B.7.7.1-1

## Results of Frozen Storage Stability in Wheat Grain

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Wheat Grain	X11393728 (XDE-729 methyl ester)	108	0.1	0.1018	102	0.0943	94
				0.1	0.1027	103	0.0951	95
				0.1	0.1052	105	0.0974	97
97	Wheat Grain	X11393728 (XDE-729 methyl ester)	96	0.1	0.0992	99	0.1033	103
				0.1	0.0921	92	0.0959	96
				0.1	0.0932	93	0.0971	97
120	Wheat Grain	X11393728 (XDE-729 methyl ester)	107	0.1	0.1086	109	0.1015	101
				0.1	0.1096	110	0.1024	102
				0.1	0.1086	109	0.1015	101
174	Wheat Grain	X11393728 (XDE-729 methyl ester)	94	0.1	0.0988	99	0.1051	105
				0.1	0.0975	98	0.1037	104
				0.1	0.1009	101	0.1073	107
366	Wheat Grain	X11393728 (XDE-729 methyl ester)	107	0.1	0.1019	102	0.0953	95
				0.1	0.1108	111	0.1036	104
				0.1	0.1068	107	0.0998	100
489	Wheat Grain	X11393728 (XDE-729 methyl ester)	100	0.1	0.1031	103	0.1031	103
				0.1	0.0988	99	0.0988	99
				0.1	0.0978	98	0.0978	98

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg

<sup>b</sup> Corrected for the mean procedural recovery %

% remaining results calculated using unrounded mg/kg result

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Wheat Grain	X11393729 (XDE-729 acid)	103	0.1	0.1055	105	0.1024	102
				0.1	0.0939	94	0.0912	91
				0.1	0.0891	89	0.0865	87
97	Wheat Grain	X11393729 (XDE-729 acid)	n/a <sup>c</sup>	0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
120	Wheat Grain	X11393729 (XDE-729 acid)	105	0.1	0.1032	103	0.0982	98
				0.1	0.1020	102	0.0971	97
				0.1	0.1012	101	0.0964	96
174	Wheat Grain	X11393729 (XDE-729 acid)	98	0.1	0.1059	106	0.1080	108
				0.1	0.1064	106	0.1086	109
				0.1	0.0977	98	0.0997	100
366	Wheat Grain	X11393729 (XDE-729 acid)	107	0.1	0.1079	108	0.1009	101
				0.1	0.1132	113	0.1058	106
				0.1	0.1068	107	0.0998	100
489	Wheat Grain	X11393729 (XDE-729 acid)	93	0.1	0.0972	97	0.1045	104
				0.1	0.0987	99	0.1061	106
				0.1	0.0936	94	0.1006	101

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg

<sup>b</sup> Corrected for the mean procedural recovery %

<sup>c</sup> The X11393729 (XDE-729 acid) data could not be used due to standard problems.

% remaining results calculated using unrounded mg/kg result

Table B.7.7.1-2

## Results of Frozen Storage Stability in Lettuce

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Lettuce	X11393728 (XDE-729 methyl ester)	98	0.1	0.0977	98	0.0997	100
				0.1	0.1015	101	0.1035	104
				0.1	0.0982	98	0.1002	100
97	Lettuce	X11393728 (XDE-729 methyl ester)	92	0.1	0.0829	83	0.0901	90
				0.1	0.0864	86	0.0939	94
				0.1	0.0844	85	0.0921	92
120	Lettuce	X11393728 (XDE-729 methyl ester)	101	0.1	0.0993	99	0.0983	98
				0.1	0.0980	98	0.0970	97
				0.1	0.1004	100	0.0994	99
174	Lettuce	X11393728 (XDE-729 methyl ester)	91	0.1	0.0861	86	0.0946	95
				0.1	0.0762	76	0.0838	84
				0.1	0.0872	87	0.0958	96
366	Lettuce	X11393728 (XDE-729 methyl ester)	95	0.1	0.0876	88	0.0922	92
				0.1	0.0884	88	0.0931	93
				0.1	0.0859	86	0.0904	90
489	Lettuce	X11393728 (XDE-729 methyl ester)	92	0.1	0.0787	79	0.0856	86
				0.1	0.0786	79	0.0854	85
				0.1	0.0780	78	0.0848	85

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %

% remaining results calculated using unrounded mg/kg result

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Lettuce	X11393729 (XDE-729 acid)	100	0.1	0.1010	101	0.1010	101
				0.1	0.1037	104	0.1037	104
				0.1	0.0945	94	0.0945	94
97	Lettuce	X11393729 (XDE-729 acid)	n/a <sup>c</sup>	0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
120	Lettuce	X11393729 (XDE-729 acid)	106	0.1	0.1023	102	0.0965	97
				0.1	0.1020	102	0.0962	96
				0.1	0.1056	106	0.0996	100
174	Lettuce	X11393729 (XDE-729 acid)	93	0.1	0.0973	97	0.1046	105
				0.1	0.0901	90	0.0968	97
				0.1	0.0954	95	0.1026	103
366	Lettuce	X11393729 (XDE-729 acid)	102	0.1	0.1074	107	0.1053	105
				0.1	0.0991	99	0.0972	97
				0.1	0.0946	95	0.0928	93
489	Lettuce	X11393729 (XDE-729 acid)	92	0.1	0.0910	91	0.0990	99
				0.1	0.0933	93	0.1014	101
				0.1	0.0932	93	0.1013	101

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %

The X11393729 (XDE-729 acid) data could not be used due to standard problems.

% remaining results calculated using unrounded mg/kg result

Table B.7.7.1-3

## Results of Frozen Storage Stability in Oilseed Rape Seed

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	100	0.1	0.1007	101	0.1007	101
				0.1	0.1015	102	0.1015	102
				0.1	0.0972	97	0.0972	97
97	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	89	0.1	0.1002	100	0.1125	113
				0.1	0.0930	93	0.1045	105
				0.1	0.0950	95	0.1068	107
120	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	108	0.1	0.1071	107	0.0992	99
				0.1	0.1058	106	0.0979	98
				0.1	0.1068	107	0.0989	99
174	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	95	0.1	0.0968	97	0.1019	102
				0.1	0.0880	88	0.0927	93
				0.1	0.0992	99	0.1044	104
366	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	104	0.1	0.1059	106	0.1019	102
				0.1	0.1028	103	0.0988	99
				0.1	0.1015	101	0.0976	98
489	Oilseed Rape Seed	X11393728 (XDE-729 methyl ester)	95	0.1	0.0930	93	0.0949	95
				0.1	0.0944	94	0.0963	96
				0.1	0.0968	97	0.0987	99

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %

% remaining results calculated using unrounded mg/kg result

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Oilseed Rape Seed	X11393729 (XDE-729 acid)	99	0.1	0.1060	106	0.1070	107
				0.1	0.1042	104	0.1053	105
				0.1	0.1038	104	0.1049	105
97	Oilseed Rape Seed	X11393729 (XDE-729 acid)	n/a <sup>c</sup>	0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
120	Oilseed Rape Seed	X11393729 (XDE-729 acid)	107	0.1	0.1028	103	0.0961	96
				0.1	0.0977	98	0.0913	91
				0.1	0.0992	99	0.0927	93
174	Oilseed Rape Seed	X11393729 (XDE-729 acid)	98	0.1	0.1032	103	0.1053	105
				0.1	0.0988	99	0.1009	101
				0.1	0.1054	105	0.1075	108
366	Oilseed Rape Seed	X11393729 (XDE-729 acid)	105	0.1	0.1171	117	0.1115	112
				0.1	0.1126	113	0.1072	107
				0.1	0.1045	105	0.0996	100
489	Oilseed Rape Seed	X11393729 (XDE-729 acid)	97	0.1	0.0999	100	0.1030	103
				0.1	0.0956	96	0.0986	99
				0.1	0.0957	96	0.0986	99

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %<sup>c</sup> The X11393729 (XDE-729 acid) data could not be used due to standard problems.

% remaining results calculated using unrounded mg/kg result

Table B.7.7.1-4

## Results of Frozen Storage Stability in Whole Oranges

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Whole Oranges	X11393728 (XDE-729 methyl ester)	102	0.1	0.0957	96	0.0938	94
				0.1	0.0983	98	0.0964	96
				0.1	0.1016	100	0.0997	100
97	Whole Oranges	X11393728 (XDE-729 methyl ester)	91	0.1	0.0894	89	0.0982	98
				0.1	0.0922	92	0.1013	101
				0.1	0.0914	91	0.1004	100
120	Whole Oranges	X11393728 (XDE-729 methyl ester)	103	0.1	0.1008	101	0.0979	98
				0.1	0.1006	101	0.0979	98
				0.1	0.1007	101	0.0977	98
174	Whole Oranges	X11393728 (XDE-729 methyl ester)	94	0.1	0.0911	91	0.0970	97
				0.1	0.1030	103	0.1095	110
				0.1	0.0871	87	0.0926	93
366	Whole Oranges	X11393728 (XDE-729 methyl ester)	98	0.1	0.0940	94	0.0960	96
				0.1	0.0945	95	0.0964	96
				0.1	0.0944	94	0.0963	96
489	Whole Oranges	X11393728 (XDE-729 methyl ester)	91	0.1	0.0834	83	0.0916	92
				0.1	0.0835	84	0.0918	92
				0.1	0.0833	83	0.0916	92

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %

% remaining results calculated using unrounded mg/kg result

Actual storage time days	Commodity	Analyte	Mean Procedural Recovery % <sup>a</sup>	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	% Remaining (Uncorrected)	Corrected Amount Found mg/kg <sup>b</sup>	% Remaining (Corrected)
Zero	Whole Oranges	X11393729 (XDE-729 acid)	99	0.1	0.0864	86	0.0873	87
				0.1	0.0939	94	0.0948	95
				0.1	0.0922	92	0.0931	93
97	Whole Oranges	X11393729 (XDE-729 acid)	n/a <sup>c</sup>	0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
				0.1	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>	n/a <sup>c</sup>
120	Whole Oranges	X11393729 (XDE-729 acid)	101	0.1	0.0966	97	0.0957	96
				0.1	0.1006	101	0.0996	100
				0.1	0.1002	100	0.0992	99
174	Whole Oranges	X11393729 (XDE-729 acid)	98	0.1	0.1037	104	0.1058	106
				0.1	0.1111	111	0.1134	113
				0.1	0.0942	94	0.0961	96
366	Whole Oranges	X11393729 (XDE-729 acid)	104	0.1	0.1041	104	0.1001	100
				0.1	0.1066	107	0.1025	102
				0.1	0.1057	106	0.1016	102
489	Whole Oranges	X11393729 (XDE-729 acid)	96	0.1	0.0925	93	0.0964	96
				0.1	0.0929	93	0.0968	97
				0.1	0.0923	92	0.0962	96

<sup>a</sup> Mean of two procedural recoveries both at 0.01 mg/kg<sup>b</sup> Corrected for the mean procedural recovery %<sup>c</sup> The X11393729 (XDE-729 acid) data could not be used due to standard problems.

% remaining results calculated using unrounded mg/kg result

**Table B.7.7.1-5 Results of Frozen Storage Stability, Averaged Values for Wheat Grain**

Actual storage time days	X11393728 (XDE-729 methyl ester)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.1033	103	0.0956	95
97	0.0948	95	0.0988	99
120	0.1089	109	0.1018	101
174	0.0991	99	0.1054	105
366	0.1065	107	0.0996	100
489	0.0999	100	0.0999	100

Actual storage time days	X11393729 (XDE-729 acid)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.0962	96	0.0934	93
97	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>
120	0.1021	102	0.0973	97
174	0.1033	103	0.1055	106
366	0.1093	109	0.1022	102
489	0.0965	97	0.1037	104

<sup>b</sup> Only the data for the X11393728 (XDE-729 methyl ester) analyte is reported at this time point. The X11393729 (XDE-729 acid) data could not be used due to an error in the preparation of the calibration standards for this analyte. A spare set of samples was analysed at an additional time point of 4 months.

% remaining results calculated using unfounded mg/kg result

**Table B.7.7.1-6 Results of Frozen Storage Stability, Averaged Values for Lettuce**

Actual storage time days	X11393728 (XDE-729 methyl ester)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.0991	99	0.1011	101
97	0.0847	85	0.0920	92
120	0.0992	99	0.0982	98
174	0.0832	83	0.0914	92
366	0.0873	87	0.0919	92
489	0.0784	79	0.0853	85

Actual storage time days	X11393729 (XDE-729 acid)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.1033	100	0.0997	100
97	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>
120	0.1033	103	0.0974	98
174	0.0943	94	0.1014	102
366	0.1004	100	0.0984	98
489	0.0925	92	0.1006	100

<sup>b</sup> Only the data for the X11393728 (XDE-729 methyl ester) analyte is reported at this time point. The X11393729 (XDE-729 acid) data could not be used due to an error in the preparation of the calibration standards for this analyte. A spare set of samples was analysed at an additional time point of 4 months.

% remaining results calculated using unrounded mg/kg result



**Table B.7.7.1-7 Results of Frozen Storage Stability, Averaged Values for Oilseed Rape Seed**

Actual storage time days	X11393728 (XDE-729 methyl ester)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.0998	100	0.0998	100
97	0.0961	96	0.1079	108
120	0.1066	107	0.0987	99
174	0.0947	95	0.0996	100
366	0.1034	103	0.0994	100
489	0.0947	95	0.0966	97

Actual storage time days	X11393729 (XDE-729 acid)			
	Average Uncorrected Amount Found mg/kg	% Remaining Uncorrected (Average)	Average Corrected Amount Found mg/kg	% Remaining Corrected (Average)
Zero	0.1047	105	0.1057	106
97	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>
120	0.0999	100	0.0934	93
174	0.1025	102	0.1046	105
366	0.1114	112	0.1061	106
489	0.0971	97	0.1001	100

<sup>b</sup> Only the data for the X11393728 (XDE-729 methyl ester) analyte is reported at this time point. The X11393729 (XDE-729 acid) data could not be used due to an error in the preparation of the calibration standards for this analyte. A spare set of samples was analysed at an additional time point of 4 months.

% remaining results calculated using unrounded mg/kg result



**Table B.7.7.1-8 Results of Frozen Storage Stability, Averaged Values for Whole Oranges**

Actual storage time days	X11393728 (XDE-729 methyl ester)			
	Average Uncorrected Amount Found	% Remaining Uncorrected (Average)	Average Corrected Amount Found	% Remaining Corrected (Average)
	mg/kg		mg/kg	
Zero	0.0985	99	0.0966	97
97	0.0910	91	0.1000	100
120	0.1008	101	0.0978	98
174	0.0937	94	0.0997	100
366	0.0943	94	0.0962	96
489	0.0834	83	0.0917	92

Actual storage time days	X11393729 (XDE-729 acid)			
	Average Uncorrected Amount Found	% Remaining Uncorrected (Average)	Average Corrected Amount Found	% Remaining Corrected (Average)
	mg/kg		mg/kg	
Zero	0.0908	91	0.0917	92
97	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>	n/a <sup>b</sup>
120	0.0992	99	0.0982	98
174	0.1030	103	0.1051	105
366	0.1054	105	0.1014	101
489	0.0926	93	0.0964	96

<sup>b</sup> Only the data for the X11393728 (XDE-729 methyl ester) analyte is reported at this time point. The X11393729 (XDE-729 acid) data could not be used due to an error in the preparation of the calibration standards for this analyte. A spare set of samples was analysed at an additional time point of 4 months.

% remaining results calculated using unrounded mg/kg result

### Conclusion

The results of this study indicate that XDE-729 methyl ester and XDE-729 acid in crop samples from field studies can be stored frozen for 16 months with no observable degradation of residues.

**Plant Matrices (Cloquintocet-Mexyl and Cloquintocet Acid)***Report Devine, H. C. (2012)**Title Cloquintocet-Mexyl and Cloquintocet Acid: Residue Stability Study in Crops Under Freezer Storage Conditions. Interim Report 1: Eleven Months Stability Data. Dow AgroSciences LLC Study Number 110564, CEMAS Study Number CEMS-4958**Guidelines EC Guideline 1607/VI/97 rev.2, Appendix H 7032/VI/95 rev.5**Good Laboratory Practices Yes***Summary**

Separate samples of agricultural commodities (lettuce, wheat grain, oilseed rape seed, and whole orange) were fortified with cloquintocet-mexyl and cloquintocet acid at 0.10 mg/kg and were stored in polyethylene containers at  $\leq 18^{\circ}\text{C}$ . The crop selection for frozen storage stability residues was chosen to represent the four European Union crop groupings (high-water content, dry, high-fat content, and high-acid content). These conditions are consistent with the storage of actual field samples. The results of this study indicate that cloquintocet-mexyl and cloquintocet acid in crop samples from field studies can be stored frozen for at least 11 months with no observable degradation of residues.

**Test Procedure**

Five-gram aliquots of the specimens were placed in separate, labelled, polypropylene screw-top bottles. The recovery samples for storage stability analysis were fortified at the beginning of the study with a mixed fortification solution containing both cloquintocet-mexyl and cloquintocet acid to achieve the fortification level of 0.10 mg/kg for each analyte. An additional six spare sets of fortified specimens for each matrix were prepared at the start of the study to allow for any required repeat analyses.

The stored fortified samples were stored in a freezer set to maintain a specimen temperature of  $\leq 18^{\circ}\text{C}$ . The bulk unfortified control specimens were also stored at  $\leq 18^{\circ}\text{C}$ .

**Analytical Method (Scope)**

The analytical method used for the determination of cloquintocet-mexyl and cloquintocet acid was Enviro-Test Laboratories Method M313, "Determination of Residues of Cloquintocet-mexyl and its Acid Metabolite in Crop Samples by Liquid Chromatography with Tandem Mass Spectrometry Detection". This method is applicable for the quantitative determination of residues of cloquintocet-mexyl and cloquintocet acid in agricultural commodities representative of the high water content and dry European crop groupings. The method was validated over the concentration range of 0.01 0.10 mg/kg with a validated limit of quantitation of 0.01 mg/kg.

**Principle**

Residues of cloquintocet-mexyl and cloquintocet acid were extracted from a 5.0 gram sample by homogenizing and shaking with two 100 mL portions of an acetone/citrate buffer (80:20) solution. A 1.0 mL aliquot of the combined extract was then purified using a Phenomenex Strata X reversed-phase polymeric solid-phase extraction (SPE) cartridge. After elution from the SPE cartridge with methanol containing 0.10% formic acid, 20 µL of a mixed stable-isotope internal standard solution was added to the eluate, which was subsequently concentrated to remove the acetone. Five-hundred microliters of water were then added to the sample to yield a final volume of approximately 2 mL. After preparation, the samples were analyzed by liquid chromatography using a Keystone Aquasil C18 column coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

**Calibration**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting.

**Method Performance**

The efficiency of the analytical method was determined at the time of analysis for each sampling event by creating two procedural recovery (freshly fortified) samples at the initial time point and at each of the following time points; 93 days, 184 days, and 338 days, and analysing them according to the above method.

For cloquintocet-mexyl, the mean recoveries were within the range of 69-112% with standard deviations within the range of 6.4-18.3%.

For cloquintocet acid, the mean recoveries were within the range 91-109% with standard deviations within the range of 3.7-7.7%.

The storage stability sample concentrations were corrected for the mean recovery values of the procedural samples.

**Table B.7.7.1-9 Results of Frozen Storage Stability in Wheat Grain**

Actual storage time days	Cloquintocet-mexyl			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.0724	0.1049	105
	0.1	0.0599	0.0868	87
	0.1	0.0703	0.1019	102
93	0.1	0.1066	0.0951	95
	0.1	0.1039	0.0928	93
	0.1	0.1121	0.1001	100
184	0.1	0.0990	0.0990	99
	0.1	0.1010	0.1010	101
	0.1	0.0982	0.0982	98
338	0.1	0.1034	0.0995	99
	0.1	0.0887	0.0853	85
	0.1	0.0926	0.0890	89

Actual storage time days	Cloquintocet-acid			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.0949	0.0940	94
	0.1	0.0950	0.0940	94
	0.1	0.0932	0.0923	92
93	0.1	0.1016	0.0996	100
	0.1	0.0893	0.0876	88
	0.1	0.0913	0.0896	90
184	0.1	0.1012	0.1044	104
	0.1	0.1033	0.1069	107
	0.1	0.0985	0.1015	102
338	0.1	0.1013	0.1034	103
	0.1	0.0853	0.0870	87
	0.1	0.0891	0.0910	91

\* Corrected for the mean procedural recovery %

**Summary of procedural recoveries in Wheat Grain**

Actual storage time days	Amount Fortified mg/kg	Cloquintocet-mexyl %	Cloquintocet-acid %
Zero	0.1	74	106
	0.1	63	95
93	0.1	120	99
	0.1	103	104
184	0.1	100	97
	0.1	100	97
338	0.1	103	97
	0.1	104	99
Average =		96	99
SD =		18.3	3.8
Range =		63 - 120	95 - 106
n =		8	8

**Table B.7.7.1-10 Results of Frozen Storage Stability in Lettuce**

Actual storage time days	Cloquintocet-mexyl			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.0831	0.1065	106
	0.1	0.0758	0.0972	97
	0.1	0.0849	0.1089	109
93	0.1	0.1128	0.1106	111
	0.1	0.0889	0.0871	87
	0.1	0.1051	0.1030	103
184	0.1	0.1114	0.1114	111
	0.1	0.1108	0.1108	111
	0.1	0.1099	0.1099	110
338	0.1	0.0991	0.0971	97
	0.1	0.0993	0.0973	97
	0.1	0.1033	0.1012	101

Actual storage time days	Cloquintocet-acid			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.0970	0.0970	97
	0.1	0.1060	0.1060	106
	0.1	0.0977	0.0977	98
93	0.1	0.0972	0.1068	107
	0.1	0.0921	0.1012	101
	0.1	0.0986	0.1083	108
184	0.1	0.1113	0.1136	114
	0.1	0.1072	0.1094	109
	0.1	0.1116	0.1139	114
338	0.1	0.0949	0.0969	97
	0.1	0.0956	0.0976	98
	0.1	0.1017	0.1038	104

\* Corrected for the mean procedural recovery %

**Summary of procedural recoveries in Lettuce**

Actual storage time days	Amount Fortified mg/kg	Cloquintocet-mexyl %	Cloquintocet-acid %
Zero	0.1	77	101
	0.1	78	98
93	0.1	99	93
	0.1	104	89
184	0.1	100	98
	0.1	100	97
338	0.1	101	97
	0.1	102	98
Average =		95	96
SD =		11.0	3.7
Range =		77 - 104	89 - 101
n =		8	8

**Table B.7.7.1-11 Results of Frozen Storage Stability in Rape Seed**

Actual storage time days	Cloquintocet-mexyl			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.1036	0.0950	95
	0.1	0.1091	0.1000	100
	0.1	0.1100	0.1010	101
93	0.1	0.1138	0.1034	103
	0.1	0.1171	0.1064	106
	0.1	0.1108	0.1007	101
184	0.1	0.1163	0.1175	118
	0.1	0.1108	0.1119	112
	0.1	0.1113	0.1124	112
338	0.1	0.1042	0.1074	107
	0.1	0.0967	0.0997	100
	0.1	0.0962	0.0992	99

Actual storage time days	Cloquintocet-acid			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.1059	0.0999	100
	0.1	0.1026	0.0968	97
	0.1	0.1023	0.0966	97
93	0.1	0.1005	0.0975	98
	0.1	0.1057	0.1026	103
	0.1	0.0972	0.0944	94
184	0.1	0.1148	0.1159	116
	0.1	0.1101	0.1112	111
	0.1	0.1119	0.1131	113
338	0.1	0.1010	0.1074	107
	0.1	0.0951	0.1011	101
	0.1	0.0943	0.1003	100

\* Corrected for the mean procedural recovery %

**Summary of procedural recoveries in Rape Seed**

Actual storage time days	Amount Fortified mg/kg	Cloquintocet-mexyl %	Cloquintocet-acid %
Zero	0.1	108	103
	0.1	109	109
93	0.1	112	102
	0.1	107	103
184	0.1	99	99
	0.1	98	99
338	0.1	97	94
	0.1	96	94
Average =		103	100
SD =		6.4	5.0
Range =		96 - 112	94 - 109
n =		8	8

**Table B.7.7.1-12 Results of Frozen Storage Stability in Whole Oranges**

Actual storage time days	Cloquintocet-mexyl			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.1087	0.0970	97
	0.1	0.1128	0.1007	101
	0.1	0.1114	0.0994	99
93	0.1	0.0925	0.1088	109
	0.1	0.1000	0.1177	118
	0.1	0.0979	0.1152	115
184	0.1	0.1190	0.1156	116
	0.1	0.1214	0.1179	118
	0.1	0.1227	0.1192	119
338	0.1	0.0944	0.0953	95
	0.1	0.0970	0.0979	98
	0.1	0.0952	0.0961	96

Actual storage time days	Cloquintocet-acid			
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg*	% Remaining
Zero	0.1	0.1066	0.0978	98
	0.1	0.1054	0.0967	97
	0.1	0.0974	0.0894	89
93	0.1	0.0866	0.0874	87
	0.1	0.0987	0.0997	100
	0.1	0.0946	0.0955	96
184	0.1	0.1221	0.1151	115
	0.1	0.1237	0.1158	116
	0.1	0.1215	0.1147	115
338	0.1	0.0898	0.0945	95
	0.1	0.0940	0.0989	99
	0.1	0.0942	0.0992	99

\* Corrected for the mean procedural recovery.

**Summary of procedural recoveries in Whole Oranges**

Actual storage time days	Amount Fortified mg/kg	Cloquintocet-mexyl %	Cloquintocet-acid %
Zero	0.1	109	110
	0.1	114	107
93	0.1	88	90
	0.1	82	108
184	0.1	100	102
	0.1	106	109
338	0.1	99	96
	0.1	98	94
Average =		100	102
SD =		10.6	7.7
Range =		82 - 114	90 - 110
n =		8	8

**Table B.7.7.1-13**

lettuce (wet crop)	Actual Storage Time (days)	Cloquintocet-Mexyl	
		Average Uncorrected Amount Found mg/kg	Percent Remaining (average)
	Zero	0.0812	81
	93	0.1023	102
	184	0.1107	111
	338	0.1006	101

**Table B.7.7.1-14**

lettuce (wet crop)	Actual Storage Time (days)	Cloquintocet Acid	
		Average Corrected Amount Found mg/kg	Percent Remaining (average)
	Zero	0.1003	100
	93	0.096	96
	184	0.1100	110
	338	0.0974	97

**Table B.7.7.1-15**

wheat grain (dry crop)	Actual Storage Time (days)	Cloquintocet-Mexyl	
		Average Corrected Amount Found mg/kg	Percent Remaining (average)
	Zero	0.0675	68
	93	0.1075	108
	184	0.0994	99
	338	0.0949	95

**Table B.7.7.1-16**

wheat grain (dry crop)	Actual Storage Time (days)	Cloquintocet Acid	
		Average Corrected Amount Found mg/kg	Percent Remaining (average)
	Zero	0.0944	94
	93	0.0941	94
	184	0.1011	101
	338	0.0919	92

**Table B.7.7.1-17**

oilseed rape seed (oily crop)	Actual Storage Time (days)	Cloquintocet-Mexyl	
		Average Corrected Amount Found mg/kg	Percent Remaining (average)
	Zero	0.1076	108
	93	0.1139	114
	184	0.1128	113
	338	0.0990	99



**Table B.7.7.1-18**

oilseed rape seed (oily crop)	Actual Storage Time (days)	Cloquintocet Acid	
		Average Corrected Amount	Percent Remaining
		Found mg/kg	(average)
	Zero	0.1036	104
	93	0.1011	101
	184	0.1123	112
	338	0.0968	97

**Table B.7.7.1-19**

orange, whole (acidic crop)	Actual Storage Time (days)	Cloquintocet-Mexyl	
		Average Corrected Amount	Percent Remaining
		Found mg/kg	(average)
	Zero	0.111	111
	93	0.968	97
	184	0.1210	121
	338	0.0955	96

**Table B.7.7.1-20**

orange, whole (acidic crop)	Actual Storage Time (days)	Cloquintocet Acid	
		Average Corrected Amount	Percent Remaining
		Found mg/kg	(average)
	Zero	0.1031	103
	93	0.0933	93
	184	0.1188	119
	338	0.0927	93

**Conclusion**

The results of this study indicate that cloquintocet-mexyl and cloquintocet-acid in crop samples from field studies can be stored frozen for 11 months with no observable degradation of residues.

**Animal Tissues (XDE-729 Methyl Ester, XDE-729 Acid, and X11449757)***Report* [REDACTED] (2012)*Title* Frozen Storage Stability of Residues of XDE 729 Methyl Ester, XDE 729 Acid, and X11449757 in Animal Matrices – Twelve Months Stability Data for XDE 729 Methyl Ester and XDE 729 Acid and Six Month Stability Data for the Relevant Metabolite X11449757.*Second Interim Report.* Document Number [REDACTED] Study Number 110768  
[REDACTED] Study Number [REDACTED] 5255*Guidelines* EC Guideline 1607/VI/97 rev.2, Appendix H 7032/VI/95 rev.5*Good Laboratory Practices* Yes

The storage stability study was initiated in 2012 to determine the stability of XDE-729 methyl ester and XDE-729 acid and the X11449757 metabolite in animal matrices when stored under frozen conditions for approximately 24 months. This interim report presents the results for up to 12 months ( $\pm 1$  month) of frozen storage for XDE-729 methyl ester and XDE-729 acid and results for up to 6 months ( $\pm 2$  weeks) of frozen storage for X11449757.

**Summary**

Separate samples of animal matrices (bovine muscle, bovine milk, poultry liver, and poultry eggs) were fortified with XDE 729 methyl ester, XDE 729 acid, and X11449757 at 0.10 mg/kg and were stored in 50 mL centrifuge tubes at  $\leq 18$  °C. These conditions are consistent with the storage of actual study samples. The results of this study indicate that XDE 729 methyl ester and XDE 729 acid in animal tissue samples from field studies can be stored frozen for at least 12 months with no observable degradation of residues. The results of this study also indicate that X11449757 in animal tissue samples from field studies can be stored frozen for at least 6 months with no observable degradation of residues.

**Test Procedure**

One-gram aliquots of the specimens were placed in separate, labeled, 50 mL centrifuge tubes. The recovery samples for storage stability analysis were fortified at the beginning of the study with a mixed fortification solution containing XDE 729 methyl ester and XDE 729 acid to achieve the fortification level of 0.10 mg/kg for each analyte. Later, additional recovery samples for storage stability analysis were fortified with X11449757 to achieve the fortification level of 0.10 mg/kg. An additional twelve spare sets of fortified specimens for each matrix were prepared at the start of the study to allow for any required repeat analyses. The stored fortified samples were stored in a freezer set to maintain a specimen temperature of  $\leq 18$  °C. The bulk unfortified control specimens were also stored at  $\leq 18$  °C.

## Analytical Method

### Scope

Two analytical methods were used for the analysis of bovine and poultry samples. The method for the determination of XDE 729 methyl ester and XDE 729 acid utilises the initial extraction procedure of Dow AgroSciences Method 110505, "Method Validation Study for the Determination of Residues of XDE 729 Methyl Ester and XDE 729 Acid in Bovine and Poultry Tissues using Offline Solid-Phase Extraction and Liquid Chromatography with Mass Spectrometry Detection" coupled with the online solid-phase extraction sample purification and analysis conditions of Dow AgroSciences Method 110005, "Determination of Residues of XDE 729 Methyl Ester and XDE 729 Acid in Agricultural Commodities and Wheat Processed Products using Online Solid-Phase Extraction and Liquid Chromatography with Mass Spectrometry".

The method for the determination of X11449757 is the same as that described above except for the addition of the appropriate mass spectrometry parameters.

Each method was validated over the concentration range of 0.01-0.10 mg/kg with a validated limit of quantitation of 0.01 mg/kg.

### Principle

For the determination of XDE 729 methyl ester and XDE 729 acid, residues were extracted from a 1.0 gram bovine or poultry sample by shaking with 20 mL of an acetonitrile/water (80:20) solution and partitioning with 20 mL of n hexanes. One-hundred microliters of a glycerin/methanol solution (10:90 w/v) containing a mixed stable-isotope internal standard were added to a 500 µL aliquot of the acetonitrile/water extraction solution and the sample was concentrated to near dryness. The sample extract was then diluted to 1.0 mL with a methanol/water (20:80) solution for analysis. After preparation, the solution was purified using a reversed-phase online solid-phase extraction procedure and analyzed by liquid chromatography using a Zorbax SB C8 column coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

For the determination of X11449757, the samples were prepared using the same procedure as described above. Residues were extracted from a 1.0 gram bovine or poultry sample by shaking with 20 mL of an acetonitrile/water (80:20) solution and partitioning with 20 mL of n hexanes. One-hundred microliters of a glycerin/methanol solution (10:90 w/v) containing a mixed stable-isotope internal standard were added to a 500 µL aliquot of the acetonitrile/water extraction solution and the sample was concentrated to near dryness. The sample extract was then diluted to 1.0 mL with a methanol/water (20:80) solution for analysis. After preparation, the solution was purified using a reversed-phase online solid-phase extraction procedure and analyzed by liquid chromatography using a Zorbax SB C8 column coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of the analyte and one MS/MS transition characteristic of the internal standard.

**Calibration**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis without weighting.

**Validation**

For each analyte, the method was validated over the concentration range of 0.01-0.10 mg/kg with a limit of quantitation of 0.01 mg/kg.

The individual recoveries were within the range of 65-114%. For the X11449757 confirmation MS/MS transition, there was one recovery (65%) which was slightly below the acceptance criteria of 70-120%.

At the 0.01 mg/kg level (LOQ), the mean recoveries were within the range of 81-107%, with relative standard deviations within the range of 1.4-16.5%.

At the 0.10 mg/kg level (10x LOQ), the mean recoveries were within the range of 93-109%, with relative standard deviations within the range of 0.6-6.8%.

The above results comply with the acceptance criteria of SANCO 825/00/rev. 8.1.

**Method Performance**

For XDE 729 methyl ester and XDE 729 acid, the efficiency of the analytical method was determined at the time of analysis for each sampling event by creating two procedural recovery (freshly fortified) samples at the initial time point and at each of the following time points; 32-33 days, 91-92 days, 147-148 days and 371-372 days, and analysing them according to the above method. For X11449757, the efficiency of the analytical method was determined at the time of analysis for each sampling event by creating two procedural recovery samples at the initial time point, at 29 days, and at 182 days and analysing them according to the above method.

For XDE 729 methyl ester, the mean recoveries were within the range of 96-98% with standard deviations within the range of 6.1-9.8%.

For XDE 729 acid, the mean recoveries were within the range 98-101% with standard deviations within the range of 6.8-8.8%.

For X11449757, the mean recoveries were within the range of 90-103% with standard deviations within the range of 5.7-10.1%.

The storage stability sample concentrations were corrected for the mean recovery values of the procedural samples.

**Table B.7.7.1-21**  
**Results of Frozen Storage Stability in Bovine Muscle**

Analysis Time Point	XDE-729 acid				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1087	0.1030	109	103
	0.1	0.1074	0.1017	107	102
	0.1	0.1068	0.1011	107	101
1 month ( $\pm$ 2 weeks) after application	0.1	0.0927	0.0909	93	91
	0.1	0.0979	0.0960	98	96
	0.1	0.0942	0.0923	94	92
3 months ( $\pm$ 2 weeks) after application	0.1	0.0987	0.1084	99	108
	0.1	0.0941	0.1034	94	103
	0.1	0.0957	0.1051	96	105
5 months ( $\pm$ 2 weeks) after application	0.1	0.0882	0.0909	88	91
	0.1	0.0868	0.0895	87	90
	0.1	0.0886	0.0913	89	91
12 months ( $\pm$ 1 Month) after application	0.1	0.0843	0.1016	84	101
	0.1	0.0791	0.0953	79	95
	0.1	0.0821	0.0989	82	99

Analysis Time Point	XDE-729 methyl ester				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1035	0.0994	104	99
	0.1	0.1033	0.0991	103	99
	0.1	0.1049	0.1007	105	101
1 month ( $\pm$ 2 weeks) after application	0.1	0.1023	0.0956	102	96
	0.1	0.1037	0.0970	104	97
	0.1	0.0982	0.0918	98	92
3 months ( $\pm$ 2 weeks) after application	0.1	0.0976	0.1027	98	103
	0.1	0.0997	0.1050	100	105
	0.1	0.1050	0.1106	105	111
5 months ( $\pm$ 2 weeks) after application	0.1	0.0893	0.0960	89	96
	0.1	0.0881	0.0948	88	95
	0.1	0.0863	0.0928	86	93
12 months ( $\pm$ 1 Month) after application	0.1	0.0804	0.1005	80	101
	0.1	0.0806	0.1007	81	101
	0.1	0.0769	0.0961	77	96

Analysis Time Point	X11449757				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.0882	0.0944	88	94
	0.1	0.0952	0.1020	95	102
	0.1	0.0936	0.1003	94	100
1 month ( $\pm$ 2 weeks) after application	0.1	0.0947	0.1040	95	104
	0.1	0.0903	0.0992	90	99
	0.1	0.0855	0.0939	85	94
3 months ( $\pm$ 2 weeks) after application	0.1	0.0894	0.0971	89	97
	0.1	0.0866	0.0941	87	94
	0.1	0.0857	0.0932	86	93
6 months ( $\pm$ 2 weeks) after application	0.1	0.0763	0.0954	76	95
	0.1	0.0734	0.0918	73	92
	0.1	0.0772	0.0966	77	97

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.7.7.1-22 Results of Frozen Storage Stability in Bovine Milk

Analysis Time Point	XDE-729 acid				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1046	0.0967	105	97
	0.1	0.1082	0.1000	103	100
	0.1	0.1078	0.0996	108	100
1 month ( $\pm$ 2 weeks) after application	0.1	0.1051	0.0992	105	99
	0.1	0.1049	0.0990	105	99
	0.1	0.1050	0.0990	105	99
3 months ( $\pm$ 2 weeks) after application	0.1	0.0990	0.1020	99	102
	0.1	0.1014	0.1046	101	105
	0.1	0.0995	0.1026	100	103
5 months ( $\pm$ 2 weeks) after application	0.1	0.0939	0.0989	94	99
	0.1	0.0898	0.0945	90	95
	0.1	0.0853	0.0897	85	90
12 months ( $\pm$ 1 Month) after application	0.1	0.0877	0.0997	88	100
	0.1	0.0856	0.0973	86	97
	0.1	0.0824	0.0936	82	94

Analysis Time Point	XDE-729 methyl ester				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1034	0.1016	103	102
	0.1	0.1063	0.1044	106	104
	0.1	0.1043	0.1024	104	102
1 month ( $\pm$ 2 weeks) after application	0.1	0.1003	0.0955	100	95
	0.1	0.0997	0.0949	100	95
	0.1	0.0996	0.0948	100	95
3 months ( $\pm$ 2 weeks) after application	0.1	0.1001	0.1065	100	107
	0.1	0.1026	0.1091	103	109
	0.1	0.0987	0.1050	99	105
5 months ( $\pm$ 2 weeks) after application	0.1	0.0921	0.1012	92	101
	0.1	0.0874	0.0960	87	96
	0.1	0.0900	0.0989	90	99
12 months ( $\pm$ 1 Month) after application	0.1	0.0803	0.1003	80	100
	0.1	0.0835	0.1043	83	104
	0.1	0.0897	0.1121	90	112

Analysis Time Point	X11449757				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1072	0.1000	107	100
	0.1	0.1090	0.1017	109	102
	0.1	0.1094	0.1021	109	102
1 month ( $\pm$ 2 weeks) after application	0.1	0.0971	0.0961	97	96
	0.1	0.0947	0.0938	95	94
	0.1	0.0999	0.0989	100	99
3 months ( $\pm$ 2 weeks) after application	0.1	0.0992	0.0963	99	96
	0.1	0.0998	0.0968	100	97
	0.1	0.1001	0.0972	100	97
6 months ( $\pm$ 2 weeks) after application	0.1	0.0937	0.0966	94	97
	0.1	0.0866	0.0893	87	89
	0.1	0.0838	0.0864	84	86

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.



Table B.7.7.1-23 Results of Frozen Storage Stability in Poultry Liver

Analysis Time Point	XDE-729 acid				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1035	0.0991	103	99
	0.1	0.1056	0.1011	100	101
	0.1	0.1081	0.1035	108	104
1 month ( $\pm$ 2 weeks) after application	0.1	0.0958	0.0968	96	97
	0.1	0.1007	0.1017	100	102
	0.1	0.0924	0.0933	92	93
3 months ( $\pm$ 2 weeks) after application	0.1	0.0884	0.0921	88	92
	0.1	0.0932	0.0971	93	97
	0.1	0.0942	0.0982	94	98
5 months ( $\pm$ 2 weeks) after application	0.1	0.0876	0.0932	88	93
	0.1	0.0833	0.0886	83	89
	0.1	0.0873	0.0928	87	93
12 months ( $\pm$ 1 Month) after application	0.1	0.0741	0.0842	74	84
	0.1	0.0738	0.0839	74	84
	0.1	0.0745	0.0847	74	85

Analysis Time Point	XDE-729 methyl ester				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.0965	0.0969	96	97
	0.1	0.0967	0.0970	97	97
	0.1	0.1027	0.1032	103	103
1 month ( $\pm$ 2 weeks) after application	0.1	0.0961	0.0924	96	92
	0.1	0.1027	0.0987	103	99
	0.1	0.0945	0.0909	95	91
3 months ( $\pm$ 2 weeks) after application	0.1	0.0993	0.1003	99	100
	0.1	0.0995	0.1005	99	100
	0.1	0.0992	0.1002	99	100
5 months ( $\pm$ 2 weeks) after application	0.1	0.0799	0.0823	80	82
	0.1	0.0807	0.0832	81	83
	0.1	0.0861	0.0888	86	89
12 months ( $\pm$ 1 Month) after application	0.1	0.0735	0.0844	73	84
	0.1	0.0702	0.0807	70	81
	0.1	0.0688	0.0791	69	79

Analysis Time Point	X11449757				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.0907	0.0841	91	84
	0.1	0.1068	0.0991	107	99
	0.1	0.1076	0.0998	108	100
1 month ( $\pm$ 2 weeks) after application	0.1	0.0899	0.0988	90	99
	0.1	0.0867	0.0953	87	95
	0.1	0.0960	0.1055	96	105
3 months ( $\pm$ 2 weeks) after application	0.1	0.0922	0.0913	92	91
	0.1	0.0881	0.0872	88	87
	0.1	0.0841	0.0833	84	83
6 months ( $\pm$ 2 weeks) after application	0.1	0.0744	0.0886	74	89
	0.1	0.0722	0.0859	72	86
	0.1	0.0720	0.0857	72	86

Table B.7.7.1-24 Results of Frozen Storage Stability in Poultry Eggs

Analysis Time Point	XDE-729 acid				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1069	0.1008	107	101
	0.1	0.1095	0.1033	110	103
	0.1	0.1081	0.1020	108	102
1 month ( $\pm$ 2 weeks) after application	0.1	0.0942	0.0924	94	92
	0.1	0.0978	0.0959	98	96
	0.1	0.0950	0.0932	95	93
3 months ( $\pm$ 2 weeks) after application	0.1	0.0973	0.0983	97	98
	0.1	0.0953	0.0963	95	96
	0.1	0.0992	0.1002	99	100
5 months ( $\pm$ 2 weeks) after application	0.1	0.0903	0.0903	90	90
	0.1	0.0946	0.0946	95	95
	0.1	0.0856	0.0856	86	86
12 months ( $\pm$ 1 Month) after application	0.1	0.0797	0.0916	80	92
	0.1	0.0838	0.0964	84	96
	0.1	0.0848	0.0975	85	97

Analysis Time Point	XDE-729 methyl ester				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.0991	0.0979	99	98
	0.1	0.1061	0.1048	106	105
	0.1	0.0991	0.0979	99	98
1 month ( $\pm$ 2 weeks) after application	0.1	0.1013	0.0965	101	96
	0.1	0.0987	0.0940	99	94
	0.1	0.1009	0.0961	101	96
3 months ( $\pm$ 2 weeks) after application	0.1	0.0976	0.1017	98	102
	0.1	0.1029	0.1072	103	107
	0.1	0.0999	0.1041	100	104
5 months ( $\pm$ 2 weeks) after application	0.1	0.0896	0.0974	90	97
	0.1	0.0862	0.0937	86	94
	0.1	0.0808	0.0878	81	88
12 months ( $\pm$ 1 Month) after application	0.1	0.0775	0.0957	77	96
	0.1	0.0781	0.0964	78	96
	0.1	0.0767	0.0947	77	95

Analysis Time Point	X11449757				
	Amount Fortified mg/kg	Uncorrected Amount Found mg/kg	Corrected Amount Found mg/kg	Uncorrected % Remaining	Corrected % Remaining
Immediately after application	0.1	0.1058	0.1008	106	101
	0.1	0.1061	0.1011	106	101
	0.1	0.1047	0.0997	105	100
1 month ( $\pm$ 2 weeks) after application	0.1	0.0966	0.1006	97	101
	0.1	0.0968	0.1008	97	101
	0.1	0.0870	0.0906	87	91
3 months ( $\pm$ 2 weeks) after application	0.1	0.0463	0.0468	46	47
	0.1	0.0965	0.0975	97	97
	0.1	0.1004	0.1014	100	101
6 months ( $\pm$ 2 weeks) after application	0.1	0.0822	0.0934	82	93
	0.1	0.0819	0.0930	82	93
	0.1	0.0710	0.0806	71	81

**Soil (XDE 729 Methyl Ester, XDE 729 Acid, and X11449757)**

*Report* Lindner, M. (2012)

*Title* Storage Stability of Residues of XDE 729 Methyl Ester, XDE 729 Acid, and the Metabolite X11449757 in Soil. **Interim Report – Twelve Months Stability Data.** Document Number Dow AgroSciences LLC Study Number 110565, Eurofins Analytical Services Study Number S11-03037

*Guidelines* EC Guideline 1607/VI/97 rev.2, Appendix H 7032/VI/95 rev.5

*Good Laboratory Practices* Yes

Summary

Separate samples of soil (LUFA 2.2, loamy sand) were fortified with XDE 729 methyl ester, XDE 729 acid, and X11449757 at 0.50 µg/kg and were stored in glass vials at ≤ 18 °C. These conditions are consistent with the storage of actual study samples. The results of this study indicate that XDE 729 methyl ester, XDE 729 acid, and X11449757 in soil samples from field studies can be stored frozen for at least 12 months with no observable degradation of residues.

Test Procedure

Five-gram aliquots of the specimens were placed in separate, labelled, glass vials. The recovery samples for storage stability analysis were fortified at the beginning of the study with a mixed fortification solution containing both XDE 729 methyl ester, XDE 729 acid, and X11449757 to achieve the fortification level of 0.50 µg/kg for each analyte. Additional spare sets of fortified specimens for each matrix were prepared at the start of the study to allow for any required repeat analyses.

The stored fortified samples were stored in a freezer set to maintain a specimen temperature of ≤ 18 °C. The bulk unfortified control specimens were also stored at ≤ 18 °C.

Analytical MethodScope

The analytical method used for the determination of XDE 729 methyl ester, XDE 729 acid, and X11449757 was Dow AgroSciences Method 110716, “Method Validation Study for the Determination of Residues of X11393728 (XDE 729 Methyl), X119393729 (XDE 729 Acid), and X11449757 (des-Methyl XDE 729 Acid) in Soil using High Performance Liquid Chromatography with Positive-Ion Electrospray Ionization Mass Spectrometry Detection.”. This method is applicable for the quantitative determination of residues of XDE 729 methyl ester, XDE 729 acid, and X11449757 in soil. The method was validated over the concentration range of 0.50 8.0 µg/kg with a validated limit of quantitation of 0.50 µg/kg.

Principle

Residues of XDE 729 methyl ester and its metabolites were extracted from a 5.0 gram soil sample with 25 mL of a methanol/water (50:50) solution containing 0.1% phosphoric acid using accelerated solvent extraction (ASE) at 90 °C and 1500 psi. After extraction, 40 µL of

a mixed stable-isotope internal standard solution were added to a 5.0 mL aliquot of the methanol/water extraction solution, which was subsequently concentrated to approximately 1 mL. One-hundred microliters of acetonitrile were added to the sample extract and the solution was then filtered prior to analysis. The samples were analyzed by liquid chromatography using a Synergi Hydro RP C18 column coupled with positive-ion electrospray tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

#### Calibration

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by power regression analysis without weighting.

#### Method Performance

The efficiency of the analytical method was determined at the time of analysis for each sampling event by creating a minimum of two procedural recovery (freshly fortified) samples at the initial time point and at each of the following time points; 98 days, 219 days, 284 and 373 days and analysing them according to the above method.

For XDE 729 methyl ester, the mean recoveries were within the range of 91-108%.

For XDE 729 acid, the mean recoveries were within the range 95-107%.

For X11449757, the mean recoveries were within the range of 79-104%.

The storage stability sample concentrations were not corrected for the mean recovery values of the procedural samples.

**Table B.7.7.1-25**

soil (loamy sand)	Actual Storage Time (days)	X11393728 (XDE-729 methyl ester)	
		Average Uncorrected Amount Found, µg/kg	Percent Remaining (average)
	Zero	0.4682	91
	98	0.3872	76
	219	0.5468	107
	284	0.5578	109
	373	0.4746	93

**Table B.7.7.1-26**

soil (loamy sand)	Actual Storage Time (days)	X11393729 (XDE-729 acid)	
		Average Uncorrected Amount Found, µg/kg	Percent Remaining (average)
	Zero	0.5303	103
	91	0.4638	91
	212	0.5363	105
	277	0.3757	74
	366	0.5099	100

**Table B.7.7.1-27**

soil (loamy sand)	Actual Storage Time (days)	X11449757	
		Average Uncorrected Amount Found, µg/kg	Percent Remaining (average)
	Zero	0.5311	104
	98	0.3717	73
	219	0.5084	99
	284	0.4728	92
	373	0.4768	93

### Stability of Residues in Sample Extracts

The stability of residues in sample extracts has been evaluated for each method and is presented in Volume 3, Annex B5, Methods of Analysis. A summary, with reference to the appropriate method is provided below for information.

### Plant Matrices

In the multiresidue method (Study Number 110293, Annex B5 Section B.5.2.1), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for storage periods ranging from 6 to 12 days. In general, the mean recoveries of the second injection of sample extracts were within 20% of the mean recoveries obtained from the first injection. Exceptions were observed for the determination of XDE 729 methyl ester in barley grain at the 0.01 mg/kg level where the recovery of the second injection (after 9 days) decreased 22% and for the determination of XDE 729 methyl ester in kale leaves at the 0.01 mg/kg level where the recovery of the second injection (after 10 days) decreased 25%.

In the enforcement method (Study Number 110004, Annex B5 Section B.5.2.3), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 11 days. For XDE 729 methyl ester, on Day 0 the recoveries ranged from 81-99%, while on Day 11, the recoveries ranged from 82-98%. For XDE 729 acid, on Day 0 the recoveries ranged from 76-95%, while on Day 11, the recoveries ranged from 82-97%.

In the data generation method (Study Number 110005, Annex B7, Section B.7.6.2 (see above)), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 4 days. For XDE 729 methyl ester, on Day 0 the recoveries ranged from 97-103%, while on Day 4, the recoveries ranged from 96-102%. For XDE 729 acid, on Day 0 the recoveries ranged from 92-105%, while on Day 4, the recoveries ranged from 90-112%.

### Animal Tissues

In the multiresidue method for bovine and poultry animal tissues (Study Number 110574, Annex B5 Section B.5.2.5), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for storage periods ranging from 8 to 12 days. At the 0.01 mg/kg level (LOQ), the mean recoveries of the second injection of the extracts were within the range of 66-101%, indicating that the sample extracts were stable.

In the multiresidue method for bovine fat (Study Number 110750, Annex B5 Section B.5.2.6), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 11 days. At the 0.01 mg/kg level (LOQ), the mean recoveries of the second injection of the extracts were within the range of 92-94%, indicating that the sample extracts were stable.

In the independent laboratory validation of the animal tissue multiresidue methods for bovine and poultry animal tissues, and bovine fat (Study Number 110294, Annex B5 Section B.5.2.7), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 8 days. At the 0.01 mg/kg (LOQ) and 0.10 mg/kg (10x LOQ) levels, the mean recoveries of the second injection of the extracts were within the range of 65-101%, indicating that the sample extracts were stable.

In the enforcement method (Study Number 110505, Annex B5 Section B.5.2.8), final sample extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 9 days. For XDE 729 methyl ester, on Day 0 the recoveries ranged from 92-95%, while on Day 9, the recoveries ranged from 92-94%. For XDE 729 acid, on Day 0 the recoveries ranged from 92-97%, while on Day 9, the recoveries ranged from 94-98%.

### Soil

In the soil method (Study Number 110716, Annex B5 Section B.5.3.1.1), final extracts containing XDE 729 methyl ester, XDE 729 acid, and X11449757 were evaluated for a storage period of 10 days and were found to be stable when refrigerated.

**Water**

In the water method (Study Number 110718, Annex B5 Section B.5.3.2.1), final extracts containing XDE 729 methyl ester, XDE 729 acid, X11449757, and X11406790 were evaluated for a storage period of 6 days and were found to be stable when refrigerated.

**Air**

In the air monitoring method (Study Number 110028, Annex B5 Section B.5.3.3.1), final extracts containing XDE 729 methyl ester and XDE 729 acid were evaluated for a storage period of 6 days and were found to be stable when stored at room temperature or when refrigerated.

**Body Fluids**

A study for the “Development and Validation of an Analytical Method for the Determination of XDE 729 Methyl Ester and Acid in Body Fluid(s)” was submitted; however, it was not relied upon since XDE-Me is not classified as toxic or highly toxic; therefore monitoring methods for human tissues and body fluids are not required.

**B.7.8 Effects of industrial processing and/or household processing (IIA 6.5, IIIA 8.4)**

Heating during processing will usually inactivate enzymes present in the substrate leaving hydrolysis as the most important degradation mechanism. Therefore, the nature of most processing practices is such that hydrolysis is route of degradation most likely to affect the nature of the residue. Under conditions representative of processing operations, <sup>14</sup>C-XDE-729 methyl is degraded with increased pH and temperature, with formation of one degradate, X11393729, accounting for up to 29.6% of the total radioactivity. <sup>14</sup>C-X11393729 can be regarded as stable to hydrolysis. Therefore, hydrolysis during RAC processing operations does not significantly affect the nature of the residues since both XDE-729 methyl and X11393729 (XDE-729 acid) are proposed as the residue definition for XDE-729 methyl in plants.

Although the levels of residue of XDE-729 methyl and XDE-729 acid in grain from supervised residue trials do not trigger a requirement for processing studies (supervised residue trials resulted in an LOQ residue situation in grain), studies with both wheat and barley were carried out to evaluate residues in processed products. The notifier states that the processing studies were planned and carried out concurrently with the year 2 supervised residue trials as a precautionary measure in the event that any higher residue levels than expected were observed among the year 2 trial results.

There were three trials each for wheat and barley carried out to evaluate the potential for transfer of any residues from grain to processed products. For both wheat and barley, GF-2573 was applied at growth stage BBCH 45 in a single application at an exaggerated rate of



XDE-729 methyl at a nominal rate 30 g ae/ha, which is 5X the maximum rate of 6 g ae/ha for application of XDE-729 methyl in the spring. The trials for both wheat and barley were carried out in Germany, Italy and Spain. Each of the three trials for both wheat and barley were carried out as balance trials with processing following industrial procedures on a laboratory scale. The processed products of wheat that were analyzed for residues were: cleaned grain, middlings, wheat germ, fine bran, coarse bran, total bran, refined flour, white bread, wholemeal bread and wholemeal flour. The processed products of barley that were analyzed for residues were: cleaned grain, pot barley, barley bran, barley flour, brewing malt, malt sprouts, spent grain, flocs, brewer's yeast and beer. Residues of XDE-729 methyl and XDE-729 acid in grain and all processed products from each of the three wheat and the three barley trials in treated as well as untreated samples were not detected (ND, <0.003 mg/kg). These studies demonstrated that residues of XDE-729 methyl are not expected to concentrate in processed fractions of grain.

**Table B.7.8-1****Summary of processing factors**

Crop/processed crop	Number of studies	Transfer factor	% Transference*
Wheat. – no residues of XDE-729 methyl or XDE-729 acid were detected (ND, <0.003 mg/kg) in grain (or processed product produced from the grain) in 3 trials with wheat treated with XDE-729 methyl at a rate of 30 g ae/ha (5X the rate for spring application) at growth stage BBCH 45.	3	N/A**	N/A**
Barley - no residues of XDE-729 methyl or XDE-729 acid were detected (ND, <0.003 mg/kg) in grain (or processed product produced from the grain) in 3 trials with barley treated with XDE-729 methyl at a rate of 30 g ae/ha (5X the rate for spring application) at growth stage BBCH 45.	3	N/A**	N/A**

\* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies.

\*\* No Transfer factor or % Transference were calculated for processed products of wheat or barley since no residues of XDE-729 methyl or XDE-729 acid were detected in grain (ND, <0.003 mg/kg). Additionally, no residues were detected in the processed products produced from the treated wheat and barley grain.

**B.7.8.1 Effects on the nature of the residue**

Report:	Ma, M. (2011) Processing Study to Determine the Nature of Residues of [14C]-XDE-729 and [14C]-X11393729 Following Industrial or Household Preparation. Dow AgroSciences, unpublished Study Number 110369, 28 Oct 2011.
Guidelines:	OECD 507 (16/10/2007) entitled, "Nature of the pesticide residues in processed commodities – high temperature hydrolysis", 16 October 2007
GLP:	Yes

A study was carried out to simulate the conditions of pasteurisation, sterilisation and baking, brewing and boiling.

1 mg/L solutions of  $^{14}\text{C}$ -XDE-729 methyl (radiochemical purity 98.6%) and  $^{14}\text{C}$ -X11393729, (radiochemical purity 95.9%) each radiolabeled in only the pyridine ring were prepared in methanol ( $^{14}\text{C}$ -XDE-729 methyl) and 1:1 methanol:water ( $^{14}\text{C}$ -X11393729). These were buffered with 20 mM citric acid and 2 N sodium hydroxide to achieve the required pH.

Three replicates per set of hydrolysis conditions were prepared for each test compound, for a total of 9 samples per test substance and 18 samples overall. Treated dose solution (10 mL) was pipetted into each labelled vial. The 45-mL samples vials were capped with a Teflon-lined septum cap. The septum was pierced with a syringe needle, which remained in position during processing, to prevent pressure build-up in the samples during heating. Each sample was weighed before and after heating. The samples were heated in a water bath (90 or 100 °C) or autoclave (120 °C) under the following representative processing conditions:

- Pasteurisation: 90°C at pH 4 for 20 min.
- Baking, brewing and boiling: 100°C at pH 5 for 60 min.
- Sterilisation: 120°C at pH 6 for 20 min.

After cooling, the samples were weighed to determine if any volume was lost during heating. Aliquots of the processed samples were analyzed by LSC and HPLC. The sample pH was also measured. Since samples were analysed on the day of the experimental processing conditions, it was unnecessary to assess storage stability. The HPLC column used was a Synergi 4  $\mu\text{m}$  Hydro- $\text{RP}$ , 150 x 4.6 mm (Phenomenex). A direct spike of each sample analyzed by HPLC was compared to the sum of the radioactivity eluted from the column and used to determine chromatographic recovery. HPLC recoveries were generally between 90% and 110%.

An UV detector at 254 nm wavelength was used to determine the retention times of non-radiolabeled standards.

As shown in Table B.7.8.1-1., the final concentrations of the dosing solutions were 1.02-1.06 µg/mL containing 0.41-0.66% co-solvent (methanol). Overall material balance for all nine XDE-729 methyl replicates was 98.7%. Material balance averaged  $97.9\% \pm 1.3\%$ ,  $98.4\% \pm 1.4\%$ , and  $99.9\% \pm 1.2\%$  at pH 4, 5, and 6, respectively. Also in Table B.7.8.1-1., overall material balance for the X11393729 experiments averaged 100.3%. Material balance averaged  $100.4\% \pm 0.2\%$ ,  $100.1\% \pm 0.2\%$ , and  $100.4\% \pm 0.1\%$  at pH 4, 5, and 6, respectively. The material balance values demonstrate that the radioactivity did not dissipate from the test systems during the processing period.

In the  $^{14}\text{C}$ -XDE-729 methyl pH 4, 5 and 6 heated replicates, 99.0%, 93.7% and 69.2% of the radioactivity remained as  $^{14}\text{C}$ -XDE-729 methyl (average replicates/dose solution in the respective tables); these values take into account the purity of the dose solution. There was one degradate formed, X11393729, accounting for 1.6%, 6.3%, and 29.6% of the radioactivity at pH 4, 5, and 6.

In the  $^{14}\text{C}$ -X11393729 pH 4, 5 and 6 heated replicates, 98.5%, 100.7%, and 100.0% of the radioactivity remained as  $^{14}\text{C}$ -X11393729 (average replicates/dose solution in the respective tables); these values take into account the purity of the dose solution. No hydrolysis of  $^{14}\text{C}$ -X11393729 occurred after heating using the three sets of conditions.

Mass spectral analysis confirmed the XDE-729 methyl degradate to be X11393729. After processing of  $^{14}\text{C}$ - XDE-729 methyl (pH 6), X11393729 was confirmed by LC-MS/MS.

**Table B.7.8.1-1.****Industrial and household preparation of XDE-729 results summary**

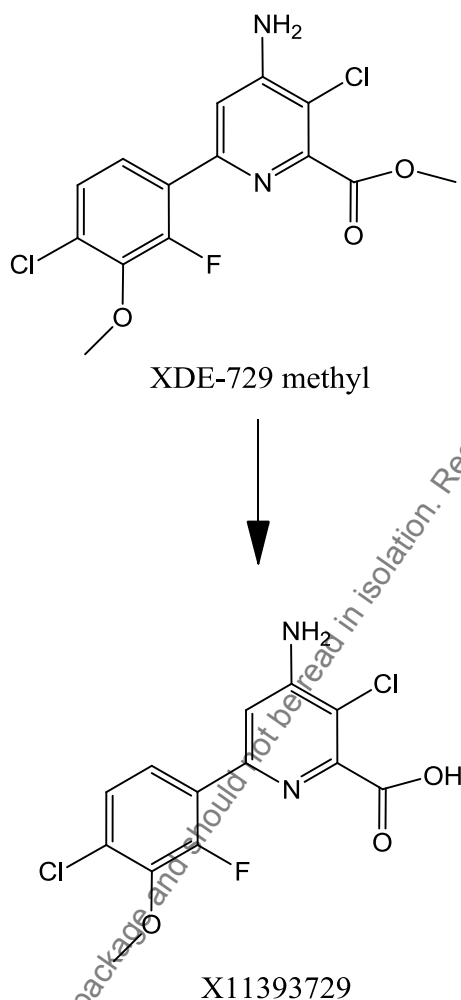
test substance	test conditions	dose conc. (µg/mL)	% recovery	dose soln % parent	average % parent after heating	average % parent as % of dose	average % X11393729 after heating
XDE-729 methyl	pH4 90 °C 20 min	1.05	97.9%	98.3%	97.3%	99.0%	1.6%
XDE-729 methyl	pH5 100 °C 60 min	1.03	98.4%	98.7%	92.5%	93.7%	6.3%
XDE-729 methyl	pH6 120 °C 20 min	1.02	99.9%	99.1%	68.5%	69.2%	29.6%
	average		98.7%				
	std dev		1.1%				
X11393729	pH4 90 °C 20 min	1.04	100.4%	98.5%	97.0%	98.5%	--
X11393729	pH5 100 °C 60 min	1.04	100.1%	96.6%	97.3%	100.7%	--
X11393729	pH6 120 °C 20 min	1.06	100.4%	97.6%	97.6%	100.0%	--
	average		100.3%				
	std dev		0.2%				
	min	1.02					
	max	1.06					

Conclusions

Average mass balance for the nine replicates for each test substance was 98.7% and 100.3%, for XDE-729 methyl and X11393729, respectively.

After processing, the samples were analyzed by HPLC, comparing retention times with an authentic standard.

Under conditions representative of processing operations, <sup>14</sup>C-XDE-729 methyl is degraded with increased pH and temperature, with formation of one degradate, X11393729, accounting for up to 29.6% of the total radioactivity. <sup>14</sup>C-X11393729 can be regarded as stable to hydrolysis.

**Figure B.7.8.1-1. Pathway for XDE-729 methyl during household and industrial Processing****B.7.8.2 Effects on residue levels**

Residues of XDE-729 methyl and XDE-729 acid in wheat and barley grain from the supervised residue trials were below the analytical limit of quantitation (i.e. <0.01 mg/kg), except for one spring barley trial in southern Europe (Bulgaria) in which XDE-729 methyl was 0.071 mg/kg, although XDE-729 acid was ND (<0.003 mg/kg). The RMS agrees with the notifier however that this result is an outlier (see section B.7.6 Residues arising from supervised trials for details). Furthermore, the applicant states that *“based on results of the plant metabolism study, quantifiable residues in grain were not anticipated. However, even if the residue value of 0.071 mg/kg for XDE-729 methyl in barley grain is included when*

*considering the requirement to conduct studies to determine the effect of processing on levels of residue in processed products, the residue level does not exceed that considered significant (i.e. does not exceed 0.1 mg/kg) and it is expected that Total Theoretical Maximum Daily Intake (TMDI) will be less than 10% of the ADI. Therefore, based on results from residue trials it is concluded that studies to evaluate the effects of industrial processing on the magnitude of the residue in processed commodities are not required”*

The above case made by the notifier is acceptable; however, despite the trials demonstrating that residue levels in cereal grains were not sufficiently high to require a processing study, a balance study with 3 trials each was carried out for both wheat and barley, and has been evaluated below for completion.

#### **B.7.8.3 Summary/assessment**

Under conditions representative of processing operations, <sup>14</sup>C-XDE-729 methyl is degraded with increased pH and temperature, with formation of one degradate, X11393729, accounting for up to 29.6% of the total radioactivity. <sup>14</sup>C-X11393729 can be regarded as stable to hydrolysis. Therefore, hydrolysis during RAC processing operations does not significantly affect the nature of the residues.

#### **B.7.8.4 Residue levels - balance studies on a core set of representative processes**

Although residue levels in cereal grains were not sufficiently high to require a processing study, a balance study with 3 trials each was carried out for both wheat and barley.

#### **Wheat Grain Processing**

The transfer of residues of XDE-729 methyl and XDE-729 acid from wheat grain to wheat processed fractions was determined following a single foliar application targeted at 30 g a.e./ha in spray volumes of 405 to 415 L/ha. The wheat grain used in this study was treated with a 5X exaggerated application rate (compared to the maximum application rate in spring of 6.0 g ae/ha) of XDE-729 methyl in order to improve the ability to quantify residues and determine the proportion of residues that transferred from treated wheat grain to processed fractions. Three trials were made in Germany, Italy, and Spain in 2011, as the major producers and representative geographies for wheat in the Northern and Southern Zones. The test material was GF-2573 formulation, an emulsifiable concentrate (EC) containing XDE-729 methyl at a nominal concentration of 7.5 g ae/L and cloquintocet-mexyl (herbicide safener) at a nominal concentrate 7.5 g a.i./L. Field samples were collected at normal commercial harvest, 47-81 days after application.

The processing phase was carried out to obtain samples of cleaned grain, refined flour, middlings, wheat germ, fine bran, coarse bran, total bran, white bread, wholemeal flour and

wholemeal bread from samples taken in the field. Wheat processing was done on a laboratory scale and fully comparable to industrial wheat processing and is shown below.

### Cleaning

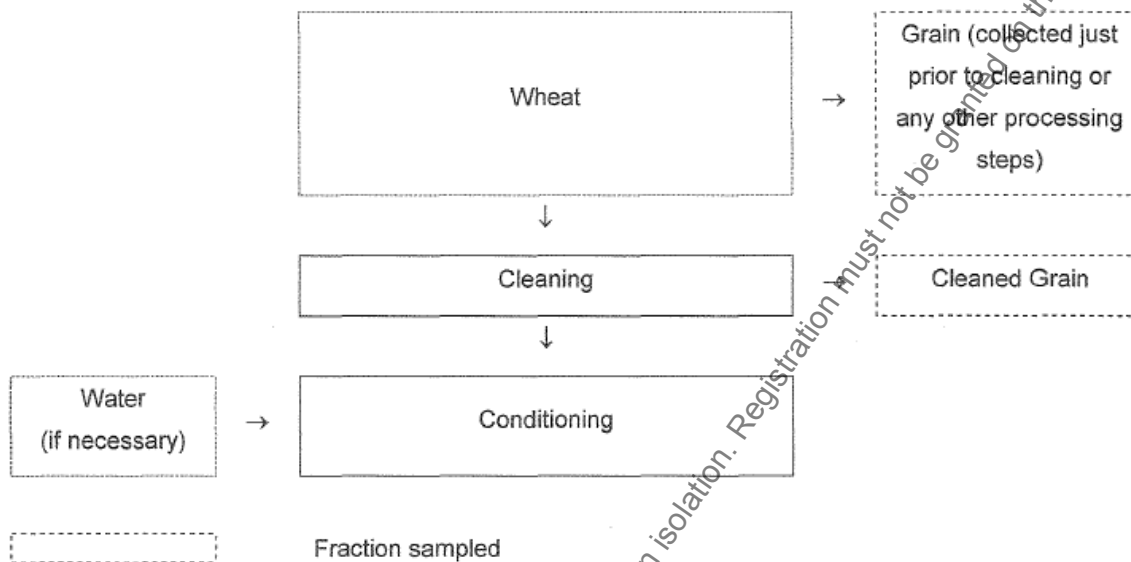
Prior to processing the samples "Grain (collected just prior to cleaning or any other processing steps)" were taken (3 independently collected samples, randomised sampling procedure).

**Cleaning:** The wheat grain was cleaned using Rationel Kornservice sample cleaner SLN3. Cleaning was done in three stages. First the grain was deawned (setting 3 - 9). In the second stage impurities were removed with help of sieves and a cyclone (aspiration setting 10). Lastly the grain was sorted by size grading (2.0mm). The throughput of the machine was set at 5. The settings of the sample cleaner were chosen to the best performance of the process. The cleaned grain material was stored under cool conditions (8.5-10.8°C) for up to 67 days.

**Conditioning:** The grain was conditioned directly one day before milling to Flour Type 550 and wholemeal flour. The moisture content of the grain was determined using a moisture analyser (PCE Europe MB-50) before the start of milling. The grain had initial moisture content between 13.4 and 15.0 %. The optimum moisture content intended was 16%. So these samples were moistened in plastic boxes for 1 day at ambient temperatures. The grain had a moisture content of 15.7-17.2% after conditioning. A second cleaning step after conditioning was not necessary. For the untreated samples the grain was then divided into 2 parts. One part was used to produce the white flour (Type 550). The other part was used to produce wholemeal flour. For the treated samples the cleaned grain was conditioned separately.

### Wheat cleaning processing flowchart

Flowchart



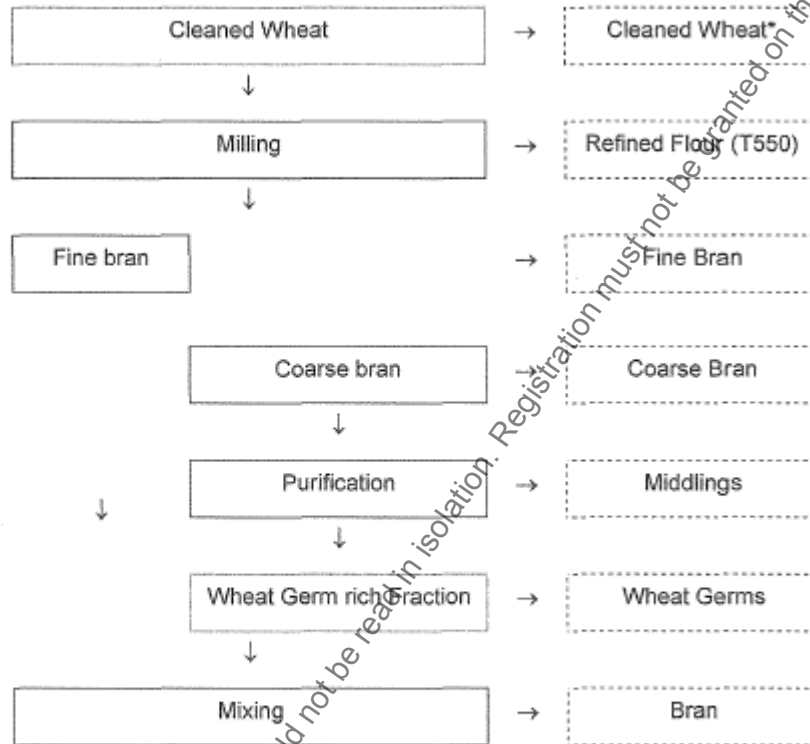
### Wheat Milling (Flour Type 550)

**Milling:** Before processing an extra sample "Cleaned Grain before Refined Flour Type 550" was taken. First a part of the wheat sample was milled to clean the mill and all continuing equipment and to get normal milling conditions at the correct working temperature of the mill. For milling a rolling mill type "Bühler Mahlautomat MLU-202" was used. The mill delivered eight different fractions. Two fractions were the bran fractions and the remaining six fractions were the flour fractions. The specimens "Refined Flour (T550)" "Fine bran" and "Coarse bran" were sampled.

**Purification:** The coarse bran fraction was cleaned with help of a bran duster (BBC Brown Bover 4 QU100LB4). The cleaning of coarse bran delivered the fraction "Wheat Germs" and the "Middlings" which were sampled.

**Mixing:** The "Fine bran" fraction and the "Wheat Germ rich fraction" were mixed by hand in the ratio 1:1. The specimen "Bran" was taken.



**Wheat Milling (Flour Type 550) processing flowchart****Flowchart**

\* Fraction sampled  
Extra cleaned wheat grain samples were taken before processing to Flour Type 550

### White Bread

**Kneading:** All ingredients were placed in the kneading machine (Alexanderwerk). The duration of mixing and kneading was 10 min.

**Fermentation:** The doughs were placed in environmental cabinets (Sanyo MLR-350HT) with a controlled climate at 25.8- 26.4 °C and a relative humidity of 80 % for 25 min. Then the dough was kneaded for 1 minute and again transferred into the cabinet for a second fermentation period of 15 min. When the second fermentation had ended the dough was shortly kneaded manually, divided and manually formed into loaves. These loaves were transferred into the baking forms. The forms were placed in the cabinet followed by a rest period of 20 min (same environmental conditions).

**Baking:** The forms were placed in the flash steam oven (Bartscher 64EX-EM12) and baked at 198.8-198.9°C for 20 min. The bread cooled down and the specimen "White Bread" was taken.

### White bread processing flowchart

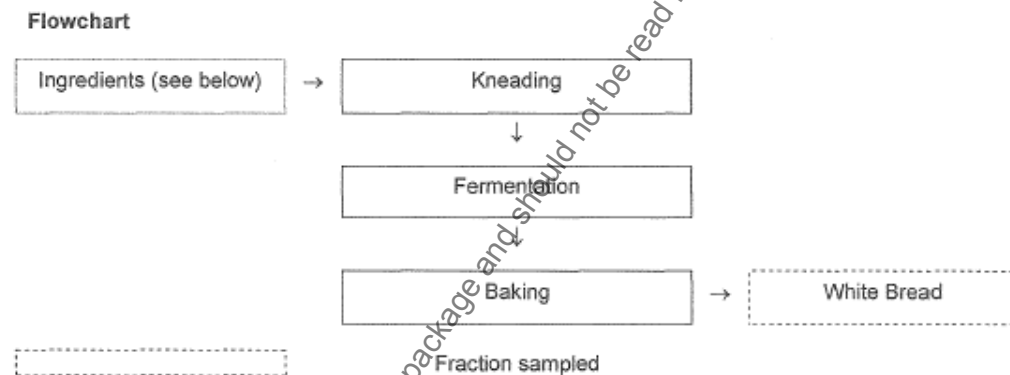


Table B.7.8.4 -1

Ingredients	Dough
Flour (Type 550)	1.5 kg
Salt	2 %
Sugar	2 %
Plant fat or butter	5 %
Ascorbic acid (0.1 % aqueous solution)	4 %
Water	0.8 kg
Powdered milk	3 %
Bread yeast (fresh)	62.31 – 62.94 g*

\* Recommended usage: 1 cube yeast (42 g) for up to 500 g flour. Batch: EX 050112

Basis of percentage is the weight of Flour Type 550 used (except for yeast).

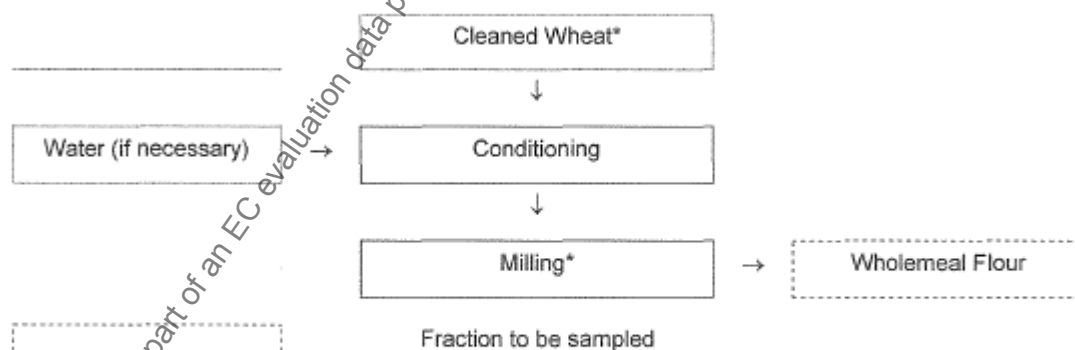
### Details of dough preparation for white bread

#### Wholemeal Flour

**Milling:** First a part of the wheat sample was milled to clean the mill and to get normal milling conditions at the correct working temperature of the mill. For milling a laboratory hammer mill (Perten 3303) was used. After milling the specimen "Wholemeal Flour" was taken.

#### Wholemeal flour processing flowchart

##### Flowchart



\* For milling to wholemeal flour a part of the cleaned conditioned grain (see 5.3 Wheat Milling (Flour Type 550)) was used.

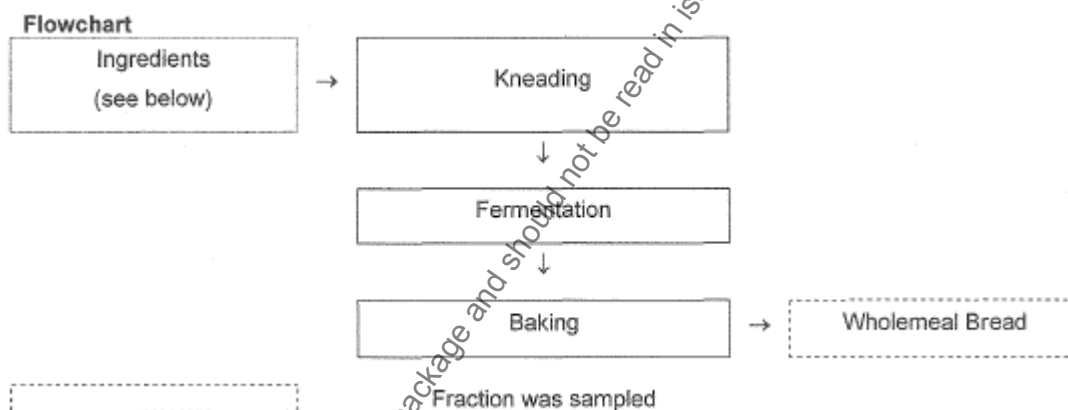
### Wholemeal Bread

**Kneading:** All ingredients were placed in the kneading machine (Aiexanderwerk). The duration of kneading was 10 min.

**Fermentation:** The dough was placed in environmental cabinets with a controlled climate at 26.9-28.2 °C and a relative humidity of 78 - 87 % for 25 min. The dough was kneaded for 1 min and again transferred into the cabinet for a second fermentation period of 15 minutes. When the second fermentation had ended the dough was kneaded manually with an extra minute and was then divided and manually formed into loaves. The loaves were transferred into the baking forms. The forms were placed in the cabinet followed by a rest of 25 min (same environmental conditions).

**Baking:** The forms were placed in the oven and baked at 201.6 - 213.0°C for 30 min. The bread cooled down and the specimen "Wholemeal Bread" was taken.

### Wholemeal Bread processing flowchart



**Table B.7.8.4 -2**

Ingredients	Dough
Wholemeal flour	1.50 kg
Salt	1 %
Sugar	1 %
Plant fat	1 %
Ascorbic acid (0.1 % solution)	10 %
Bread yeast (fresh yeast)	61.41 g – 62.60 g*
Water	0.70 – 0.71 kg

\* Recommended usage: 1 cube yeast (42 g) for up to 500 g flour.

Basis of percentage is the weight of whole meal flour used (except for yeast). Weight of water was adapted to the properties of the flour.

#### Details of dough preparation for wholemeal bread

Residues of XDE-729 methyl and XDE-729 acid were determined using Dow AgroSciences Crop Method 110005 with liquid chromatography / mass spectrometry. The limit of detection (LOD) and limit of quantitation (LOQ) for XDE-729 methyl and XDE-729 acid in wheat grain, cleaned grain, refined flour, middlings, wheat germ, fine bran, coarse bran, total bran, white bread, wholemeal flour and wholemeal bread were 0.003 mg/kg and 0.01 mg/kg, respectively. Recoveries in wheat grain averaged 101±6% for XDE-729 methyl and 97±14% for XDE-729 acid. Recoveries in wholemeal bread averaged 100±5% for XDE-729 methyl and 94±7% for XDE-729 acid. Recoveries in wholemeal flour averaged 100±7% for XDE-729 methyl and 95±10% for XDE-729 acid. Recoveries in middlings averaged 96±2% for XDE-729 methyl and 90±13% for XDE-729 acid. Recoveries in refined flour averaged 96±3% for XDE-729 methyl and 85±14% for XDE-729 acid. Recoveries in coarse bran averaged 99±4% for XDE-729 methyl and 90±14% for XDE-729 acid. Recoveries in fine bran averaged 98±3% for XDE-729 methyl and 86±10% for XDE-729 acid. Recoveries in total bran averaged 103±4% for XDE-729 methyl and 97±13% for XDE-729 acid. Recoveries in white bread averaged 101±3% for XDE-729 methyl and 94±9% for XDE-729 acid. Recoveries in wheat germ averaged 97±6% for XDE-729 methyl and 94±6% for XDE-729 acid. Residue results were reported down to the LOD level, otherwise declared as non-detected (ND).

Residues of XDE-729 methyl or XDE-729 acid in wheat grain and processed fractions at normal commercial harvest were all ND (<0.003 mg/kg). Transfer factors were not

calculated in wheat since quantifiable residues were not attained in the RAC's and processed commodities. Residue data generated on wheat grain and processed fractions in support of the transfer factors and MRL setting is summarized in the table below.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

**Table B.7.8.4-3 Residues in wheat and wheat processed commodities after a single foliar broadcast application with GF-2573**

Trial details			Crop		Country		Application Details				Residues found				
Trial no.	DAS Study ID	Year	Crop	Variety	Country	Zone	Rate g as/ha	Water (L/ha)	G.S at last appl.	PHI (days)	Substrate (portion analysed)	XDE-729 Methyl (mg/kg)	Mean recovery XDE-729 Methyl (%)	XDE-729 Acid (mg/kg)	Mean recovery XDE-729 acid (%)
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Grain	ND, ND	101	ND, ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	101	ND, ND, ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Cleaned Grain	ND, ND, ND	101	ND, ND, ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Cleaned Grain (before flour type 550)	ND	101	ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Refined Flour (flour type 550)	ND, ND	96	ND, ND	85
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Middlings	ND, ND	96	ND, ND	90
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Wheat Germ	ND, ND	97	ND, ND	94
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Fine Bran	ND, ND	98	ND, ND	86
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Coarse Bran	ND, ND	99	ND, ND	90
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Total Bran	ND, ND	103	ND, ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	White Bread	ND, ND	101	ND, ND	94
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Cleaned Grain (before Wholemeal flour)	ND	101	ND	97
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Wholemeal Flour	ND, ND	100	ND, ND	95
5003A	110435	2011	Spring Wheat	Amaretto	Germany	NZ	30.4	405	BBCH. 45	80	Wholemeal Bread	ND, ND	100	ND, ND	94
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Grain	ND, ND	101	ND, ND	97
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	101	ND, ND, ND	97
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Cleaned Grain	ND, ND, ND	101	ND, ND, ND	97
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Cleaned Grain (before flour type 550)	ND	101	ND	97

**XDE 729 Methyl (Halauxifen-methyl)****Volume 3, Annex B.7**

5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Refined Flour (flour type 550)	ND, ND	96	ND, ND	85
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Middlings	ND, ND	96	ND, ND	90
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Wheat Germ	ND, ND	97	ND, ND	94
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Fine Bran	ND, ND	98	ND, ND	86
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Coarse Bran	ND, ND	99	ND, ND	90
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Total Bran	ND, ND	103	ND, ND	97
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	White Bread	ND, ND	101	ND, ND	94
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Cleaned Grain (before Wholemeal flour)	ND	101	ND	97
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Wholemeal Flour	ND, ND	100	ND, ND	95
5003B	110435	2011	Spring Wheat	Palesio	Italy	SZ	31.1	415	BBCH. 45	47	Wholemeal Bread	ND, ND	100	ND, ND	94
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Grain	ND, ND	101	ND, ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	101	ND, ND, ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Cleaned Grain	ND, ND, ND	101	ND, ND, ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Cleaned Grain (before flour type 550)	ND	101	ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Refined Flour (flour type 550)	ND, ND	96	ND, ND	85
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Middlings	ND, ND	96	ND, ND	90
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Wheat Germ	ND, ND	97	ND, ND	94
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Fine Bran	ND, ND	98	ND, ND	86
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Coarse Bran	ND, ND	99	ND, ND	90
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Total Bran	ND, ND	103	ND, ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	White Bread	ND, ND	101	ND, ND	94
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Cleaned Grain (before Wholemeal flour)	ND	101	ND	97
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Wholemeal Flour	ND, ND	100	ND, ND	95
5003C	110435	2010	Spring Wheat	Sarina	Spain	SZ	38.4	409	BBCH. 45	81	Wholemeal Bread	ND, ND	100	ND, ND	94

**Not-Detected: ND (<0.003 mg/kg).**

WARNING: This document forms part of an EC evaluation. The package and should not be re-used for the purpose of this document. Registration must not be based on this document.



## Barley Grain Processing

The transfer of residues of XDE-729 methyl and XDE-729 acid from barley grain to barley processed fractions was determined following a single foliar application targeted at 30 g a.e./ha in spray volumes of 389 to 417 L/ha. The barley grain used in this study was treated with a 5X exaggerated application rate (compared to the maximum application rate in spring of 6.0 g ae/ha) of XDE-729 methyl in order to improve the ability to quantify residues and determine the proportion of residues that transferred from treated barley grain to processed fractions. Three trials were made in Germany, Italy, and Spain in 2011, as the major producers and representative geographies for barley in the Northern and Southern Zones. The test material was GF-2573 formulation, an emulsifiable concentrate (EC) containing XDE-729 methyl at a nominal concentration of 7.5 g ae/L and cloquintocet-mexyl (herbicide safener) at a nominal concentrate 7.5 g a.i./L. Field samples were collected at normal commercial harvest, 55-66 days after application.

The processing phase was carried out to obtain samples of cleaned barley, pot barley, brewing malt, malt sprouts, spent grain, flocs, brewer's yeast, beer, barley bran and barley flour from samples taken in the field. Barley processing was done on a laboratory scale and fully comparable to industrial barley processing and is shown below.

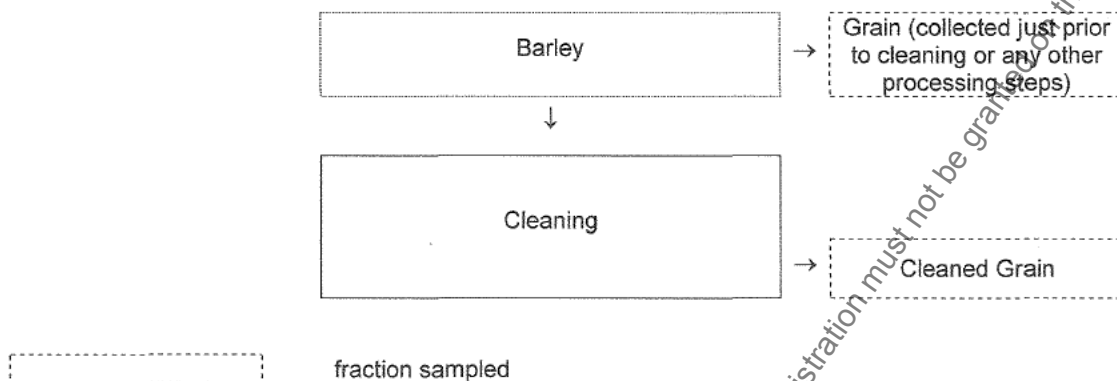
### Cleaning

Prior to cleaning the specimen "grain" (collected just prior to cleaning or any other processing steps) was taken.

**Cleaning:** The barley grain was cleaned using Rationel Kornservice sample cleaner SLN3. Cleaning was done in three steps. First the grain was de-awned (setting 3-8). In the second step impurities were removed with the help of sieves and a cyclone (aspiration setting 10). Lastly the grain was sorted by size grading (2.5 mm). The throughput of the machine was set at 5. The settings of the sample cleaner were chosen to the best performance of the process. The specimen "Cleaned Grain" (before storage) were taken. One part of the cleaned grain was used to produce pot barley, another part to produce barley flour and another part was used to produce brewing malt, beer and associated fractions.

### Barley cleaning processing flowchart

#### Flowchart



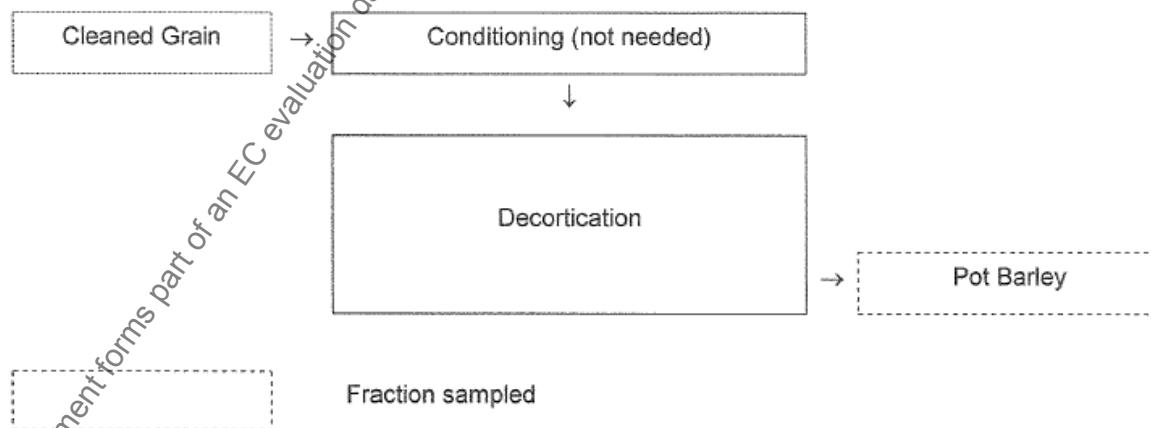
#### Pot Barley

**Conditioning:** The moisture content of the grain was determined using a moisture analyser (PCE Europe MB-50) before the start of decortication (abrasion). The grain had an initial moisture content of 14.4 - 15.0 %. Therefore the conditioning was not necessary. A second cleaning step after conditioning was also not necessary.

**Decortication (abrasion):** The cleaned grain was placed in a suitable decorticator (Vertikalschäler Fa. Schule). The abrasion rate was between 8.8- 11.9%. The fraction "Pot Barley" was sampled. In a pre-test the time was determined to get an abrasion of 8-10 %. The sieving rests and the rub-off obtained directly after decortication were discarded.

### Pot barley processing flowchart

#### Flowchart



### Malting

**Dormancy:** After cleaning, the grain was stored cooled at 8.5- 10.8°C for 42-58 days.

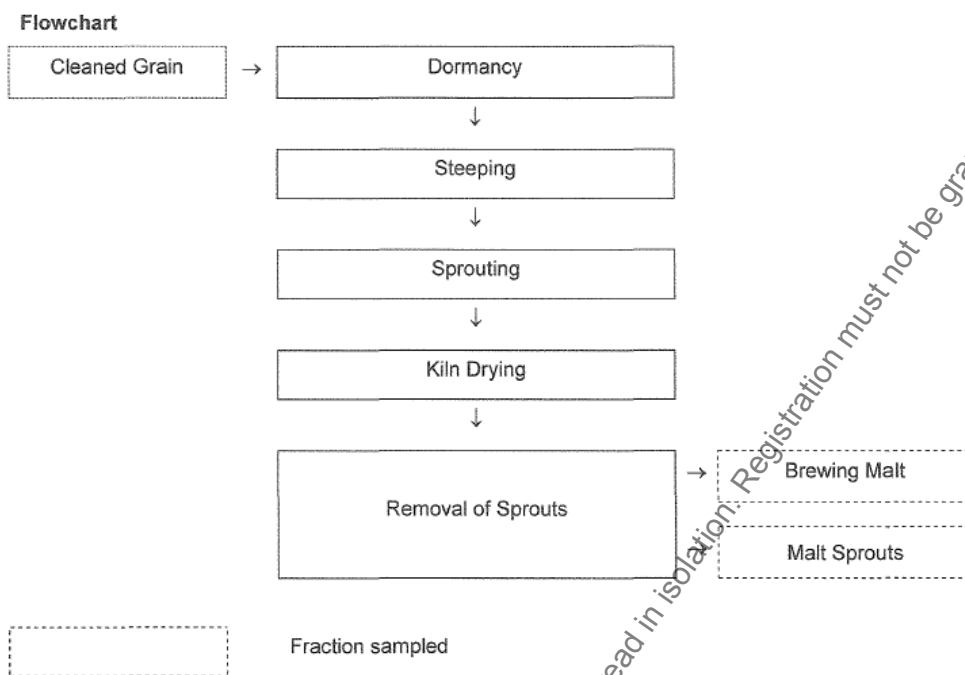
**Steeping:** The grain was steeped by covering with tap water such that the whole grain was covered with water. 8.3- 9.6 kg grain was used (ratio water/grain between 1.0 and 1.3 and stored for 23- 24.5 h at room temperature). Impurities were removed with the water. The steeping water was discarded.

**Sprouting:** Sprouting was conducted using a climatic exposure cabinet in the dark. During the sprouting process the temperature was between 10.7 - 12.1°C and the air was kept in a high humidity. The malt was turned by hand and was periodically moistened with tap water. The emergence period was 5 - 7 days.

**Kiln drying:** After sprouting, the green malt was immediately kiln dried using a drying oven. The malt was dried for approximately 6 hours at approximately 50°C. Then the drying temperature was continually elevated for approximately 8 hours, followed by a generally constant temperature of approximately 85°C for another 5- 10 hours.

**Removal of sprouts:** After kiln drying the malt sprouts were separated mechanically from the grain with a sample cleaner "Rational Kornservice SLN 3" (settings: deawning: 3-4, aspiration: 11-13 throughput 3-5, size grading: 2.5mm). The specimens "Malt Sprouts" and "Brewing Malt" were collected. The malt for brewing was stored for 3-22 days at 6.6-10.7°C until brewing.

### Malting processing flowchart



### Brewing

The brewing process was done on a laboratory scale, but the notifier states that it is fully comparable to the industrial brewing process. The equipment used was the "Speidel Braumeister".

Along with the malt prepared as described, the following ingredients were used for brewing:

- <sup>2</sup> Dried and ground hops (organically grown, "Bioland Perle Typ 90")
- <sup>3</sup> Dry yeast for brewing
- <sup>4</sup> Drinking water

Before processing the equipment used was cleaned carefully. The brewing temperature profile was recorded using a calibrated data logger with two sensors (one placed in the mash and another in the heating water).

The malt was ground coarsely before brewing. For grinding a "Corona" mill was used.

**Mashing:** 20.05 - 20.51 kg of brewing water was heated in order to produce mash. The mashing temperature was 32-40°C. Approximately 4.5- 5.3 kg of malt was placed into the water.

**Brewing:** After more than 30 minutes of rest at approximately 52°C the mash was heated to a temperature of approximately 62 °C. After another rest of approximately 30 minutes the

mash was heated to approximately 72 °C. After a rest of approximately 20 minutes the iodine reaction was tested to ensure saccharification had occurred.

**Lautering:** After heating to approximately 78°C and a subsequent rest, the mash was removed and rinsed with 4.86 - 5.65 L of hot water (78 - 87 °C). The specimen "Spent Grain" was taken.

**Wort Cooking:** After lautering the wort was cooked for approximately 80 minutes and the original extract content was determined at 10.5 -11.4°P.

Approximately 10 minutes after the start of cooking approximately 40 g of hops was added. After approximately another 60-70 minutes a further amount of approximately 20 g of hops was added.

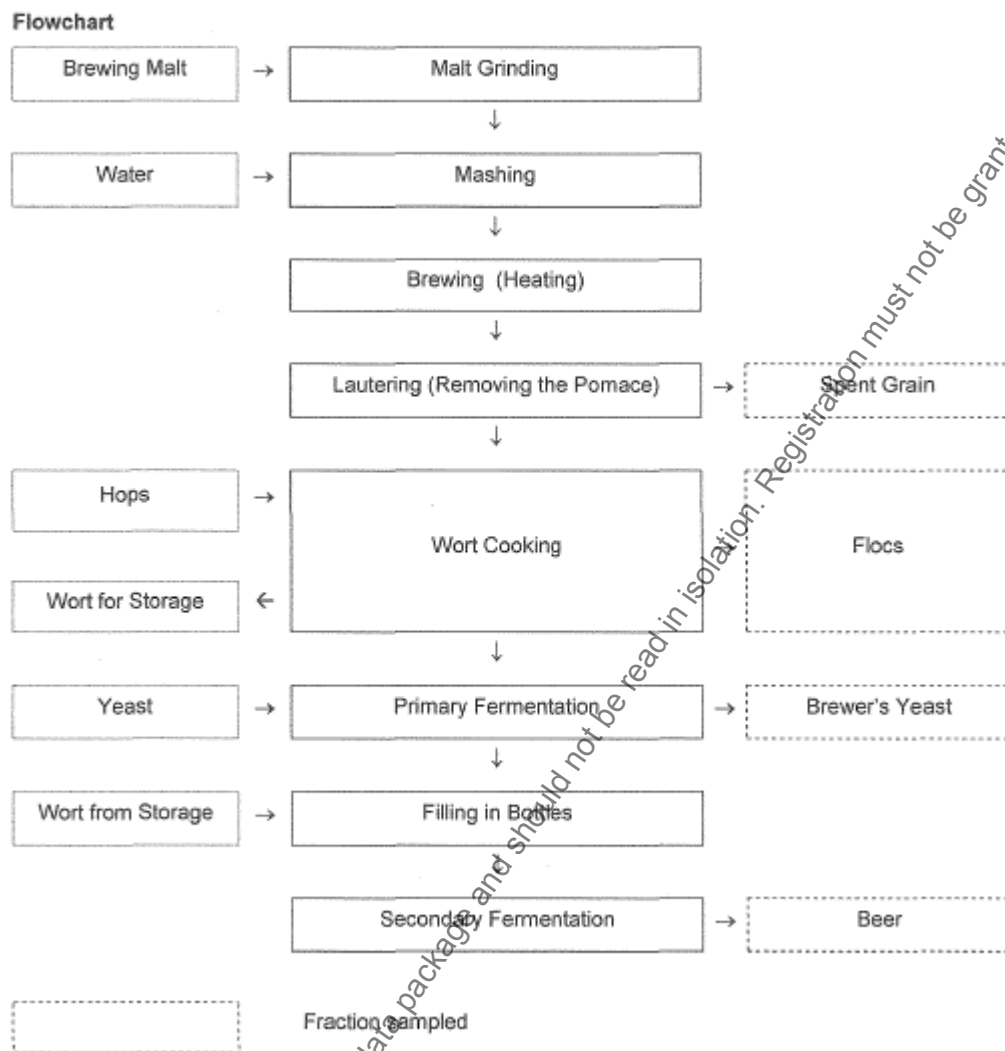
After the wort had cooled the deposited flocs (trub or hops draf) was removed. The wort was placed in an open fermenting tank after additional filtration. The specimen "Flocs" was taken. 11.7- 16.2 % of wort was stored for the secondary fermentation.

**Filtration:** After brewing a filtration step was done using a pump (Vinobi 35/230; G. Wein GmbH & Co) and 5 depth filters (Pall Corporation K900). Pump performance was adjusted success-related to the filtration.

**Primary fermentation:** The fermentation was started by adding the dried yeast (9.8 - 11.8 g). For 8 -14 days the primary fermentation was conducted at 12.5- 14.2°C. When the fermentation finished the stored wort was added to increase the sugar content. For this purpose it was ensured that it had the same temperature as the content of the fermentation tank. For samples CSR 5004-004 (3), -009 ( 1) and -014 (1) the stored wort was destroyed due to a lab accident. Therefore the fermentation was carried out without adding the stored wort. After primary fermentation, the extract content was 3.2 - 4.1 °P. The specimen "brewer's yeast" was taken.

**Secondary fermentation:** 1-2 hours after the induction of the additional wort, the beer was poured into bottles and stored for secondary fermentation. The fermentation duration was 20-27 days, fermentation temperature was between 12.5- 13.7°C. At the end of the second fermentation the beer samples were stored deep-frozen.

### Brewing processing flowchart



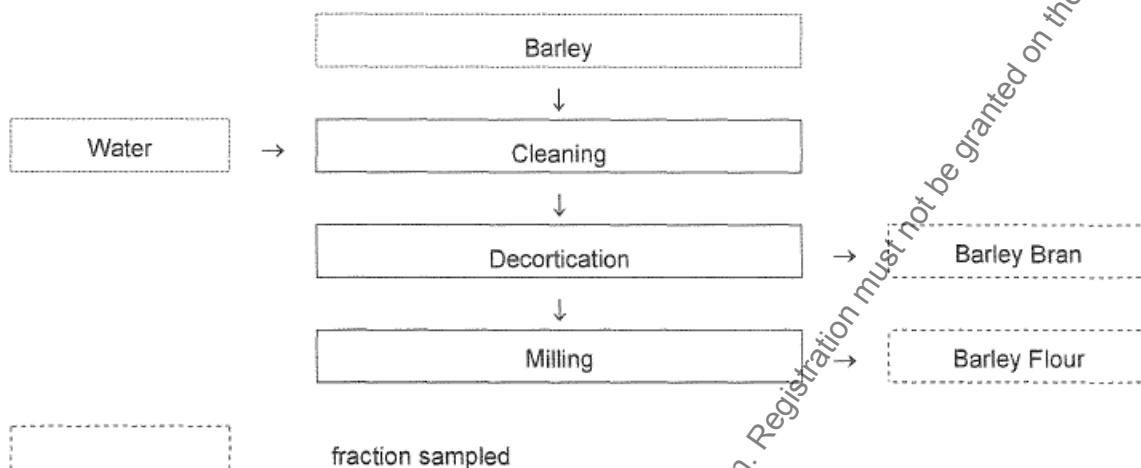
#### Barley Flour

**Decortication:** The cleaned grain was filled in a suitable decorticator (Vertika/schaler Fa. Schute). The cleaned grain was decorticated using the vertical shelling machine. The specimen "Barley Bran" was taken.

**Milling:** The peeled barley was milled using the hammer mill (Pertent). The specimen "Barley Flour" was taken.

### Barley flour processing flowchart

#### Flowchart



Residues of XDE-729 methyl and XDE-729 acid were determined using Dow AgroSciences Crop Method 110005 with liquid chromatography-mass spectrometry. The limit of detection (LOD) and limit of quantitation (LOQ) for XDE-729 methyl and XDE-729 acid in barley grain (including cleaned barley), pot barley, brewing malt, malt sprouts, spent grain, flocs, brewer's yeast, beer, barley bran and barley flour were 0.003 mg/kg and 0.01 mg/kg, respectively. Recoveries in barley grain averaged  $100\pm3\%$  for XDE-729 methyl and  $92\pm22\%$  for XDE-729 acid. Recoveries in barley bran averaged  $96\pm3\%$  for XDE-729 methyl and  $98\pm9\%$  for XDE-729 acid. Recoveries in barley flour averaged  $101\pm4\%$  for XDE-729 methyl and  $99\pm10\%$  for XDE-729 acid. Recoveries in brewer's yeast averaged  $98\pm2\%$  for XDE-729 methyl and  $89\pm18\%$  for XDE-729 acid. Recoveries in brewing malt averaged  $97\pm6\%$  for XDE-729 methyl and  $105\pm15\%$  for XDE-729 acid. Recoveries in malt sprouts averaged  $99\pm7\%$  for XDE-729 methyl and  $100\pm9\%$  for XDE-729 acid. Recoveries in pot barley averaged  $100\pm3\%$  for XDE-729 methyl and  $92\pm16\%$  for XDE-729 acid. Recoveries in flocs averaged  $94\pm5\%$  for XDE-729 methyl and  $94\pm7\%$  for XDE-729 acid. Recoveries in spent grain averaged  $92\pm5\%$  for XDE-729 methyl and  $93\pm6\%$  for XDE-729 acid. Recoveries in beer averaged  $90\pm6\%$  for XDE-729 methyl and  $94\pm8\%$  for XDE-729 acid. Residue results were reported down to the LOD level, otherwise declared as non-detected (ND).

Residues of XDE-729 methyl or XDE-729 acid in barley grain and processed fractions at normal commercial harvest were all ND ( $<0.003$  mg/kg). Transfer factors were not calculated in barley since quantifiable residues were not attained in the RAC's and processed commodities. Residue data generated on barley grain and processed fractions in support of the transfer factors and MRL setting is summarized in the table below.

**Table B.7.8.4-4 Residues in barley and barley processed commodities after a single foliar broadcast application with GF-2573**

Trial details			Crop		Country		Application Details				Residues found				
Trial no.	DAS Study ID	Year	Crop	Variety	Country	Zone	Rate g as/ha	Water (L/ha)	G.S at last appl.	PHI (days)	Substrate (portion analysed)	XDE-729 Methyl (mg/kg)	Mean recovery XDE-729 Methyl (%)	XDE-729 Acid (mg/kg)	Mean recovery XDE-729 acid (%)
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Grain	ND, ND	99	ND, ND	92
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	99	ND, ND, ND	92
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Cleaned Barley Grain	ND, ND, ND, ND, ND	99	ND, ND, ND, ND, ND	92
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Pot Barley	ND, ND	100	ND, ND	92
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Brewing Malt	ND, ND	97	ND, ND	105
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Malt Sprouts	ND, ND	99	ND, ND	100
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Spent Grain	ND, ND	92	ND, ND	93
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Flocs	ND, ND	94	ND, ND	94
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Brewer's Yeast	ND, ND	98	ND, ND	89
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Beer	ND, ND	90	ND, ND	94
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Barley Bran	ND, ND	96	ND, ND	97
5004A	110436	2011	Spring Barley	Ingmar	Germany	NZ	29.4	391	BBCH. 45	63	Barley Flour	ND, ND	101	ND, ND	99
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Grain	ND, ND	99	ND, ND	92
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	99	ND, ND, ND	92
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Cleaned Barley Grain	ND, ND, ND, ND, ND	99	ND, ND, ND, ND, ND	92
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Pot Barley	ND, ND	100	ND, ND	92
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Brewing Malt	ND, ND	97	ND, ND	105
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Malt Sprouts	ND, ND	99	ND, ND	100
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Spent Grain	ND, ND	92	ND, ND	93



## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Flocs	ND, ND	94	ND, ND	94
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Brewer's Yeast	ND, ND	98	ND, ND	89
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Beer	ND, ND	90	ND, ND	94
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Barley Bran	ND, ND	96	ND, ND	97
5004B	110436	2011	Spring Barley	Rondo	Italy	SZ	31.3	417	BBCH. 45	55	Barley Flour	ND, ND	101	ND, ND	99
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Grain	ND, ND	99	ND, ND	92
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Grain (collected just prior to cleaning or any other processing steps)	ND, ND, ND	99	ND, ND, ND	92
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Cleaned Barley Grain	ND, ND, ND, ND, ND	99	ND, ND, ND, ND, ND	92
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Pot Barley	ND, ND	100	ND, ND	92
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Brewing Malt	ND, ND	97	ND, ND	105
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Malt Sprouts	ND, ND	99	ND, ND	100
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Spent Grain	ND, ND	92	ND, ND	93
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Flocs	ND, ND	94	ND, ND	94
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Brewer's Yeast	ND, ND	98	ND, ND	89
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Beer	ND, ND	90	ND, ND	94
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Barley Bran	ND, ND	96	ND, ND	97
5004C	110436	2010	Spring Barley	Cristalia	Spain	SZ	29.2	389	BBCH. 45	66	Barley Flour	ND, ND	101	ND, ND	99

Not-Detected: ND (&lt;0.003 mg/kg).

**B.7.9 Livestock feeding studies (IIA 6.4, IIIA 8.3 )****Overall conclusions**

Based on feed commodities considered in this submission, only cereal grain is a potential contributor to residues in the poultry diet. Since residues of XDE-729 methyl and XDE-729 acid were ND (not-detected, <0.003 mg/kg) or <0.01 mg/kg in grain, dietary intake of residues in poultry is expected to be insignificant. Results from the poultry NOR / metabolism study presented above along with the insignificant dietary intake of residues from grain indicates that residues in poultry commodities would be expected to be non-detectable (<0.003 mg/kg). Therefore, no poultry feeding study was required.

Based on residue trials conducted in the EU according to the critical GAP and resulting residues in cereal grain and straw, intake of XDE-729 methyl and XDE-729 acid in the dairy cattle diet is a maximum 0.021 mg/kg on a dry matter (DM) basis (0.0008 mg/kg bw/day). Although residues from uses proposed in the EU do not result in sufficient dietary burden to trigger the requirement for a cattle feeding study, a study was conducted to support uses in other regions of the world where the dietary burden is greater, due primarily to the potential for use of cereals as forage and hay with short PHIs. Although a cattle feeding study is not required for the proposed uses in the EU, it was presented for information and to provide additional data for use in considering potential transfer of residues from the cattle diet to edible tissues and milk. The notifier states that uses proposed in other regions of the world may result in cattle dietary intake of 1 mg/kg to 2.7 mg/kg in the diet on a DM basis (0.04 mg/kg bw/day to 0.1 mg/kg bw/day). Even with this level of dietary intake of residues, extrapolation of results from the goat NOR / metabolism study summarized above indicated that residues of XDE-729 methyl or XDE-729 acid at or above the LOQ of 0.01 mg/kg in milk or tissues was not expected. However, to more fully evaluate potential residue transfer to cattle / ruminant commodities since there was potential for significant dietary intake of XDE-729 methyl and XDE-729 acid residues, a feeding study was conducted with lactating dairy cattle. Animals were orally dosed for 28 or 29 consecutive days with a compound feed containing the test item, XDE-729 methyl. In the cattle feeding study, cows were divided into 4 separate treatment groups / dose levels. (Control, 0x, 1x, 3.1x and 15.6x). Based on dose levels of XDE-729 methyl administered along with actual feed consumption levels during the period of dosing, the average dose levels of XDE-729 methyl expressed as concentrations in the diet of treated cattle on a dry weight basis were: 1.06 mg/kg (1x), 3.16 mg/kg (3.1x) and 15.31 mg/kg (15.6x). No adverse treatment-related effects were observed on body weight, feed consumption or milk production. Additionally, no treatment-related behavioural reactions or systemic signs of toxicity were noted. Gross necropsies showed no effects that appeared to be treatment-related. Results showed that residues of XDE-729 methyl and XDE-729 acid above the LOQ do not transfer into whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat or perirenal fat at any of the dose levels. Residues of the metabolite X11449757 above the LOQ do not transfer into whole milk, skim milk, cream, muscle, subcutaneous fat, mesenteric fat or perirenal fat, with the exception of a single residue of 0.012 mg/kg in mesenteric fat and a single residue of 0.014 mg/kg in perirenal fat from cows in the highest (15.6x) dose level group. Residues of

X11449757 above the LOQ transfer into liver at the 1x, 3.1x and 15.6x dose levels and into kidney at the 3.1x and 15.6x dose levels. Although levels of X11449757 were monitored in milk and tissues, X11449757 is not proposed for inclusion in the residue definition in livestock. Depuration data generated using the 12 cows in the 15.6x (15.31 mg/kg) dose level showed that residues of X11449757 declined rapidly in liver and kidney following withdrawal of the test items from the cows' diet. All residues were below the LOQ by Day 31 of the study (3 days of depuration) and at that time, except for liver from one cow with a detectable residue that was <LOQ (residue of 0.004 mg/kg), all other residue values were ND (<0.003 mg/kg).

As discussed above, metabolism of XDE-729 methyl is similar in ruminants (goats) and rodents (rats). Therefore, there is no requirement to conduct a feeding study in pigs / swine since results from the feeding study conducted in dairy cattle may be extrapolated to swine / pigs. However, of the feed commodities considered in this submission, only cereal grain is a potential contributor to residues in the swine diet. Since residues of XDE-729 methyl and XDE-729 acid were ND (not detected, <0.003 mg/kg) or <0.01 mg/kg in grain, dietary intake of residues in swine is expected to be insignificant. Results from the goat NOR / metabolism study as well as from the cattle feeding study summarized above together with the insignificant dietary intake of residues indicate that no feeding study / feeding study results are necessary for swine for this submission since residues in swine commodities would be expected to be non-detectable (ND, <0.003 mg/kg).

#### **B.7.9.1 Poultry**

Based on feed commodities considered in this submission, only cereal grain is a potential contributor to residues in the poultry diet. Since residues of XDE-729 methyl and XDE-729 acid were ND or <0.01 mg/kg in grain, dietary intake of residues in poultry is insignificant. Results from the poultry NOR / metabolism study along with the insignificant dietary intake of residues in poultry indicates that residues in poultry commodities would be expected to be non-detectable (<0.003 mg/kg). Therefore, no poultry feeding study is needed.

#### **B.7.9.2 Pigs**

No feeding study is required in pigs. Since metabolism of XDE-729 methyl in ruminants (goats) is similar to the metabolism observed in rodents (rats), the feeding study conducted with dairy cattle may be extrapolated to pigs / swine. However, due to the very low level of potential dietary intake of residues in pigs (grain residues <0.01 mg/kg) there is no requirement for feeding study results for pigs and residues in edible tissues of pigs are expected to be far below the LOQ of 0.01 mg/kg.

**B.7.9.3 Lactating ruminants (goat or cow)**

Reference: [REDACTED] "XDE-729 Livestock Feeding Study: Magnitude of Residue in Milk, Muscle, Fat, Liver and Kidney of Lactating Dairy Cattle"; Unpublished Report of [REDACTED] (Report ID: [REDACTED]-5266); [REDACTED] Study Reference ID: 020077; 13 July 2012.

Guidelines: EC Council Directive 91/414/EEC – Working Document 7031/VI/95 rev. 4; OECD Guidance Document: Overview for Residue Chemistry Studies (2006); OECD Guidelines for the Testing of Chemicals, No. 505: Residues in Livestock (2007); APVMA Residue Guideline No. 1 – Animal Transfer Studies.

GLP: Yes, OECD Principles of Good Laboratory Practice [ENV/MC/CHEM(98)17]

**EXECUTIVE SUMMARY:**

Residues from uses proposed in the EU do not result in sufficient dietary burden to trigger the requirement for a cattle feeding study. Feeding studies have been conducted however to address the higher residue levels seen within the Australian supervised field trials. Although the feeding study is included here for information, it has not been relied upon for the EU evaluation. The feeding dose was 1.0 mg/kg XDE-729 methyl which is ca. 48 fold the estimated maximum dietary burden for dairy cattle in the EU (0.021 mg/kg DM basis).

Lactating Friesian/Holstein dairy cows were dosed orally for 28 or 29 consecutive days via a compound feed containing the test item, XDE-729 methyl (X11393728). The test item was added to the compound feed as a solution in acetone on two occasions each day (AM and PM feeding). The animals were divided into 4 separate treatment groups. One treatment group of 3 cows was an untreated control group, which was dosed by adding acetone only to the compound feed. The remaining groups were treated with XDE-729 methyl, targeted at a nominal dose equivalent to a concentration in the animals' diet (on a dry matter (DM) basis) of:

1.0 mg/kg XDE-729 methyl (1x, 4 cows)

3.1 mg/kg XDE-729 methyl (3.1x, 4 cows)

15.6 mg/kg XDE-729 methyl (15.6x, 16 cows)

The animals were dosed for 28 or 29 consecutive days. Twelve of the cows in the 15.6 mg/kg treatment group were used to generate depuration data. At the end of the dosing period, they

were transferred to the control diet to measure the decline in residues following withdrawal of the test item from the diet.

Based on actual feed consumption during the period of dosing, the average dose levels of XDE-729 methyl were 1.06 mg/kg (1x), 3.16 mg/kg (3.1x) and 15.31 mg/kg (15.6x). These dose levels represent 106%, 102% and 98% of the nominal/target dose levels for the 1x, 3.1x and 15.6x treatment groups, respectively. If the daily dosage of XDE-729 methyl is expressed on the basis of bodyweight of the individual cows (mg/kg bw/day), the average dosage over the four weeks of dosing was 0.037 mg/kg bw/day, 0.109 mg/kg bw/day and 0.533 mg/kg bw/day, for the 1x, 3.1x and 15.6x treatment groups, respectively.

All animals were observed at least twice daily for general health. No adverse treatment-related effects were observed on body weight, feed consumption or milk production. Additionally, no treatment-related behavioural reactions or systemic signs of toxicity were noted. Gross necropsies showed no effects that appeared to be treatment-related.

Residues of XDE-729 methyl, XDE-729 acid (X11393729) and X11449757 in milk and tissues were measured using an analytical method based on LC-MS/MS. The limit of detection (LOD) and limit of quantitation (LOQ) for each of the analytes in milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat were 0.003 mg/kg and 0.01 mg/kg, respectively. Overall average procedural recovery for the three analytes (XDE-729 methyl, XDE-729 acid and X11449757) in all matrices (whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat) ranged from 89% to 105%.

Results showed that residues of XDE-729 methyl and XDE-729 acid above the LOQ do not transfer into whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat or perirenal fat at any of the dose levels. Residues of X11449757 above the LOQ do not transfer into whole milk, skim milk, cream, muscle, subcutaneous fat, mesenteric fat or perirenal fat, with the exception of a single residue of 0.012 mg/kg in mesenteric fat and a single residue of 0.014 mg/kg in perirenal fat from cows in the highest (15.31 mg/kg) dose level group.

Residues of X11449757 above the LOQ transfer into liver at the 1.06 mg/kg, 3.16 mg/kg and 15.31 mg/kg dose levels and into kidney at the 3.16 mg/kg and 15.31 mg/kg dose levels.

Regression analysis for X11449757 in liver and kidney across dose levels demonstrated a linear relationship between the dose level and the resulting residue concentration. No regression analysis has been performed for X11449757 in other matrices, or for XDE-729 methyl or XDE-729 acid in any matrices, because in almost all cases residues were not detected (ND, <0.003 mg/kg) or fell below the LOQ of 0.01 mg/kg.

Depuration data generated using the 12 cows in the 15.31 mg/kg dose level showed that residues of X11449757 declined rapidly in liver and kidney following withdrawal of the test items from the cows' diet. All residues were below the LOQ by 3 days of depuration (Day 31 of the study) and at that time, except for liver from one cow with a detectable residue that was <LOQ (residue of 0.004 mg/kg), all other residue values were ND (<0.003 mg/kg) by 3 days of depuration.

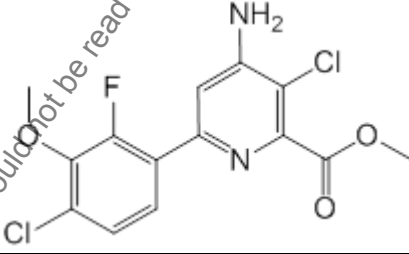
**BACKGROUND INFORMATION**

Residues from uses proposed in the EU do not result in sufficient dietary burden to trigger the requirement for a cattle feeding study. Feeding studies have been conducted however to address the higher residue levels seen within the Australian supervised field trials. Although the feeding study is included here for completion, it has not been relied upon for the EU evaluation. For information, the feeding dose was 1.0 mg/kg XDE-729 methyl which is ca. 48 fold the estimated maximum dietary burden for dairy cattle in the EU (0.021 mg/kg DM basis).

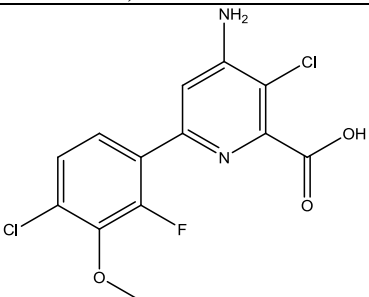
This study was conducted to quantify the transfer of residues of XDE-729 methyl and its metabolites XDE-729 acid and X11449757 in the ruminant diet to milk and tissues (muscle, fat, liver and kidney).

The chemical structure and nomenclature for XDE-729 methyl, XDE-729 acid and X11449757 are listed in the tables below.

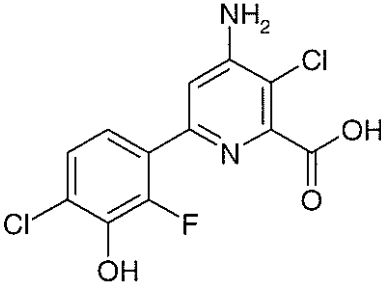
**Nomenclature and Identification Information for XDE-729 methyl**

Active Ingredient	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate 
Common Name:	N/A
Company Experimental Name:	XDE-729 methyl
Company Experimental Number (X Number)	X11393728
IUPAC Name:	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate
Molecular Formula	C <sub>14</sub> H <sub>11</sub> Cl <sub>2</sub> F N <sub>2</sub> O <sub>3</sub>
Molecular Weight	345.16
CAS Name	N/A
CAS Number	N/A
Test Substance Number	TSN031117-0004
Lot Number	E2837-51
Analyzed Content of Active Ingredient	97.2%
Expiry Date	30 November 2013

Nomenclature and Identification Information for XDE-729 acid

Name:	XDE-729 acid (X11393729)
	
Common Name	N/A
Company Experimental Name	XDE-729 acid
Company Experimental Number (X Number)	X11393729
IUPAC Name	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylic acid
CAS Name	N/A
CAS No.	N/A
Molecular Formula	C <sub>13</sub> H <sub>9</sub> Cl <sub>2</sub> FN <sub>2</sub> O <sub>3</sub>
Molecular Weight	331.13
TSN	TSN030751-0004
Lot Number	DC6-E2622-77
Analyzed Content of Compound	99%
Expiry Date	02 November 2013

Nomenclature and Identification Information for X11449757

Name	X11449757
	
Common Name	N/A
Company Experimental Name	N/A
Company Experimental Number (X Number)	X11449757
IUPAC Name	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxyphenyl)pyridine-2-carboxylic acid
CAS Name	N/A
CAS No.	N/A
Molecular Formula	C <sub>12</sub> H <sub>7</sub> Cl <sub>2</sub> FN <sub>2</sub> O <sub>3</sub>
Molecular Weight	317.11
TSN	TSN031413-0003
Lot Number	YB1-100780-103
Analyzed Content of Compound	99%
Expiry Date	25 January 2014



Descriptive information concerning the lactating dairy cows used in this study is provided below in the Table.

#### Description of Livestock Used in the Feeding Study

**Table B.7.9.3-1**

Species	Breed	Age	Weight at study initiation (kg)	Health status	Description of housing/holding area
Lactating dairy cows ( <i>Bos taurus</i> )	Friesian/Holstein	Multiparous , range of 4-13 yrs.	475 to 692 kg	All cows selected for use in the study were examined and identified as fit, healthy and suitable for use in the study prior to transport to the In-Life phase test facility.	Cows were housed in a building in individual pens approximately 3.75m x 3.45m. Wood shavings were used for bedding material with manure removed twice daily. The building where the animals were housed was naturally ventilated. Animals were housed under natural light with artificial light supplemented as needed.

Twenty-seven multiparous Friesian/Holstein dairy cows were selected for use in the study and were assigned to one of four treatment groups based on the dose level of test substance (0 mg/kg – untreated control, 1.06 mg/kg, 3.16 mg/kg, and 15.31 mg/kg). The 0 mg/kg, 1.06 mg/kg, 3.16 mg/kg, and 15.31 mg/kg treatment groups are also described in text and tables in the study report as Dose Groups A, B, C, and D, respectively. Three cows were assigned to Dose Group A, the untreated control dose group. Four cows were assigned to each of the Dose Groups B and C (1.06 mg/kg and 3.16 mg/kg dose groups, respectively). Cows in the Dose Group D (15.31 mg/kg dose group) were used to evaluate residue depuration and were assigned to one of five separate slaughter dates after administration of the final dose (0-days, 3-days, 5-days, 10-days, and 15-days after final dosing). For the purpose of allocation to treatment, the different slaughter dates within the Group D were regarded as separate treatments. Four cows were assigned to the Dose Group D slaughter group to be euthanized on the day of final dose administration (0-day after final dose) and three cows each were assigned to the four other slaughter groups in Dose Group D (3-days, 5-days, 10-days, and 15-days after final dosing).

Milk production was used as a blocking factor when allocating cows to Dose Groups/treatments in an effort to manage variability among Dose Groups. All cows were individually identified with unique ear tags and freeze brands.

Each cow was offered 8 kg of pelleted compound feed per day, split into two feeds (AM and PM). The pelleted compound feed was composed primarily of wheat, palm kernel expeller and rape seed meal. Other ingredients included wheat feed, sunflower seed meal, sugar cane molasses, soybean meal, minerals and vitamins. In addition to the pelleted compound feed,

each cow was offered grass silage fed to appetite throughout the study. Dry matter content of the pelleted compound feed and grass silage were determined weekly. Individual feed consumption was measured daily during the acclimation period and throughout the remainder of the study until sacrifice. Total dry matter consumption for each cow on a daily basis was determined. A summary of the dietary regime is provided in Table 6.4.2-5.

**Table B.7.9.3-2 Test Animal Dietary Regime**

Composition of Diet (Fresh weight or as-fed basis)	Feed consumption (kg/day) – Average consumption of combined feed sources ( <b>dry weight basis</b> ) during the dosing period	Water	Acclimation, Dosing and Withdrawal Period
Pelleted compound feed (Containing 18% protein, 9% fiber, 5% oil and 7-8% ash) – 8 kg/day,  Grass silage fed to appetite	Group A (0 mg/kg, Control): 22.3 Dose Group B (1.06 mg/kg): 20.6 Dose Group C (3.16 mg/kg): 21.3 Dose Group E (15.31 mg/kg): 21.4	Water offered <i>ad libitum</i> with use of water troughs. Cows in different treatment groups did not share water troughs	A 14-day acclimation period was used in this study.  Dietary regime was the same through all phases of the study.

The maximum anticipated dietary residues used for selection of the 1x dose level (Dose Group B) in this study were based on preliminary results from initial crop residue trials in cereals conducted in multiple regions of the world (North America, Australia, and Europe) as well as residue trials carried out in brassicas in Australia. These trials were carried out based on proposed use patterns that were expected to produce maximum residue levels globally (i.e. maximum intended use rate, maximum number of applications, shortest retreatment interval, if more than one application, and maximum growth stage at treatment application).

Data available at the time dose levels were selected indicated that based on diet composition for ruminant livestock together with anticipated residue levels in the associated crops and expected regional use patterns for XDE-729 methyl, ruminant livestock in Australia could potentially have the highest level of dietary residue intake globally, depending on the pre-grazing interval for cereal forage and brassica forages selected following treatment. Consequently, the 1x dose level was based on potential dietary residue intake in cattle in Australia. Preliminary residue results available at the time the dose levels were selected for this study indicated that, based on a diet of 100% forage, the combined residues of XDE-729 methyl and XDE-729 acid expressed as XDE-729 methyl equivalents would be approximately 1 mg/kg in the diet on a dry weight / dry matter basis in cereal forage at 1-day after treatment or approximately 3 mg/kg in the diet on a dry weight / dry matter basis for brassica forage at 1-day after treatment. Therefore, XDE-729 methyl at 1.0 mg/kg dry weight in the diet was selected for use as the 1x dose level and 3.1 mg/kg dry weight in the diet was selected as the 3.1x dose level. Lower levels of residue intake that were expected to be associated with proposed use of XDE-729 methyl in cereals in Europe and North America were not used in setting a 1x dose level for this livestock feeding study since extrapolation of results from the metabolism / nature of the residue study with [14C]-XDE-729 methyl in

goats indicated that residues of XDE-729 methyl or XDE-729 acid were unlikely to be detected in milk or edible tissues if XDE-729 methyl was present at levels less than 1.0 mg/kg dry weight in the diet. Likewise, the level of the metabolite X11449757 was expected to be below the limit of detection (LOD) in milk, muscle, fat and kidney or below the limit of quantitation (LOQ) of 0.01 mg/kg in liver if XDE-729 methyl was present at levels of less than 1.0 mg/kg dry weight in the diet.

**Based on the above, the 1x dose of XDE-729 methyl for the feeding study was targeted at 1.0 mg/kg in the diet on a dry matter basis.** In addition to the target 1x dose level, to allow for residues that may occur with brassica forage or other future potential uses that may increase residue levels in the diet and to comply with guideline requirements for feeding studies, the compound was also tested at two higher dose levels, which in this case were targeted at 3.1x and 15.6x the dose level targeted for the 1x dose.

To summarize, the dosing levels of XDE-729 methyl were targeted at 1.0 mg/kg (1.0x, (Group B), 3.1 mg/kg (3.1x, Group C) and 15.6 mg/kg (15.6x, Group D). The study also contained an untreated control group (0x, Group A).

In order to more closely match the target dose level in each animal's diet, the amount of test substance added to a given animal's diet was adjusted individually based on that animal's recent feed consumption on a DM (dry matter) basis along with the dose level specified for the dose group to which the animal was assigned. The dry matter intake on which the amount of test substance administered to each animal was based was determined during a five day period during acclimation.

The test substance was administered to the cows by preparing solutions containing the XDE-729 methyl dissolved in acetone and adding this solution to the pelleted compound feed just prior to offering it to each cow. The volume of solution required to deliver the required amount of XDE-729 methyl was added to the pelleted compound feed for each individual animal just prior to offering the feed to the animal. The solution was administered to the compound feed at the time it was offered twice per day (AM and PM feeding), resulting in the test substance being administered twice daily. Acetone only (without test substance) was added to the pelleted compound feed given to the cows in the untreated control group (Dose Group A). The pelleted compound feed was palatable to the cows and addition of the dosing solution did not appear to affect palatability. Consumption of the compound feed was checked by visual examination of the feed buckets and any incomplete uptake was recorded. In nearly all instances the compound feed was completely consumed. An incomplete uptake of between 0.05 kg and 0.36 kg out of 8 kg of compound feed offered was recorded on only three occasions during the study (0.05 kg and 0.36 kg out of a total of 8 kg represents only 0.6% and 4.5% of the total, respectively). In each case, the rejected feed was weighed and then added to the forage (grass silage) in front of the cow so that there was still the opportunity for consumption of any unconsumed treated pelleted feed. This very low level of compound feed refusal gives confidence in the complete consumption of the test item.

The dosing solutions used to treat the pelleted feed were prepared fresh weekly and were stored refrigerated at approximately 5°C. The dose solutions were analyzed both to confirm

expected concentration and to evaluate stability. Results of the analysis confirmed that the dosing solutions had been prepared correctly and also confirmed stability of test substances in the dosing solution for a period of at least 14 days. The solutions used for dosing cows were stored for a maximum of 10 days before use.

The actual dose level (expressed as mg XDE-729 methyl per kg of dry matter consumed) is affected by the level of feed consumption during the dosing period. The actual dose levels attained for XDE-729 methyl in Dose Groups B, C, and D expressed as a percentage of the target dose level averaged 106%, 102%, and 98%, respectively. A summary of information concerning dose administration is presented in the table below.

**Table B.7.9.3-3** Dosing Regime – XDE-729 methyl

Treatment group	Treatment Type	Level of administered dose - XDE-729 methyl (mg/day) <sup>a, b</sup>	Residue intake in diet - XDE-729 methyl (mg/kg) <sup>a</sup>	Vehicle <sup>c</sup>	Timing/ Duration
Untreated control (Dose Group A)	Oral – twice per day	0	0	Acetone added to pelleted feed (no test substance added)	29 days (feed treated with acetone only)
Dose Group B (1.06 mg/kg)	Oral – twice per day	21.8	1.06	XDE-729 methyl in acetone solution added to pelleted feed	28 days
Dose Group C (3.16 mg/kg)	Oral – twice per day	67.3	3.16	XDE-729 methyl in acetone solution added to pelleted feed	29 days
Dose Group D (15.31 mg/kg)	Oral – twice per day	153.1	15.31	XDE-729 methyl in acetone solution added to pelleted feed	28 days

<sup>a</sup> Average for treatment group over dosing period

<sup>b</sup> Calculated based on average daily dry matter consumption of 22.3 kg, 20.6 kg, 21.3 kg, and 21.4 kg for Dose Groups A, B, C, and D, respectively, together with average residue intake in the diet of 0 mg/kg, 1.06 mg/kg, 3.16 mg/kg and 15.31 mg/kg for Dose Groups A, B, C, and D, respectively.

<sup>c</sup> Test substances dissolved in acetone and added to pelleted feed which was fed to cows on two occasions each day. Solution added to the feed immediately before it was offered to the cow for consumption.

Milk from each cow was collected twice per day and the quantity recorded at each time (at both the AM and PM milkings) through all phases of the study. Samples of whole milk were collected from each cow for residue analysis the day before dosing began (study day -1), and on study days 1, 3, 5, 7, 10, 14, 18, 20, 22, 24, 28, 29, 30, 31, 33, 35, 36, 40, and 42, including samples collected during the depuration phase of the study. Milk from the PM and AM milking for an individual cow was pooled to form a single whole milk sample used for residue analysis for a given day for each cow. For each cow, a combined proportional sample for a given sample day was constructed from the PM and AM samples, on the basis of milk yields recorded at the corresponding milkings. For example, the proportional sample

for Day 10 consisted of the morning sample for Day 10 and the evening sample for Day 9. On study days 22 and 26, additional aliquots of pooled milk samples were collected and mechanically separated into cream and skim milk fractions.

With the exception of the cows used in the depuration phase of the study, all cows were euthanized within 8 hours of administration of the final dose. Tissue samples were collected immediately after slaughter. Muscle specimens comprised approximately equal quantities of hind leg or flank, loin and diaphragm muscle. Samples of mesenteric, subcutaneous and perirenal fat were collected separately and maintained as separate samples. For each liver sample, tissue was sub-sampled from at least six areas of the whole liver. For each kidney sample, tissue was sub-sampled from at least three areas from each of the two kidneys. A summary of sample collection is presented in the table below.

**Table B.7.9.3-3 Sample Collection**

Milk collected	Amount of milk produced during normal production	Urine, feces and cage wash collected	Interval from last dose to sacrifice (days)	Tissues harvested and analysed
<u>Milk:</u> Day before dosing (study day -1) and dosing (study) days 1, 3, 5, 7, 10, 14, 18, 20, 22, 24, 28, and 29. <u>Skim milk and cream:</u> Study days 22 and 26 <u>Depuration period:</u> Milk collected on study days 29, 30, 31, 33, 35, 36, 40, and 42 (i.e. 1, 2, 3, 5, 7, 8, 12 and 14 days after administration of final dose).	Average yields by dose group were generally in the range of 25 – 30 kg per day throughout the study.	N/A - None	<b>8 hours or less</b>  Depuration of residues in tissues also evaluated at 3, 5, 10, and 15 days after administration of final dose.	Muscle – approx. 1kg Fat (separate samples of mesenteric, subcutaneous and perirenal fat - approx. 1kg Liver - approx. 1kg Kidney - approx. 1kg

### Sampling Handling and Preparation

At the In-life phase facility, samples of whole milk, cream or skim milk collected from the AM or PM milking for each cow were stored in a refrigerator set to  $5 \pm 3^{\circ}\text{C}$  for a period not exceeding 24 hours for all contributing samples until combined proportionately to form a pooled sample for each individual cow for a given Study Day. The pooled proportional samples were then transferred to a freezer set to maintain a temperature of less than  $-15^{\circ}\text{C}$  while at the In-life phase facility. At the In-life phase facility, upon collection all tissue samples were double-wrapped in polythene bags and immediately were stored in a polystyrene box containing ice packs to quickly reduce the sample temperature and then transferred to a freezer within approximately three hours of collection, which was set to maintain a temperature of less than  $-15^{\circ}\text{C}$ .

Whole milk, cream, skim milk and tissue samples were transported frozen in a freezer truck from ADAS, the In-Life phase facility, to CEMAS for sample preparation and residue analysis. All samples were received at CEMAS on the day of shipment. Upon receipt by CEMAS, samples were checked for identification with the previously assigned sample numbers. All samples remained frozen during shipment and were stored in temperature-monitored freezers at approximately  $\leq -18^{\circ}\text{C}$  on arrival.

Complete samples of muscle, fat, liver and kidney were homogenised in a Robot Coupe processor in the presence of dry ice (dry ice was not required for muscle samples). After appropriate mixing of each sample, samples were transferred to HDPE plastic containers. No preparation was required for milk, skim milk or cream samples.

### Analytical Methodology

Residues of XDE-729 methyl, XDE-729 acid and X11449757 were determined using the analytical method described in the study report. Full validation data is shown below (Section B.7.9.4). A summary of the method follows:

Residues were extracted from a 1.0-gram portion of muscle, liver, or kidney by homogenising with 20.0 mL of an acetonitrile/water (80:20) solution. Residues were extracted from a 1.0-gram portion of milk or fat by homogenising with 20.0 mL of an acetonitrile/water (80:20) solution plus 20.0 mL of n-hexanes. The sample was shaken and centrifuged and a 500- $\mu\text{L}$  aliquot of the acetonitrile/water layer was mixed with 100  $\mu\text{L}$  of a 50-ng/mL stable isotope internal standard and 1400  $\mu\text{L}$  of water. After mixing and filtration, residues were analysed by high performance liquid chromatography with positive-ion electrospray (ESI) tandem mass spectrometry (LC/MS/MS).

The limit of detection (LOD) and limit of quantitation (LOQ) of XDE-729 methyl, XDE-729 acid and X11449757 in all matrices were 0.003 mg/kg and 0.01 mg/kg, respectively.

This method is validated for the determination of XDE-729 methyl, XDE-729 acid and X11449757 in whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat as part of this study. Method validation was carried out within the feeding study for XDE-729, XDE-729 acid and X11449757 in each matrix by the analysis of five control samples fortified at the LOQ (0.01 mg/kg) and five control samples fortified at 10 x LOQ (0.1 mg/kg). The validation was carried during the first analytical batch for whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat and detailed results for quantitation ion and confirmatory ion are included in the study report. Validation recovery data, based on the quantitation ion, showed overall recovery averages for the analytes (XDE-729, XDE-729 acid and X11449757) in all matrices (whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat) ranged from 89% to 106%.

## RESULTS AND DISCUSSION

### Animal Health

All animals were observed at least twice daily for general health. No adverse treatment-related effects were observed on body weight, feed consumption or milk production.

Additionally, no treatment-related behavioural reactions or systemic signs of toxicity were noted. Gross necropsies showed no effects that appeared to be treatment-related. Cow 27 (treatment group D, 15-day depuration) was found to be lame on 02 March 12. On veterinary advice, this cow was exchanged with cow 24 (treatment group D, 10-day depuration) on humane grounds. As a result of this change, cow 27 was sacrificed after 10 days of depuration and cow 24 after 15 days of depuration.

#### Storage Stability

The whole milk, cream and skim milk samples from this study were stored frozen up to 91 days, 74 days and 70 days, respectively, from the date of sampling to analysis. Samples of muscle, liver, kidney and fat were stored up to 70 days, 69 days, 68 days and 70 days, respectively, from the date of sampling to analysis.

A storage stability test was performed as a separate study for residues of XDE-729 methyl, XDE-729 acid and X11449757 in matrices of animal origin and is currently on-going, but results to this point have been provided in an interim report, which is validated above in Section B.7.6.2 *Analytical method for residues determination*. In this study storage stability was evaluated in bovine milk, bovine muscle, poultry liver, and poultry eggs as representative matrices for materials of animal origin. Interim results from this study demonstrated that residues of XDE-729 methyl and XDE-729 acid remain stable in poultry liver, poultry eggs, bovine milk and bovine muscle for at least 371 days. The period of demonstrated frozen storage stability for XDE-729 methyl and XDE-729 acid exceeds the maximum period for which samples from the feeding study were stored before analysis and therefore shows adequate frozen storage stability for residues of XDE-729 methyl and XDE-729 acid in the feeding study samples. The storage stability study demonstrates that residues of X11449757 do not exhibit any significant degradation for at least 182 days in bovine muscle, bovine milk, poultry liver and poultry eggs while stored under frozen conditions. In line with XDE-729 methyl and XDE-729 acid, the storage stability exceeds the maximum period for which samples from the feeding study were stored before analysis and therefore shows adequate frozen storage stability for residues of X11449757.

Where extract solutions needed to be stored during the extraction process this was done in a cold room set at 4°C. The procedural recoveries demonstrate the stability of the analyte during this storage (up to 6 days).

**Table B.7.9.3-4 Summary of Sample Frozen Storage Conditions**

Matrix	Storage Temperature (°C) <sup>a</sup>	Maximum Storage Duration (days)	Interval of Demonstrated Frozen Storage Stability – Interim Report (days) <sup>b</sup>
Whole milk	≤ -18	91	371 <sup>b</sup> / 182 <sup>c</sup>
Skim milk	≤ -18	70	371 <sup>b</sup> / 182 <sup>c</sup>
Cream	≤ -18	74	371 <sup>b</sup> / 182 <sup>c</sup>
Muscle	≤ -18	70	371 <sup>b</sup> / 182 <sup>c</sup>
Subcutaneous Fat	≤ -18	70	371 <sup>b</sup> / 182 <sup>c</sup>
Mesenteric Fat	≤ -18	70	371 <sup>b</sup> / 182 <sup>c</sup>
Perirenal Fat	≤ -18	69	371 <sup>b</sup> / 182 <sup>c</sup>
Liver	≤ -18	69	371 <sup>b</sup> / 182 <sup>c</sup>
Kidney	≤ -18	68	371 <sup>b</sup> / 182 <sup>c</sup>

<sup>a</sup> Storage temperature at the analytical laboratory (CEMAS) was -18°C or less.

<sup>b</sup> Interim report, maximum storage interval currently evaluated for XDE-729 methyl and XDE-729 acid

<sup>c</sup> Interim report, maximum storage interval currently evaluated for X11449757. Additional data for longer intervals will become available as the study continues

### Analytical Method Performance

The efficiency of the analytical method was determined at the time of analysis of each set of samples by fortifying aliquots of the appropriate control matrix with analyte and analysing according to the method. An unfortified control matrix, reagent blank, and control matrix fortified at the limit of detection (LOD) were included in each set as well. The LOD recovery samples were analysed only to demonstrate observable peaks at the LOD level. Therefore, the percent recovery of analyte is not reported for these samples. Recoveries were corrected for any apparent residue in the corresponding control sample.

Fortified recoveries were analysed over a range of 0.01 mg/kg to 1.0 mg/kg (liver and kidney) and 0.01 mg/kg to 0.1 mg/kg (all other matrices). Overall average procedural recovery for the three analytes (XDE-729 methyl, XDE-729 acid and X11449757) in all matrices (whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat) ranged from 89% to 105%, and are therefore acceptable.

### Residues in Whole Milk

A summary of XDE-729 methyl, XDE-729 acid and X11449757 residues in whole milk during the dosing and depuration periods is presented in the tables below. Since no residues above the LOQ were found in whole milk, there was not an opportunity to demonstrate that a plateau level of residue had been reached before dosing ended. Although residues did not exceed the LOQ in any whole milk sample and in most cases were ND (<0.003 mg/kg), the dosing period of 28 to 29 consecutive days is considered sufficient since this meets guideline requirements and is expected to be sufficient time for residues to begin to appear in milk if there was potential for appreciable transfer of residues to milk. Except for one sample of



milk with a detectable residue of XDE-729 methyl (Group C) and a few samples of milk from the 15.31 mg/kg (Group D) dose level with detectable residues of X11449757 (0.003-0.008 mg/kg range), residues in the milk samples were ND (not detected, below the LOD of 0.003 mg/kg). Average residues in milk are listed below, but since residues were typically not detected (ND), all averages are also ND. These results are consistent with those observed in the NOR (Nature of the Residue) study conducted with XDE-729 methyl in goats since in that study residues of XDE-729 methyl, XDE-729 acid and X11449757 were not observed in milk above the analytical LOD of 0.003 mg/kg when the goats were dosed with [<sup>14</sup>C]-XDE-729 methyl at a level equivalent to approximately 10 mg/kg in dry feed.

#### Skim Milk and Cream

Samples of whole milk collected on study days 22 and 26 were mechanically separated into skim milk and cream in order to determine if residues partition preferentially with either fraction. Results of residue analysis for XDE-729 methyl, XDE-729 acid and X11449757 in skim milk and cream are presented in **Table B.7.9.3-9**. There was no indication of residue concentration in either the cream or skim milk fractions as residues in all samples were ND (<0.003 mg/kg); however, residues were not detected in corresponding whole milk samples.

#### Residues in Tissues (Muscle, Fat, Liver and Kidney)

Residues of XDE-729 methyl, XDE-729 acid and X11449757 in muscle, fat, liver and kidney from animals slaughtered upon completion of the dosing period (slaughtered within 8 hours of administration of final dose) are listed in **Table B.7.9.3-10**. Additionally, a summary of average XDE-729 methyl, XDE-729 acid and X11449757 residues in muscle, fat, liver and kidney is shown in **Table B.7.9.3-11**.

Residues of XDE-729 methyl were ND (<0.003 mg/kg) at all dose levels in all tissues evaluated (muscle, fat, liver and kidney). Residues of XDE-729 acid were ND (<0.003 mg/kg) at all dose levels in muscle, fat and liver, but were detected at levels below the LOQ of 0.01 mg/kg in kidney from one cow in the 1.06 mg/kg dose group and in two cows in the 15.31 mg/kg dose group. Residues of X11449757 were ND (<0.003 mg/kg) at all dose levels in muscle. However, X11449757 was detected at levels below the LOQ of 0.01 mg/kg in kidney from cows in the 1.06 mg/kg dose level group and was found at levels above the LOQ in kidney in the 3.16 mg/kg and 15.31 mg/kg dose level groups. In liver, X11449757 was found at levels above the LOQ in all dose level groups. Additionally, X11449757 was ND (<0.003 mg/kg) in fat in the 1.06 mg/kg and 3.16 mg/kg dose level groups, but was detected ( $\geq 0.003$  mg/kg) or above the LOQ in several of the fat samples from the 15.31 mg/kg (Group D) dose level.

Regression graphs for residues of X11449757 in liver and kidney by dose level of XDE-729 methyl in the diet are shown in **Table B.7.9.3-12**. The regression analysis demonstrated a linear relationship between the dose level and the resulting residue concentration. Regression analysis was not performed for XDE-729 methyl or XDE-729 acid, or for X11449757 in tissues other than liver and kidney or in milk, as in almost all cases the residues were below the LOQ.

Depuration of residues of XDE-729 methyl, XDE-729 acid and X11449757 from muscle, fat, liver and kidney was evaluated in specified cows in the 15.31 mg/kg (Group D) dose level at

3, 5, 10 and 15 days after administration of the final dose on Study Day 28. Depuration data is reported in the bottom portion of the same tables with other tissue residue data for XDE-729 methyl, XDE-729 acid and X11449757 (i.e. depuration data for tissues begins on Study Day 31, which is 3 days after the administration of the final dose on Study Day 28). All residues in the depuration animals were below the LOQ by Day 31 of the study (3 days after withdrawal of the test item from the cows' diet). At 3 days after withdrawal (Day 31), residues were ND ( $<0.003$  mg/kg) in milk and all tissues evaluated, except for one liver sample in which residues of X11449757 were detected ( $\geq 0.003$  mg/kg), but were below the LOQ.

Table B.7.9.3-5 Summary of Procedural Recoveries

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Whole milk	XDE-729 Methyl	0.01	32	96, 97, 105, 101, 103, 99, 92, 96, 100, 103, 95, 104, 103, 109, 104, 104, 97, 92, 89, 88, 108, 93, 96, 97, 99, 94, 92, 126, 96, 103, 100, 94	99	7.3
		0.10	23	100, 98, 98, 101, 100, 94, 105, 92, 95, 101, 101, 96, 104, 80, 97, 104, 103, 96, 95, 92, 101, 96, 103	98	5.6
				Overall mean	99	6.6
Skim milk	XDE-729 Methyl	0.01	5	89, 88, 95, 90, 96	92	4.0
		0.10	5	89, 96, 95, 95, 94	94	3.0
				Overall mean	93	3.5
Cream	XDE-729 Methyl	0.01	5	102, 105, 96, 108, 108	104	4.8
		0.10	5	101, 99, 97, 101, 95	99	2.6
				Overall mean	101	4.6
Muscle	XDE-729 Methyl	0.01	5	100, 89, 103, 96, 86	95	7.6
		0.10	5	105, 104, 93, 103, 86	98	8.5
				Overall mean	97	7.8

Table B.7.9.3-5 Summary of Procedural Recoveries (cont.)

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Liver	XDE-729 Methyl	0.01	5	93, 90, 93, 95, 100	94	3.9
		0.10	5	102, 100, 99, 94, 99	99	3.0
		1.0	2	101, 96	99	3.6
				Overall mean	97	4.0
Kidney	XDE-729 Methyl	0.01	5	94, 97, 103, 96, 97	97	3.5
		0.10	5	93, 99, 101, 101, 100	99	3.4
		1.0	2	91, 97	94	4.5
				Overall mean	97	3.7
Subcutaneous Fat	XDE-729 Methyl	0.01	5	93, 103, 100, 94, 97	97	4.3
		0.10	5	96, 89, 94, 100, 94	95	4.2
				Overall mean	96	4.3
Mesenteric Fat	XDE-729 Methyl	0.01	5	105, 97, 103, 92, 106	101	5.9
		0.10	5	100, 92, 97, 102, 102	99	4.3
				Overall mean	100	5.0
Perirenal Fat	XDE-729 Methyl	0.01	5	106, 88, 97, 107, 97	99	7.9
		0.10	5	104, 93, 106, 103, 93	100	6.3
				Overall mean	99	6.7

Table B.7.9.3-5 Summary of Procedural Recoveries (cont.)

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Whole milk	XDE-729 Acid	0.01	32	102, 106, 106, 90, 91, 86, 109, 91, 100, 109, 114, 75, 106, 116, 90, 101, 97, 95, 91, 91, 110, 95, 96, 96, 95, 97, 112, 109, 106, 92, 95, 98	99	9.3
		0.10	23	101, 106, 97, 100, 108, 103, 108, 104, 96, 99, 101, 100, 105, 77, 94, 102, 109, 104, 92, 103, 109, 93, 103	101	7.1
				Overall mean	100	8.4
Skim milk	XDE-729 Acid	0.01	5	104, 99, 108, 106, 94	102	5.6
		0.10	5	98, 108, 104, 99, 101	102	4.0
				Overall mean	102	4.6
Cream	XDE-729 Acid	0.01	5	89, 108, 101, 119, 97	103	11.1
		0.10	5	105, 106, 111, 104, 106	106	2.5
				Overall mean	105	7.7
Muscle	XDE-729 Acid	0.01	5	104, 101, 102, 79, 99	97	10.5
		0.10	5	104, 94, 88, 108, 90	97	9.1
				Overall mean	97	9.3

Table B.7.9.3-5 Summary of Procedural Recoveries (cont.)

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Liver	XDE-729 Acid	0.01	5	100, 108, 94, 100, 109	102	6.1
		0.10	5	99, 94, 105, 100, 99	99	3.9
		1.0	2	99, 96	98	2.2
				Overall mean	100	4.9
Kidney	XDE-729 Acid	0.01	5	103, 92, 101, 93, 94	97	5.2
		0.10	5	97, 98, 103, 100, 99	99	2.3
		1.0	2	99, 99	99	0.0
				Overall mean	98	3.7
Subcutaneous Fat	XDE-729 Acid	0.01	5	70, 99, 106, 109, 110	99	16.9
		0.10	5	103, 109, 99, 102, 99	102	4.0
				Overall mean	101	11.5
Mesenteric Fat	XDE-729 Acid	0.01	5	108, 78, 101, 96, 119	100	15.1
		0.10	5	100, 93, 103, 109, 97	100	6.0
				Overall mean	100	10.9
Perirenal Fat	XDE-729 Acid	0.01	5	103, 108, 95, 109, 79	99	12.5
		0.10	5	107, 106, 106, 110, 100	106	3.4
				Overall mean	102	9.1

**Table B.7.9.3-5 Summary of Procedural Recoveries (cont.)**

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Whole milk	X11449757	0.01	32	108, 96, 93, 106, 105, 98, 108, 101, 107, 106, 96, 120, 102, 104, 93, 89, 97, 106, 104, 89, 92, 87, 90, 87, 97, 110, 99, 98, 109, 109, 101, 103	100	7.9
		0.10	23	103, 110, 115, 115, 111, 105, 110, 107, 111, 109, 110, 108, 111, 88, 108, 107, 110, 103, 103, 107, 108, 110, 103	107	5.1
				Overall mean	103	7.5
Skim milk	X11449757	0.01	5	102, 103, 108, 100, 103	103	2.9
		0.10	5	107, 100, 111, 116, 103	107	5.9
				Overall mean	105	4.9
Cream	X11449757	0.01	5	94, 98, 103, 97, 86	96	6.6
		0.10	5	107, 103, 108, 111, 101	106	3.8
				Overall mean	101	7.3
Muscle	X11449757	0.01	5	86, 110, 79, 101, 94	94	13.0
		0.10	5	110, 100, 91, 108, 94	101	8.3
				Overall mean	97	10.7

Table B.7.9.3-5 Summary of Procedural Recoveries (cont.)

Matrix	Analyte	Fortification Level (mg/kg)	Number of Samples	Recoveries (%)	Mean Recovery (%)	RSD (%)
Liver	X11449757	0.01	5	99, 83, 90, 92, 96	92	6.7
		0.10	5	109, 109, 102, 106, 105	106	2.8
		1.0	2	100, 100	101	0.7
				Overall mean	99	8.0
Kidney	X11449757	0.01	5	79, 104, 84, 98, 79	89	13.0
		0.10	5	94, 97, 97, 103, 99	98	3.4
		1.0	2	96, 96	96	0.0
				Overall mean	94	9.1
Subcutaneous Fat	X11449757	0.01	5	101, 88, 91, 74, 77	86	12.7
		0.10	5	87, 93, 93, 97, 88	92	4.5
				Overall mean	89	9.3
Mesenteric Fat	X11449757	0.01	5	90, 85, 107, 98, 86	93	9.9
		0.10	5	105, 102, 102, 109, 95	103	5.0
				Overall mean	98	8.8
Perirenal Fat	X11449757	0.01	5	88, 110, 94, 102, 115	102	10.9
		0.10	5	102, 92, 109, 105, 89	99	8.6
				Overall mean	101	9.4



**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing**XDE-729 Methyl** <sup>a, b</sup>

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	1	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	2	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	4	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	5	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	6	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	7	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	8	<0.01	<0.01	<0.01	<0.01	<0.01	(0.008) <sup>c</sup>	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	9	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	10	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	11	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	12	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	13	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	14	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	15	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.<sup>c</sup> the LOD is <0.003 mg/kg, the notifier has recorded this sample as 0.008 mg/kg, although it is noted that the method is validated to an LOQ of <0.01 mg/kg.

**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing (cont.)**XDE-729 methyl**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
D	16	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	17	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	18	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	19	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	20	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	21	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	22	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	23	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	24	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	25	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	26	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	27	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing (cont.)**XDE-729 Acid**<sup>a, b</sup>

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	1	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	2	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	4	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	5	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	6	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	7	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	8	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	9	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	10	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	11	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	12	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	13	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	14	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	15	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing (cont.)**XDE-729 Acid**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
D	16	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	17	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	18	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	19	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	20	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	21	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	22	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	23	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	24	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	25	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	26	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	27	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing (cont.)**X11449757**<sup>a, b</sup>

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	1	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	2	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
A	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	4	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	5	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	6	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
B	7	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	8	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	9	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	10	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
C	11	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	12	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	13	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	14	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	15	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-6** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Dosing (cont.)**X11449757**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
D	16	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	17	<0.01	-	-	-	-	-	(0.004)	-	-	<0.01	-	(0.004)	-
D	18	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	19	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	20	<0.01	-	-	-	-	-	(0.003) <sup>c</sup>	-	-	<0.01	-	<0.01	-
D	21	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	22	<0.01	-	-	-	-	-	<0.01	-	-	(0.003)	-	<0.01	-
D	23	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	24	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	25	<0.01	-	-	-	-	-	<0.01	-	-	(0.003)	-	(0.003)	-
D	26	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-
D	27	<0.01	-	-	-	-	-	<0.01	-	-	<0.01	-	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.<sup>c</sup> the LOD is <0.003 mg/kg, the notifier has recorded this sample as 0.008 mg/kg, although it is noted that the method is validated to an LOQ of <0.01 mg/kg.

**Table B.7.9.3-7** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Depuration**XDE-729 Methyl** <sup>a, b</sup>

Dose Group	Cow Number	Study Day							
		29	30	31	33	35	36	40	42
D	16	<0.01	<0.01	-	-	-	-	-	-
D	17	<0.01	<0.01	-	-	-	-	-	-
D	18	<0.01	<0.01	-	-	-	-	-	-
D	19	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	20	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	21	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	22	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	23	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	24	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	25	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	26	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	27	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-7** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Depuration (cont.)**XDE-729 Acid**<sup>a, b</sup>

Dose Group	Cow Number	Study Day							
		29	30	31	33	35	36	40	42
D	16	<0.01	<0.01	-	-	-	-	-	-
D	17	<0.01	<0.01	-	-	-	-	-	-
D	18	<0.01	<0.01	-	-	-	-	-	-
D	19	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	20	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	21	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	22	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	23	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	24	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	25	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	26	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	27	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.



**Table B.7.9.3-7** Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk During Depuration (cont.)**X11449757**<sup>a, b</sup>

Dose Group	Cow Number	Study Day							
		29	30	31	33	35	36	40	42
D	16	<0.01	<0.01	-	-	-	-	-	-
D	17	<0.01	<0.01	-	-	-	-	-	-
D	18	<0.01	<0.01	-	-	-	-	-	-
D	19	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	20	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	21	<0.01	<0.01	<0.01	<0.01	-	-	-	-
D	22	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	23	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
D	24	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	25	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	26	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
D	27	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-8** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk**XDE-729 methyl**<sup>a, b</sup> - Dosing period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	0.0	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	1.06	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	3.16	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

**XDE-729 methyl**<sup>a, b</sup> - Depuration period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day							
		29	30	31	33	35	36	40	42
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-8** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk (cont.)**XDE-729 acid**<sup>a, b</sup> - Dosing period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	0.0	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	1.06	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	3.16	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

**XDE-729 acid**<sup>a, b</sup> - Depuration period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day							
		29	30	31	33	35	36	40	42
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-8** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Milk (cont.)**X11449757<sup>a, b</sup>** - Dosing period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day												
		-1	1	3	5	7	10	14	18	20	22	24	28	29
A	0.0	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
B	1.06	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-
C	3.16	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-	<0.01
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-

**X11449757<sup>a, b</sup>** - Depuration period

Dose Group	Dietary Dose, DM (mg/kg)	Study Day							
		29	30	31	33	35	36	40	42
D	15.31	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-9** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Skim Milk and Cream**XDE-729 Methyl**

Dose Group <sup>a</sup>	Cow Number	Residue (mg/kg)			
		Skim Milk		Cream	
		22 <sup>b</sup>	26 <sup>b</sup>	22 <sup>b</sup>	26 <sup>b</sup>
A	1	<0.01	<0.01	<0.01	<0.01
A	2	<0.01	<0.01	<0.01	<0.01
A	3	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
B	4	<0.01	<0.01	<0.01	<0.01
B	5	<0.01	<0.01	<0.01	<0.01
B	6	<0.01	<0.01	<0.01	<0.01
B	7	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
C	8	<0.01	<0.01	<0.01	<0.01
C	10	<0.01	<0.01	<0.01	<0.01
C	11	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
D	12	<0.01	<0.01	<0.01	<0.01
D	13	<0.01	<0.01	<0.01	<0.01
D	14	<0.01	<0.01	<0.01	<0.01
D	15	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01

<sup>a</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

<sup>b</sup> Study Day.

**Table B.7.9.3-9** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Skim Milk and Cream (cont.)**XDE-729 Acid**

Dose Group <sup>a</sup>	Cow Number	Residue (mg/kg)			
		Skim Milk		Cream	
		22 <sup>b</sup>	26 <sup>b</sup>	22 <sup>b</sup>	26 <sup>b</sup>
A	1	<0.01	<0.01	<0.01	<0.01
A	2	<0.01	<0.01	<0.01	<0.01
A	3	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
B	4	<0.01	<0.01	<0.01	<0.01
B	5	<0.01	<0.01	<0.01	<0.01
B	6	<0.01	<0.01	<0.01	<0.01
B	7	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
C	8	<0.01	<0.01	<0.01	<0.01
C	10	<0.01	<0.01	<0.01	<0.01
C	11	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
D	12	<0.01	<0.01	<0.01	<0.01
D	13	<0.01	<0.01	<0.01	<0.01
D	14	<0.01	<0.01	<0.01	<0.01
D	15	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01

<sup>a</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

<sup>b</sup> Study Day

**Table B.7.9.3-9** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Skim Milk and Cream (cont.)**X11449757**

Dose Group <sup>a</sup>	Cow Number	Residue (mg/kg)			
		Skim Milk		Cream	
		22 <sup>b</sup>	26 <sup>b</sup>	22 <sup>b</sup>	26 <sup>b</sup>
A	1	<0.01	<0.01	<0.01	<0.01
A	2	<0.01	<0.01	<0.01	<0.01
A	3	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
B	4	<0.01	<0.01	<0.01	<0.01
B	5	<0.01	<0.01	<0.01	<0.01
B	6	<0.01	<0.01	<0.01	<0.01
B	7	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
C	8	<0.01	<0.01	<0.01	<0.01
C	10	<0.01	<0.01	<0.01	<0.01
C	11	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01
D	12	<0.01	<0.01	<0.01	<0.01
D	13	<0.01	<0.01	<0.01	<0.01
D	14	<0.01	<0.01	<0.01	<0.01
D	15	<0.01	<0.01	<0.01	<0.01
Mean		<0.01	<0.01	<0.01	<0.01

<sup>a</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

<sup>b</sup> Study Day

**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat**XDE-729 Methyl**<sup>a, b</sup>

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Muscle	Liver	Kidney
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	<0.01	<0.01
B	5	28	0	<0.01	<0.01	<0.01
B	6	28	0	<0.01	<0.01	<0.01
B	7	28	0	<0.01	<0.01	<0.01
C	8	29	0	<0.01	<0.01	<0.01
C	9	29	0	<0.01	<0.01	<0.01
C	10	29	0	<0.01	<0.01	<0.01
C	11	29	0	<0.01	<0.01	<0.01
D	12	28	0	<0.01	<0.01	<0.01
D	13	28	0	<0.01	<0.01	<0.01
D	14	28	0	<0.01	<0.01	<0.01
D	15	28	0	<0.01	<0.01	<0.01
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	<0.01	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	24	38	10	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg/kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.



**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**XDE-729 Methyl**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	<0.01	<0.01
B	5	28	0	<0.01	<0.01	<0.01
B	6	28	0	<0.01	<0.01	<0.01
B	7	28	0	<0.01	<0.01	<0.01
C	8	29	0	<0.01	<0.01	<0.01
C	9	29	0	<0.01	<0.01	<0.01
C	10	29	0	<0.01	<0.01	<0.01
C	11	29	0	<0.01	<0.01	<0.01
D	12	28	0	<0.01	<0.01	<0.01
D	13	28	0	<0.01	<0.01	<0.01
D	14	28	0	<0.01	<0.01	<0.01
D	15	28	0	<0.01	<0.01	<0.01
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	<0.01	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	27	38	10	<0.01	<0.01	<0.01
D	24	43	15	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**XDE-729 Acid**<sup>a, b</sup>

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Muscle	Liver	Kidney
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	<0.01	(0.004)
B	5	28	0	<0.01	<0.01	<0.01
B	6	28	0	<0.01	<0.01	<0.01
B	7	28	0	<0.01	<0.01	<0.01
C	8	29	0	<0.01	<0.01	<0.01
C	9	29	0	<0.01	<0.01	<0.01
C	10	29	0	<0.01	<0.01	<0.01
C	11	29	0	<0.01	<0.01	<0.01
D	12	28	0	<0.01	<0.01	(0.004)
D	13	28	0	<0.01	<0.01	(0.004)
D	14	28	0	<0.01	<0.01	<0.01
D	15	28	0	<0.01	<0.01	<0.01
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	<0.01	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	27	38	10	<0.01	<0.01	<0.01
D	24	43	15	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively. respectively.

**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**XDE-729 Acid**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	<0.01	<0.01
B	5	28	0	<0.01	<0.01	<0.01
B	6	28	0	<0.01	<0.01	<0.01
B	7	28	0	<0.01	<0.01	<0.01
C	8	29	0	<0.01	<0.01	<0.01
C	9	29	0	<0.01	<0.01	<0.01
C	10	29	0	<0.01	<0.01	<0.01
C	11	29	0	<0.01	<0.01	<0.01
D	12	28	0	<0.01	<0.01	<0.01
D	13	28	0	<0.01	<0.01	<0.01
D	14	28	0	<0.01	<0.01	<0.01
D	15	28	0	<0.01	<0.01	<0.01
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	<0.01	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	24	38	10	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively. respectively.

**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**X11449757<sup>a, b</sup>**

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Muscle	Liver	Kidney
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	0.010	(0.005)
B	5	28	0	<0.01	0.012	(0.004)
B	6	28	0	<0.01	0.011	(0.004)
B	7	28	0	<0.01	(0.008)	(0.004)
C	8	29	0	<0.01	0.045	0.022
C	9	29	0	<0.01	0.036	0.020
C	10	29	0	<0.01	0.036	0.024
C	11	29	0	<0.01	0.026	0.014
D	12	28	0	<0.01	0.216	0.048
D	13	28	0	<0.01	0.145	0.054
D	14	28	0	<0.01	0.164	0.045
D	15	28	0	<0.01	0.169	0.066
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	(0.004)	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	24	38	10	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively. respectively.

**Table B.7.9.3-10** Summary of Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**X11449757**<sup>a, b</sup> - continued

Dose Group	Cow Number	Study Day	Days After Last Dose	Residue (mg/kg)		
				Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	1	29	0	<0.01	<0.01	<0.01
A	2	29	0	<0.01	<0.01	<0.01
A	3	29	0	<0.01	<0.01	<0.01
B	4	28	0	<0.01	<0.01	<0.01
B	5	28	0	<0.01	<0.01	<0.01
B	6	28	0	<0.01	<0.01	<0.01
B	7	28	0	<0.01	<0.01	<0.01
C	8	29	0	<0.01	<0.01	<0.01
C	9	29	0	<0.01	<0.01	<0.01
C	10	29	0	<0.01	<0.01	<0.01
C	11	29	0	<0.01	<0.01	<0.01
D	12	28	0	(0.003)	<0.01	0.014
D	13	28	0	(0.004)	0.012	(0.005)
D	14	28	0	<0.01	<0.01	<0.01
D	15	28	0	(0.007)	<0.01	(0.004)
D	16	31	3	<0.01	<0.01	<0.01
D	17	31	3	<0.01	<0.01	<0.01
D	18	31	3	<0.01	<0.01	<0.01
D	19	33	5	<0.01	<0.01	<0.01
D	20	33	5	<0.01	<0.01	<0.01
D	21	33	5	<0.01	<0.01	<0.01
D	22	38	10	<0.01	<0.01	<0.01
D	23	38	10	<0.01	<0.01	<0.01
D	27	38	10	<0.01	<0.01	<0.01
D	24	43	15	<0.01	<0.01	<0.01
D	25	43	15	<0.01	<0.01	<0.01
D	26	43	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg.<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg /kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-11** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat**XDE-729 Methyl**<sup>a, b</sup>

Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Muscle	Liver	Kidney
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	<0.01	<0.01
C	3.16	-	<0.01	<0.01	<0.01
D	15.31	-	<0.01	<0.01	<0.01
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	<0.01	<0.01
C	3.16	-	<0.01	<0.01	<0.01
D	15.31	-	<0.01	<0.01	<0.01
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg/kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-11** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**XDE-729 Acid**<sup>a, b</sup>

Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Muscle	Liver	Kidney
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	<0.01	<0.01
C	3.16	-	<0.01	<0.01	<0.01
D	15.31	-	<0.01	<0.01	<0.01
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	<0.01	<0.01
C	3.16	-	<0.01	<0.01	<0.01
D	15.31	-	<0.01	<0.01	<0.01
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg/kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.

**Table B.7.9.3-11** Average Residues of XDE-729 methyl, XDE-729 acid and X11449757 in Muscle, Liver, Kidney and Fat (cont.)**X11449757**<sup>a, b</sup>

Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Muscle	Liver	Kidney
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	0.010	(0.004)
C	3.16	-	<0.01	0.036	0.020
D	15.31	-	<0.01	0.174	0.053
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

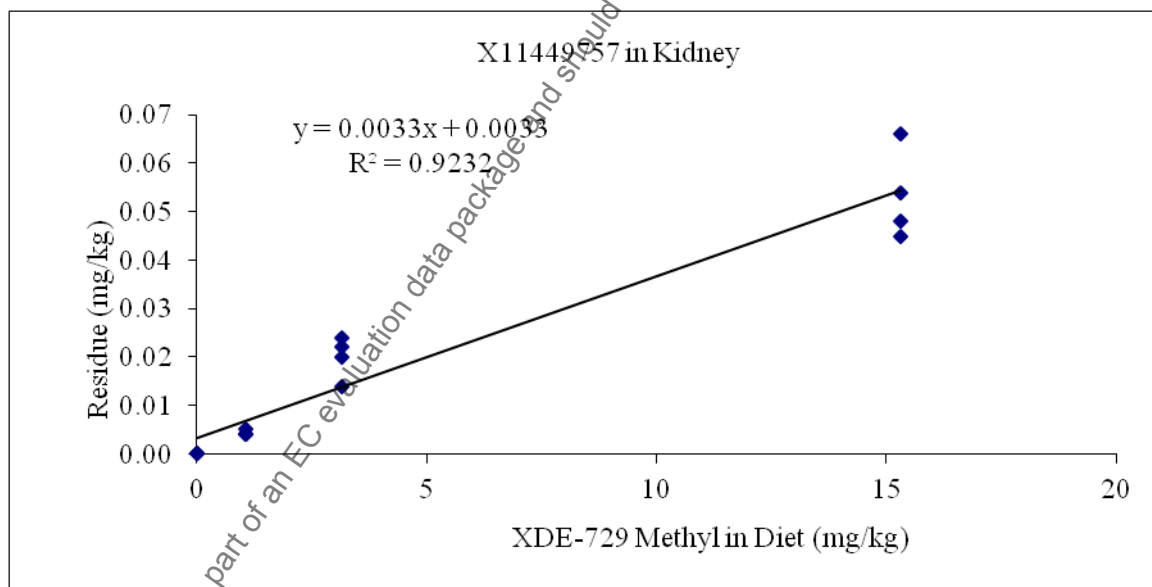
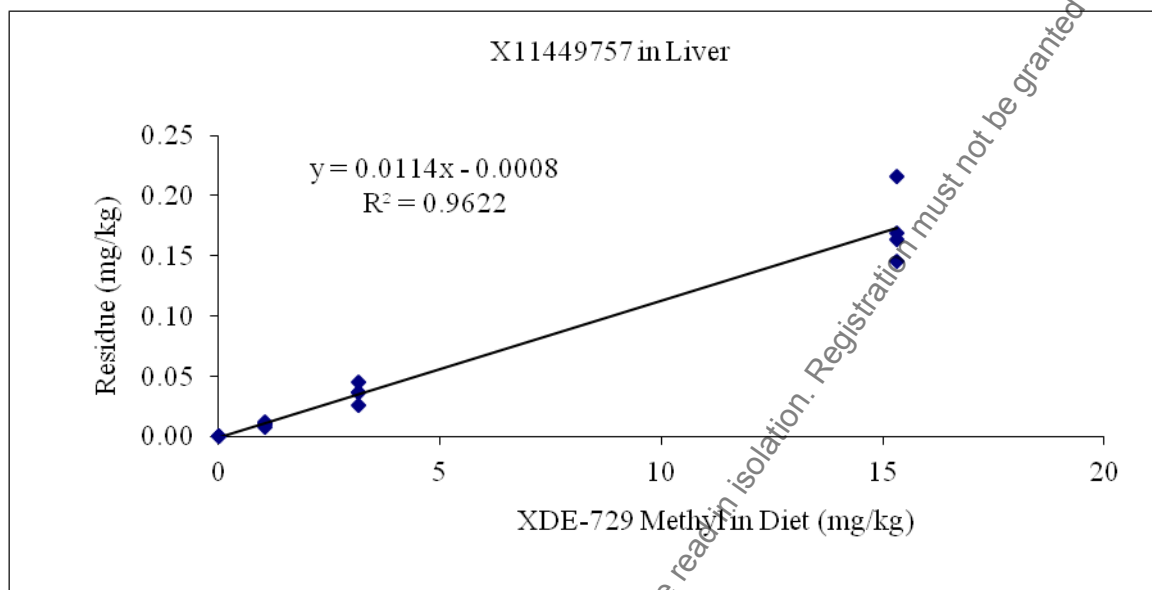
Dose Group	Dietary Dose, DM (mg/kg)	Days of Depuration	Average Residue (mg/kg)		
			Subcutaneous Fat	Mesenteric Fat	Perirenal Fat
A	0.0	-	<0.01	<0.01	<0.01
B	1.06	-	<0.01	<0.01	<0.01
C	3.16	-	<0.01	<0.01	<0.01
D	15.31	-	(0.004)	(0.003)	(0.006)
D	15.31	3	<0.01	<0.01	<0.01
D	15.31	5	<0.01	<0.01	<0.01
D	15.31	10	<0.01	<0.01	<0.01
D	15.31	15	<0.01	<0.01	<0.01

<sup>a</sup> All concentrations are expressed in mg/kg. Averages are calculated from individual results, rounded to 3 decimal places. Residues below the LOD (ND) are classed as 0 mg/kg for the purposes of calculating mean values.

<sup>b</sup> Average dose levels of XDE-729 methyl attained when expressed on the basis of concentration in the diet (mg/kg dry matter) for Dose Groups A, B, C and D were 0.00 mg/kg, 1.06 mg/kg, 3.16 mg/kg, 15.31 mg/kg, respectively.



**Table B.7.9.3-12** Linear Regression of X11449757 Residue Concentration in Liver and Kidney vs. XDE-729 Methyl Dosing Level



Residues are plotted against the actual calculated concentration of XDE-729 methyl in the diet for each dosing group.

## CONCLUSIONS

There is no requirement for animal feeding studies for the EU. However, feeding studies have been carried out to address the higher level of residues found in the Australian residue trials. This data has not been relied upon for the current evaluation, but has been presented for information. In the feeding study, lactating dairy cows were dosed with XDE-729 methyl to evaluate transfer of these compounds from the diet to milk, muscle, fat, kidney and liver. A 1x dose level was set based on maximum estimated residues in the Australian dairy cattle diet and this compound was also tested at two other dose levels (3.16 mg/kg and 15.31 mg/kg). The actual 1x dose level attained in the study expressed as mg/kg feed on a dry matter basis for XDE-729 methyl was 1.06 mg/kg. Dosing was carried out twice daily for 28 or 29 consecutive days.

No adverse treatment-related effects were observed on body weight, feed consumption or milk production. Additionally, no treatment-related behavioural reactions or systemic signs of toxicity were noted. Gross necropsies showed no effects that appeared to be treatment-related.

Residues of XDE-729 methyl and XDE-729 acid above the LOQ do not transfer into whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat or perirenal fat at any of the dose levels. Residues of X11449757 above the LOQ do not transfer into whole milk, skim milk, cream, muscle, subcutaneous fat, mesenteric fat or perirenal fat, with the exception of a single residue of 0.012 mg/kg in mesenteric fat and a single residue of 0.014 mg/kg in perirenal fat from cows in the highest (15.31 mg/kg) dose level group.

Residues of X11449757 above the LOQ transfer into liver at the 1.06 mg/kg, 3.16 mg/kg and 15.31 mg/kg dose levels and into kidney at the 3.16 mg/kg and 15.31 mg/kg dose levels.

Regression analysis for X11449757 in liver and kidney across dose levels demonstrated a linear relationship between the dose level and the resulting residue concentration. No regression analysis was performed for X11449757 in other matrices, or for XDE-729 methyl or XDE-729 acid in any matrices, because in almost all cases residues fell below the LOQ.

Depuration data generated using the 12 cows in the 15.31 mg/kg dose level showed that residues of X11449757 declined rapidly in liver and kidney following withdrawal of the test items from the cows' diet. All residues were below the LOQ by Day 31 of the study (3 days of depuration) and at that time, except for liver from one cow with a detectable residue that was <LOQ (residue of 0.004 mg/kg), all other residue values were ND (<0.003 mg/kg) by 3 days of depuration.

To conclude, results from the goat (ruminant) metabolism study with XDE-729 methyl suggest that no quantifiable residues of XDE-729 methyl or XDE-729 acid would be present in milk or edible tissues when dietary intake of XDE-729 methyl is 0.035 mg/kg or less in feed. Data from the lactating ruminant feeding study shown above provide further evaluation of the potential transfer of XDE-729 methyl residues from the diet of dairy or beef cattle to milk and edible tissues. The lowest dose level evaluated in that study was equivalent to XDE-729 methyl at 1.06 mg/kg feed on a DM (dry matter) basis or 0.037 mg/kg bw/day, if expressed on the basis of bodyweight. At this dose level, residues of XDE-729 methyl and XDE-729 acid in milk, muscle, fat and liver were not detected (ND, <0.003 mg/kg). In kidney, in one cow the residue of XDE-729 acid was <0.01 mg/kg and in the other three cows was not detected (ND, <0.003 mg/kg). The lowest dose level used in the cattle feeding study was 22N or 46N greater than the maximum expected dietary intake of residues in beef or dairy cattle, respectively (0.037 mg/kg bw/day / 0.0017 mg/kg bw/day = 22, or

0.037 mg/kg bw/day / 0.0008 mg/kg bw/day = 46). Based on these results residues of XDE-729 methyl or XDE-729 acid in milk or edible tissues are not expected to be detectable (ND, 0.003 mg/kg) based on dietary intake of residues resulting from the proposed uses of XDE-729 methyl in cereals.

#### B.7.9.4 Validation of Analytical Method of Analysis Used to Determine Residues in Animal Tissues.

Reference: [REDACTED] "XDE-729 Livestock Feeding Study: Magnitude of Residue in Milk, Muscle, Fat, Liver and Kidney of Lactating Dairy Cattle"; Unpublished Report of [REDACTED] (Report ID: [REDACTED]-5266), [REDACTED] Study Reference ID: 120077; 13 July 2012.

Guidelines: EC Council Directive 91/414/EEC – Working Document 7031/VI/95 rev. 4; OECD Guidance Document: Overview for Residue Chemistry Studies (2006); OECD Guidelines for the Testing of Chemicals, No. 505: Residues in Livestock (2007); APVMA Residue Guideline No. 1 – Animal Transfer Studies.

GLP: Yes, OECD Principles of Good Laboratory Practice [ENV/MC/CHEM(98)17]

Guidelines	SANCO/3029/99 rev. 4	
Matrix, limit of quantitation	bovine whole milk	0.01 mg/kg
	bovine skim milk	0.01 mg/kg
	bovine cream	0.01 mg/kg
	bovine muscle	0.01 mg/kg
	bovine liver	0.01 mg/kg
	bovine kidney	0.01 mg/kg
	bovine subcutaneous fat	0.01 mg/kg
	bovine mesenteric fat	0.01 mg/kg
	bovine perirenal fat	0.01 mg/kg
Description	<p><u>Scope</u></p> <p>This method is applicable for the quantitative determination of residues of XDE-729 methyl, XDE-729 acid and X11449757 in bovine tissues. The method was validated over the concentration range of 0.01-0.10 mg/kg with a validated limit of quantitation of 0.01 mg/kg.</p> <p>Method validation was carried out within the feeding study for XDE-729,</p>	

XDE-729 acid and X11449757 in each matrix by the analysis of five control samples fortified at the LOQ (0.01 mg/kg) and five control samples fortified at 10 x LOQ (0.1 mg/kg). The validation was carried during the first analytical batch for whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat and detailed results for quantitation ion and confirmatory ion are included in the study report. Validation recovery data, based on the quantitation ion, showed overall recovery averages for the analytes (XDE-729, XDE-729 acid and X11449757) in all matrices (whole milk, skim milk, cream, muscle, liver, kidney, subcutaneous fat, mesenteric fat and perirenal fat) ranged from 89% to 106%.

#### Principle

Residues were extracted from a 1.0-gram portion of muscle, liver, or kidney by homogenising with 20.0 mL of an acetonitrile/water (80:20) solution. Residues were extracted from a 1.0-gram portion of milk or fat by homogenising with 20.0 mL of an acetonitrile/water (80:20) solution plus 20.0 mL of n-hexanes. The sample was shaken and centrifuged and a 500- $\mu$ L aliquot of the acetonitrile/water layer was mixed with 100  $\mu$ L of a 50-ng/mL stable isotope internal standard and 1400  $\mu$ L of water. After mixing and filtration, residues were analysed by high performance liquid chromatography (Agilent Zorbax SB-C8, 4.6 x 75 mm, 3.5  $\mu$ m column, gradient elution: mobile phase A – water containing 0.10% formic acid, mobile phase B – methanol containing 0.1% formic acid) with positive-ion electrospray (ESI) tandem mass spectrometry (LC/MS/MS), monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard.

#### Calibration

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least squares equation which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of seven standards over the concentration range of 0.0375-5 ng/mL (equivalent to 0.003 mg/kg-0.5 mg/kg) demonstrated linearity with coefficients of determination ( $r^2$ ) of at least 0.999.

#### Validation

For each analyte, the method was validated over the concentration range of 0.01-0.10 mg/kg with a limit of quantitation of 0.01 mg/kg.

At the 0.01-mg/kg level (LOQ), the mean recoveries were within the range of 86-105%, with relative standard deviations within the range of 2.9-16.9%.

At the 0.10-mg/kg level (10x LOQ), the mean recoveries were within the range of 92-109%, with relative standard deviations within the range of 2.3-9.1%.

The above results comply with the acceptance criteria of SANCO/3029/99 rev. 4

#### Selectivity/Confirmation

The LC/MS/MS method is highly selective for both the quantitation and confirmation of XDE-729 methyl, XDE-729 acid and X11449757. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

XDE-729 methyl	$m/z$ 345/250 (quantitation)
	$m/z$ 345/235 (confirmation)
(M+6 ISTD)	$m/z$ 351/256 (quantitation)
XDE-729 acid	$m/z$ 331/250 (quantitation)
	$m/z$ 331/235 (confirmation)
(M+6 ISTD)	$m/z$ 337/256 (quantitation)
X11449757	$m/z$ 317/236 (quantitation)
	$m/z$ 319/238 (confirmation)
(M+6 ISTD)	$m/z$ 323/242 (quantitation)

The confirmation ratios for each analyte were determined by calculating the peak area ratios of the confirmation transition to the quantitation transition. Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards. This data is contained in the report.

#### Crossover factor

In this assay, the analytes and internal standards are quantitated using MS/MS transitions characteristic of each compound. When using stable-isotope labelled internal standards, there is a possibility that isotopic contributions will occur between the transitions used for quantitation of the

	<p>unlabelled and labelled compounds. The degree of isotopic crossover for each analyte and its respective stable isotope internal standard was determined and expressed as the crossover factor. In the case of X11449757, the analyte peak areas were corrected to take into account a crossover factor, which was applied to compensate for traces of 11449757 in the stable isotope internal standard. The study report stated that application of a crossover factor was not required for the calculation of XDE-729 methyl or XDE-729 acid residues.</p>
--	--

Summaries of the Validation Recoveries are shown below:

**Table B.7.9.4-1 Whole Milk – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	92	97	4.4
		96		
		100		
		103		
		95		
	0.10	100	97	4.4
		94		
		105		
		92		
		95		
Overall			97	4.7
XDE-729 Acid	0.01	109	105	8.7
		91		
		100		
		109		
		114		
	0.10	108	104	4.7
		103		
		108		
		104		
		96		
Overall			104	6.6
X11449757	0.01	108	104	4.9
		101		
		107		
		106		
		96		
	0.10	111	109	2.5
		105		
		110		
		107		
		111		
Overall			106	4.4

**Table B.7.9.4-2 Skim Milk – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	89	92	4.0
		88		
		95		
		90		
		96		
	0.10	89	94	3.0
		96		
		95		
		95		
		94		
Overall		93	3.5	
XDE-729 Acid	0.01	104	102	5.6
		99		
		108		
		106		
		94		
	0.10	98	102	4.0
		108		
		104		
		99		
		101		
Overall		102	4.6	
X11449757	0.01	102	103	2.9
		103		
		108		
		100		
		103		
	0.10	107	107	5.9
		100		
		111		
		116		
		103		
Overall		105	4.9	



**Table B.7.9.4-3 Cream – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	102	104	4.8
		105		
		96		
		108		
		108		
	0.10	101	99	2.6
		99		
		97		
		101		
		95		
Overall			101	4.6
XDE-729 Acid	0.01	89	103	11.1
		108		
		101		
		119		
		97		
	0.10	105	106	2.5
		106		
		111		
		104		
		106		
Overall			105	7.7
X11449757	0.01	94	96	6.6
		98		
		109		
		97		
		86		
	0.10	107	106	3.8
		103		
		108		
		111		
		101		
Overall			101	7.3

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

**Table B.7.9.4-4 Muscle – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	100	95	7.6
		89		
		103		
		96		
		86		
	0.10	105	98	8.5
		104		
		93		
		103		
		86		
Overall		97	7.8	
XDE-729 Acid	0.01	104	97	10.5
		101		
		102		
		79		
		99		
	0.10	104	97	9.1
		94		
		88		
		108		
		90		
Overall		97	9.3	
X11449757	0.01	86	94	13.0
		110		
		79		
		101		
		94		
	0.10	110	101	8.3
		100		
		91		
		108		
		94		
Overall		97	10.7	

**Table B.7.9.4-5 Liver – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	93	94	3.9
		90		
		93		
		95		
		100		
	0.10	102	99	3.0
		100		
		99		
		94		
		99		
Overall		97	4.1	
XDE-729 Acid	0.01	100	102	6.1
		108		
		94		
		100		
		109		
	0.10	99	99	3.9
		94		
		105		
		100		
		99		
Overall		101	5.1	
X11449757	0.01	99	92	6.7
		83		
		90		
		92		
		96		
	0.10	109	106	2.8
		109		
		102		
		106		
		105		
Overall		99	8.8	

**Table B.7.9.4-6 Kidney – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	94	97	3.5
		97		
		103		
		96		
		97		
	0.10	93	99	3.4
		99		
		101		
		101		
		100		
Overall			98	3.3
XDE-729 Acid	0.01	103	97	5.2
		92		
		101		
		93		
		94		
	0.10	97	99	2.3
		98		
		103		
		100		
		99		
Overall			98	4.1
X11449757	0.01	79	89	13.0
		104		
		84		
		98		
		79		
	0.10	94	98	3.4
		97		
		97		
		103		
		99		
Overall			93	10.0

**Table B.7.9.4-7 Subcutaneous Fat – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	93	97	4.3
		103		
		100		
		94		
		97		
	0.10	96	95	4.2
		89		
		94		
		100		
		94		
Overall		96	4.3	
XDE-729 Acid	0.01	70	99	16.9
		99		
		106		
		109		
		110		
	0.10	103	102	4.0
		109		
		99		
		102		
		99		
Overall		101	11.5	
X11449757	0.01	101	86	12.7
		88		
		91		
		94		
		77		
	0.10	87	92	4.5
		93		
		93		
		97		
		88		
Overall		89	9.3	

**Table B.7.9.4-8 Mesenteric Fat – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	105	101	5.9
		97		
		103		
		92		
		106		
	0.10	100	99	4.3
		92		
		97		
		102		
		102		
Overall		100	5.0	
XDE-729 Acid	0.01	108	100	15.1
		78		
		101		
		96		
		119		
	0.10	100	100	6.0
		93		
		103		
		109		
		97		
Overall		100	10.9	
X11449757	0.01	90	93	9.9
		85		
		100		
		98		
		86		
	0.10	105	103	5.0
		102		
		102		
		109		
		95		
Overall		98	8.8	

**Table B.7.9.4-9 Perirenal Fat – Quantitation Ion**

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean Recovery (%)	RSD (%)
XDE-729 Methyl	0.01	106	99	7.9
		88		
		97		
		107		
		97		
	0.10	104	100	6.3
		93		
		106		
		103		
		93		
Overall		99	6.7	
XDE-729 Acid	0.01	103	99	12.5
		108		
		95		
		109		
		79		
	0.10	107	106	3.4
		106		
		106		
		110		
		100		
Overall		102	9.1	
X11449757	0.01	88	102	10.9
		110		
		94		
		102		
		115		
	0.10	102	99	8.6
		92		
		109		
		105		
		89		
Overall		101	9.4	

**Conclusion**

Full validation data were obtained for the primary (quantitation) MS/MS transition according to SANCO/3029/99 rev. 4 and were acceptable.

It is noted that the method does rely on stable isotope labelled internal standards. Although this has no bearing on pre-registration, for post-registration it has been confirmed by the notifier that the stable isotope labelled internal standards would be made available in line with guidance.

**B.7.10 Residues in succeeding or rotational crops (IIA 6.6, IIIA 8.5)**

Based on results from the confined rotational crop study, which indicated a very low potential for residues in succeeding crops, no field residue trials with succeeding crops are expected to be necessary.

**B.7.11 Proposed pre-harvest intervals for envisaged uses or withholding periods, in the case of post harvest uses (Annex IIA 6.8, Annex IIIA 8.7)**

Based on the critical GAP the maximum growth stage of cereals at the time of application of XDE-729 methyl is BBCH 45. Therefore, application of XDE-729 methyl to these crops occurs during vegetative growth and prior to development of grain. Given this use pattern, it is proposed that it is more appropriate to establish a maximum growth stage at the latest timing for application of XDE-729 methyl rather than a PHI since the period between the latest timing for application and crop harvest would be several weeks. Consequently, no PHI is proposed. Instead, it is proposed that XDE-729 methyl should not be applied to cereals after a maximum growth stage of BBCH 45.

**B.7.12 Community MRL's and MRL's in EU Member States (IIIA 12.2)**

XDE-729 is a new compound to the EU, as such there are no extant authorisations for the use of XDE-729 in the EU.

**B.7.13 Proposed EU MRLs and justification for the acceptability of those MRL's (IIA 6.7, IIIA 8.6)**

Based on the proposed residue definition along with results from crop residue trials, MRLs are proposed. A residue value for both grain and straw from a spring barely trial was identified as a statistical outlier and was excluded from consideration when calculating MRLs for grain (the RMS note that EU MRLs are not currently required for commodities used as livestock feed; however, in this case estimated MRLs for straw have been presented in Table B.7.6.1-2 and Table B.7.6.1-3 (see section B.7.6.1) for information only, with a view to when MRLs will be set for animal feed commodities in future). After excluding the outlier, residues of XDE-729 methyl (sum of residues of XDE-729 methyl and XDE-729 acid expressed as XDE-729 methyl equivalents) in grain in winter wheat, spring wheat, winter barley and spring barley trials were not detected (<0.003 mg/kg) or were less than the LOQ (<0.01 mg/kg). Consequently, the calculated MRL in each case was 0.02 mg/kg (the residue definition for both risk assessment and enforcement is XDE-729 methyl ester and XDE-729 acid. The residue level is the sum of the two components in the residue definition). Since the straw for winter barely had somewhat higher residues than in the other cereal crops, it is anticipated that in future the proposed MRL for XDE-729 methyl in cereal straw will be based on winter barley and then proposed by extrapolation for the other cereals on which use is requested. For consistency, it is proposed that the MRL for XDE-729 methyl in grain be based on that for winter barley and then established in the other cereal grains also at 0.02 mg/kg by extrapolation.



**Therefore, a MRL for XDE-729 methyl of 0.02 mg/kg is proposed for the following cereal grains: barley (including spring and winter barley) and by extrapolation wheat, to include spring wheat, winter wheat, soft wheat, durum wheat, triticale and spelt), and rye.**

No MRL's are proposed for food commodities from livestock since dietary intake of residues in ruminants, poultry and swine is insignificant (<0.01 mg/kg) and secondary residues of XDE-729 methyl and XDE-729 acid in commodities from these animals are expected to be non-detectable (ND).

Residues of cloquintocet mexyl and cloquintocet acid in grain and straw in these trials were ND (<0.003 mg/kg) and are within levels previously evaluated for other approved uses of cloquintocet mexyl in the EU and therefore do not require further evaluation. Since cloquintocet-mexyl is safener rather than an active substance, no MRLs are established.

**B.7.14 Proposed EU Import tolerances and justification for the acceptability of those residues**

No EU import tolerances are requested at this time.

**B.7.15 Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRL's**

There are currently no existing or proposed Codex MRLs for XDE-729.

### B.7.16 Estimates of potential and actual dietary exposure through diet and other means (IIA 6.9, IIIA 8.8)

#### B.7.16.1 Intakes by domestic animals.

An assessment of the theoretical maximum daily intakes by domestic animals from the consumption of treated feed commodities (wheat and barley (straw and grain)) which may contain residues of XDE-729 has been made. The following assumptions have been made:

- (i) The highest likely inclusion rate of all crops which may have been treated has been used with the proviso that the aggregate does not exceed 100% diet.
- (ii) All crops which may have been treated have been treated and contain residues at the following levels:

**Table B.7.16.1-1**

Commodity	STMR (mg/kg)	HR (mg/kg)
Wheat grain	0.02	0.02
Wheat straw	0.02	0.03
Barley grain	0.02	0.02
Barley straw	0.02	0.05

- (iii) There is no loss of residue during transport, storage, processing or preparation of feed prior to consumption.

#### Intakes calculated using STMR input (median dietary burden)

Animal	mg/kg DM Basis	mg/kg AR Basis	mg/animal/day	mg/kg b.w./day
Dairy cattle *	0.014	0.012	0.2791	0.0005
Beef cattle	0.023	0.020	0.3488	0.0010
Pig *	0.019	0.016	0.0558	0.0007
Chicken *	0.016	0.014	0.0020	0.0010

\* Less than 100% of diet employed (DM diet)

#### Intakes calculated using HR input (maximum dietary burden)

Animal	mg/kg DM Basis	mg/kg AR Basis	mg/animal/day	mg/kg b.w./day
Dairy cattle *	0.021	0.018	0.4186	0.0008
Beef cattle	0.041	0.035	0.6105	0.0017
Pig *	0.019	0.016	0.0558	0.0007
Chicken *	0.016	0.014	0.0020	0.0010

\* Less than 100% of diet employed (DM diet)

Inclusion rates used are given in Appendix 6 (Annex 2) of the "Data Requirements for Approval under the Control of Pesticides Regulations 1986"

Based on the intakes calculated above, animal intakes are not triggered (i.e.  $<0.1$  mg/kg) for dairy beef and cattle, pig or chicken on a dry matter (DM) or as received (AR) basis.

### **Dairy and Beef Cattle:**

The animal intakes support the findings from the goat (ruminant) metabolism study with XDE-729 methyl, which suggest that no quantifiable residues of XDE-729 methyl or XDE-729 acid would be present in milk or edible tissues when dietary intake of XDE-729 methyl is 0.035 mg/kg or less in feed. Although the animal intakes and metabolism study did not trigger the need for a feeding study, data from the lactating ruminant feeding study were presented by the notifier for further evaluation of the potential transfer of XDE-729 methyl residues from the diet of dairy or beef cattle to milk and edible tissues. The lowest dose level evaluated in that study was equivalent to XDE-729 methyl at 1.06 mg/kg feed on a DM (dry matter) basis or 0.037 mg/kg bw/day, if expressed on the basis of bodyweight. At this dose level, residues of XDE-729 methyl and XDE-729 acid in milk, muscle, fat and liver were not detected (ND,  $<0.003$  mg/kg). In kidney, in one cow the residue of XDE-729 acid was  $<0.01$  mg/kg and in the other three cows was not detected (ND,  $<0.003$  mg/kg). The lowest dose level used in the cattle feeding study was 22N or 46N greater than the maximum expected dietary intake of residues in beef or dairy cattle, respectively ( $0.037$  mg/kg bw/day /  $0.0017$  mg/kg bw/day = 22, or  $0.037$  mg/kg bw/day /  $0.0008$  mg/kg bw/day = 46). Based on these results residues of XDE-729 methyl or XDE-729 acid in milk or edible tissues are not expected to be detectable (ND,  $<0.003$  mg/kg) based on dietary intake of residues resulting from the proposed uses of XDE-729 methyl in cereals. Therefore, no MRLs for XDE-729 methyl are proposed for edible commodities from dairy or beef cattle or other ruminant livestock.

### **Poultry**

Cereal straw is not used as feed for poultry. Although cereal grain is used as feed for poultry, residues of XDE-729 methyl and XDE-729 acid in grain in the critical GAP-compliant residue trials were  $<0.01$  mg/kg (not considering the result from one residue trial which was excluded since it was considered to be an outlier). Consequently, intake of XDE-729 methyl in the poultry diet is insignificant. Additionally, in consideration of the results from the poultry metabolism study and potential dietary residue intake, residues of XDE-729 methyl in eggs and edible poultry tissues are expected to be non-detectable (ND,  $<0.003$  mg/kg). Therefore, no MRLs are proposed for poultry commodities.

### **Pigs**

Cereal straw is not used as feed for pigs. Although cereal grain is used as feed for pigs, residues of XDE-729 methyl and XDE-729 acid in grain in the critical GAP-compliant residue trials were  $<0.01$  mg/kg (not considering the result from one residue trial which was excluded since it was considered to be an outlier). Consequently, intake of XDE-729 methyl in the pig diet is insignificant. Additionally, in consideration of the results from the goat metabolism study as well as results from the cattle feeding study and potential dietary residue intake, residues of XDE-

729 methyl in edible tissues are expected to be non-detectable (ND, <0.003 mg/kg). Therefore, no MRLs are proposed for commodities from pigs.

### B.7.16.2 Intakes by humans

#### B.7.16.2.1 Chronic (long term) dietary intake assessment

##### NEDIs

##### (a) Risk assessment – UK diets

The UK NEDIs for the active and commodities listed below have been calculated for ten consumer groups as detailed in the Regulatory Update 21/2005. The following assumptions have been made:

- (i) Upper range of normal (97.5th percentile) consumption of each individual crop which may have been treated.
- (ii) All produce eaten which may have been treated, has been treated and contains residues at the appropriate supervised trials median residue (STMR) level found in the trials considered to support the GAP:

**Table B.7.16.2.1-1**

Commodity	STMR (mg/kg)
Wheat grain	0.02*
Barley grain	0.02*

\*: Indicates lower limit of analytical determination (i.e. <LOQ)

The residue definition for both risk assessment and enforcement is **XDE-729 methyl ester and XDE-729 acid**. The residue level is the sum of the two components in the residue definition

- (iii) There is no loss of residue during transport, storage, processing or preparation of foods prior to consumption.

The UK NEDIs for the consumption of wheat and barley treated with XDE-729 are presented in the table above. The proposed Acceptable Daily Intake (ADI) is 0.058 mg/kg bw/day – see Volume 3, Annex B.6 of the DAR for details. Based on these calculations all intakes for the population groups assessed are below the ADI. Therefore, no health effects due to chronic dietary exposure are expected in UK consumers.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

Table B.7.16.2.1-2

Active substance:		XDE-729 methyl		ADI:		0.058 mg/kg bw /day		Source:		Toxicology Evaluation									
				TOTAL INTAKE based on 97.5th percentile															
				ADULT	INFANT	TODDLER	4-6 YEARS	7-10 YEARS	11-14 YEARS	15-18 YEARS	VEGETARIAN	ELDERLY (OWN HOME)	ELDERLY (RESIDENTIAL)						
mg/kg bw/day				0.00008	0.00008	0.00018	0.00019	0.00015	0.00010	0.00009	0.00010	0.00007	0.00007						
% of ADI				<1%	<1%	<1%	<1%	<1%	<1%	<1%	<1%	<1%	<1%						
STMR		P	COMMODITY INTAKES																
Commodity	(mg/kg)	(mg/kg bw/day)																	
Barley	0.02		0.00000	L/C	0.00001	0.00001	0.00002	0.00000	0.00000	0.00001	0.00001	0.00000							
Wheat	0.02		0.00007	0.00006	0.00017	0.00018	0.00013	0.00010	0.00008	0.00009	0.00007	0.00007							
Rye	0.02		0.00001	0.00003	0.00001	0.00001	0.00001	0.00001	0.00000	0.00001	0.00001	0.00000							
* 0.00000 corresponds to <0.000005 mg/kg bw /day (any value ≥0.000005 is rounded to 0.00001)																			
L/C Low consumption (<0.1 g/day) or low number of consumers (<4)																			

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

**(b) Risk assessment – EU diets**

The EU MS national NEDIs from the consumption of wheat and barley have been calculated using PRIMo – Pesticide Residues Intake Model (revision 2). The following assumptions have been made:

- (i) All produce eaten which may have been treated, has been treated and contains residues at the STMR level found in the trials considered to support GAP:

**Table B.7.16.2.1-3**

<b>Commodity</b>	<b>STMR (mg/kg)</b>
Wheat grain	0.02*
Barley grain	0.02*

\*: Indicates lower limit of analytical determination (i.e. <LOQ which is 0.02 mg/kg)

The residue definition for both risk assessment and enforcement is **XDE-729 methyl ester and XDE-729 acid**. The residue level is the sum of the two components in the residue definition

- (ii) There is no loss of residue during transport or storage of foods prior to consumption.

A full description of PRIMo and the underlying assumptions is in the document: 'Reasoned opinion on the potential chronic and acute risks to consumers' health arising from proposed temporary EC MRLs 15 March 2007' – see PRIMo, instructions worksheet, cell B7.

The relevant intake estimates are presented in **Table B.7.16.2.1-4**. Based on these calculations the consumer groups with the highest intakes are DK child and WHO Cluster diet B, with intakes that account for 0.3% of the ADI. Chronic intakes for all consumer groups are below the ADI and therefore no health effects due to chronic dietary exposure are expected in EU consumers.

**Volume 3, Annex B.7**

<div style="text-align: center; border: 1px solid black; padding: 5px;"> <b>XDE-729</b> </div> <div style="display: flex; justify-content: space-between; font-size: 0.8em;"> <div>Status of the active substance:</div> <div>Code no.</div> </div> <div style="display: flex; justify-content: space-between; font-size: 0.8em;"> <div>LOQ (mg/kg bw):</div> <div>0.01</div> <div>proposed LOQ:</div> </div> <div style="text-align: center; background-color: #cccccc; font-weight: bold; font-size: 0.8em;"> <b>Toxicological end points</b> </div> <div style="display: flex; justify-content: space-between; font-size: 0.8em;"> <div>ADI (mg/kg bw/day):</div> <div>0.058</div> <div>ARfD (mg/kg bw):</div> <div>2.5</div> </div> <div style="display: flex; justify-content: space-between; font-size: 0.8em;"> <div>Source of ADI:</div> <div>Tox eval</div> <div>Source of ARfD:</div> <div>Tox eval</div> </div> <div style="display: flex; justify-content: space-between; font-size: 0.8em;"> <div>Year of evaluation:</div> <div>2013</div> <div>Year of evaluation:</div> <div>2013</div> </div>				Prepare workbook for refined calculations				
				Undo refined calculations				
Explain choice of toxicological reference values. The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL). The pTMRLs have been submitted to EFSA in September 2006.								
Chronic risk assessment								
		TMDI (range) in % of ADI minimum - maximum						
		No of diets exceeding ADI:						
Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
0.3	DK child	0.2	Wheat	0.2	Rye		FRUIT (FRESH OR FROZEN)	
0.3	WHO Cluster diet B	0.3	Wheat	0.0	Barley	0.0	Rye	
0.2	WHO cluster diet D	0.2	Wheat	0.0	Rye	0.0	Barley	
0.2	IT kids/toddler	0.2	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	
0.2	WHO cluster diet E	0.1	Wheat	0.0	Barley	0.0	Rye	
0.2	WHO Cluster diet F	0.1	Wheat	0.0	Rye	0.0	Barley	
0.2	NL child	0.2	Wheat	0.0	Rye	0.0	Barley	
0.2	DE child	0.1	Wheat	0.0	Rye	0.0	Barley	
0.2	ES child	0.2	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	
0.1	IT adult	0.1	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	
0.1	PT General population	0.1	Wheat	0.0	Rye	0.0	Barley	
0.1	UK Toddler	0.1	Wheat	0.0	Barley	0.0	Rye	
0.1	IE adult	0.1	Wheat	0.0	Barley	0.0	Rye	
0.1	SE general population 90th percentile	0.1	Wheat	0.0	Rye		FRUIT (FRESH OR FROZEN)	
0.1	WHO regional European diet	0.1	Wheat	0.0	Barley	0.0	Rye	
0.1	FR all population	0.1	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	
0.1	ES adult	0.1	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	
0.1	DK adult	0.1	Wheat	0.0	Rye		FRUIT (FRESH OR FROZEN)	
0.1	FR toddler	0.1	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.1	UK Infant	0.1	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.1	NL general	0.1	Wheat	0.0	Barley	0.0	Rye	
0.1	LT adult	0.0	Rye	0.0	Wheat	0.0	Barley	
0.1	UK vegetarian	0.1	Wheat	0.0	Barley	0.0	Barley	
0.1	UK Adult	0.1	Wheat	0.0	Barley	0.0	Rye	
0.1	FI adult	0.0	Wheat	0.0	Rye	0.0	Barley	
0.0	FR infant	0.0	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	PL general population		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
<b>Conclusion:</b> The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of XDE-729 is unlikely to present a public health concern.								

**TMDIs**

As residues in grain at harvest are <LOQ then the NEDIs determined above will be the same as the TMDIs.

**B.7.16.2.2 Acute (short term) dietary intake assessment****(a) Risk assessment – UK diets**

The UK NESTIs for the active and commodities listed below have been calculated for ten consumer groups as detailed in the Regulatory Update 21/2005. The following assumptions have been made:

- (i) Upper range of normal (97.5th percentile) consumption of each individual crop which may have been treated.
- (ii) All produce eaten which may have been treated, has been treated and contains residues at the highest residue (HR, which is also the proposed MRL) level found in the trials considered to support the GAP.

**Table B.7.16.2.2-1**

<b>Commodity</b>	<b>HR (mg/kg)</b>
Wheat grain	0.02*
Barley grain	0.02*

\*: Indicates lower limit of analytical determination (i.e. <LOQ which is 0.02 mg/kg)

The residue definition for both risk assessment and enforcement is **XDE-729 methyl ester and XDE-729 acid**. The residue level is the sum of the two components in the residue definition

- (iii) There is no loss of residue during transport, storage, processing or preparation of foods prior to consumption.

The UK NESTIs for the consumption of wheat and barley treated with XDE-729 are presented in **Table B.7.16.2.2-2**. The proposed Acute Reference Dose (ARfD) is 2.5 mg/kg bw/day – see Volume 3, Annex B.6 of the DAR for details. Based on these calculations all of the consumer groups demonstrate intakes below 1% of the ARfD. Therefore, no health effects due to acute dietary exposure are expected in UK consumers.



**Table B.7.16.2.2-2**

[illegible]

**(b) Risk assessment – EU diets**

The EU MS national NESTIs from the consumption of wheat and barley have been calculated using PRIMo – Pesticide Residues Intake Model (revision 2). The following assumptions have been made:

- (i) All produce eaten which may have been treated, has been treated and contains residues at the highest residue (HR, which is also the MRL) level found in the trials considered to support GAP:

**Table B.7.16.2.2-3**

Commodity	HR (mg/kg)
Wheat grain	0.02*
Barley grain	0.02*

\*: Indicates lower limit of analytical determination (i.e. < LOQ which is 0.02 mg/kg)

The residue definition for both risk assessment and enforcement is **XDE-729 methyl ester and XDE-729 acid**. The residue level is the sum of the two components in the residue definition

- (ii) There is no loss of residue during transport or storage of foods prior to consumption.

A full description of PRIMo and the underlying assumptions is in the document: 'Reasoned opinion on the potential chronic and acute risks to consumers' health arising from proposed temporary EC MRLs, 15 March 2007' – see PRIMo, instructions worksheet, cell B7.

The relevant intake estimates are presented in **Table B.7.16.2.2-4**. Acute intakes for all consumer groups are below the ARfD and therefore no health effects due to acute dietary exposure are expected in EU consumers.

**Volume 3, Annex B.7**

**Table B.7.16.2.2-4**

Acute risk assessment / children						Acute risk assessment / adults / general population						
The acute risk assessment is based on the ARfD.												
For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.												
In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.												
In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variability factor of 3.												
Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100 % of the ARfD.												
Unprocessed commodities	No of commodities for which ARfD/ADI is exceeded (IESTI 1):			No of commodities for which ARfD/ADI is exceeded (IESTI 2):			No of commodities for which ARfD/ADI is exceeded (IESTI 1):			No of commodities for which ARfD/ADI is exceeded (IESTI 2):		
	IESTI 1			IESTI 2			IESTI 1			IESTI 2		
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -
	0.0	Rye	0.02 / -	0.0	Rye	0.02 / -	0.0	Barley	0.02 / -	0.0	Barley	0.02 / -
	0.0	Barley	0.02 / -	0.0	Barley	0.02 / -	0.0	Rye	0.02 / -	0.0	Rye	0.02 / -
No of critical MRLs (IESTI 1)			No of critical MRLs (IESTI 2)			No of critical MRLs (IESTI 1)			No of critical MRLs (IESTI 2)			
Processed commodities	No of commodities for which ARfD/ADI is exceeded:			No of commodities for which ARfD/ADI is exceeded:			No of commodities for which ARfD/ADI is exceeded:			No of commodities for which ARfD/ADI is exceeded:		
	IESTI 1			IESTI 2			IESTI 1			IESTI 2		
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)
	0.0	Wheat flour	0.02 / -				0.0	Bread/pizza	0.02 / -			
*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.												
**) pTMRL: provisional temporary MRL												
***) pTMRL: provisional temporary MRL for unprocessed commodity												
Conclusion:												
For XDE-729 IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.												
No exceedance of the ARfD/ADI was identified for any unprocessed commodity.												
For processed commodities, no exceedance of the ARfD/ADI was identified.												

### B.7.16.3 Conclusions on estimates of dietary exposure

UK and EU chronic and acute consumer risk assessments (UK NEDI, NESTI and EU PRIMo) have been performed using appropriate residue endpoints (chronic: STMR; acute: HR) which were derived from supervised residue trials that support the proposed GAP. It is noted that since residues in grain at harvest are <LOQ, the NEDIs determined above will be the same as the TMDIs, and the MRL has been taken account of since it is the same as the HR.

Chronic intakes for all consumer groups are below the proposed ADI of 0.058 mg/kg bw/day and therefore no health effects are expected.

Acute intakes for all consumer groups are below the proposed ARfD of 2.5 mg/kg bw/day and therefore no health effects are expected.

#### B.7.16.4.1 Dietary Exposure Assessment of the XDE-729 Methyl Metabolites X11406790 and X11449757

As discussed previously under the wheat metabolism study evaluation, and definition of the residue for risk assessment, the notifier was asked to address the relative toxicity of the non-conjugated metabolites X11406790 and X11449757 in comparison with XDE-729 methyl and XDE-729 acid (X11393729), in order to support the residue definition of XDE-729 methyl and XDE-729 acid for Risk Assessment and Enforcement/Monitoring purposes. Details of the notifiers case to address the toxicology of these metabolites using QSAR analysis is given under the section discussing the wheat metabolism study, where it was concluded that no toxicity concerns have been identified for the metabolites

In addition to the QSAR analysis, the notifier also stated that *“In the case of the 6 metabolites for which limited toxicity data exists, it was decided to address the risk of potential human exposure by utilizing the concept of ‘threshold of toxicological concern’ (TTC) as used in the European regulation of pesticide metabolites (European Commission, 2003) and described in the open literature (Felter et al., 2009) and in an EFSA Scientific Opinion (EFSA, 2012).”*

*A dietary exposure assessment for the metabolites X11406790 and X11449757 is also presented as further evidence that the metabolites should not be added to the residue definition for XDE-729 methyl (the proposed residue definition is for XDE-729 methyl and XDE-729 acid only). The toxicological based assessment of the metabolites shows the metabolites to be of no toxicological concern with respect to genotoxicity”.*

#### TTC assessment of X11406790 and X11449757:

*The only dietary route of exposure to XDE-729 methyl and its metabolites that is relevant to humans is by the consumption of cereal grains. The Nature of Residue study submitted as part of the XDE-729 methyl dossier showed that the Total Radioactive Residue (TRR) associated with cereal grains was 0.004 mg equivalents/kg. Due to the low levels of residue observed there was no requirement to further characterize the constituents of the TRR. Therefore, as a conservative worst-case approach*

*in the presented TTC assessment, 0.004 mg/kg is assumed to be the residue level in cereal grain for each individual metabolite.*

*To assess the dietary exposure of X11406790 and X11449757 the EFSA PRIMo was used. Residue levels for relevant cereals (wheat, barley and rye) were set at 0.004 mg/kg and the relevant TTC value was inserted into the model calculator in place of an ADI.*

*The QSAR analyses of the metabolites X11406790 and X11449757 and the interpretation of the results with supporting experimental data shows that the metabolites and their associated conjugated forms are not genotoxic.*

*The initial Tier I TTC value used was 1.5 µg/person per day (0.025 µg/kg bw/day) for non-genotoxic chemicals (EC, 2003; Kroes et al., 2005; Felter et al., 2009). Estimated dietary intake was at 198% of the TTC. Following decision trees used in a number of publications (Kroes et al., 2005; Felter et al., 2009, EFSA, 2012) if exceedance of the Tier I TTC is observed the next relevant TTC value to be used for non-carbamate/organophosphate compounds is the TTC value for Cramer structural class III compounds at 90 µg/person per day (1.5 µg/kg bw/day). Based on this TTC the estimated intake of any of the individual metabolites (or all of the metabolites combined) was at 3% of the TTC. Again, referring to the decision tree that is generally used if a compound has an estimated intake below the Cramer class III TTC then the 'substance would not be expected to be a safety concern'. As the worst-case estimated exposure is 33-fold lower than the relevant TTC, it is possible to conclude that the exposure is of no concern with respect to human safety.*

#### **B.7.16.4.2 Conclusions on Dietary Exposure Assessment of the XDE-729 Methyl Metabolites X11406790 and X11449757**

The estimated intake assessment shows the exposure to any or all of the metabolites in question (X11406790, X11449757 and/or their glucuronide and sulphate conjugates) is below the relevant TTC. The presented exposure assessment is conservative in nature as it assumes the residue value is for metabolites only, whereas in reality the residue is likely to consist of more than one component including XDE-729 methyl and XDE-729 acid (i.e. actual levels of the metabolites are likely to be lower than the 0.004 mg/kg assumed).

In conclusion, the metabolites X11406790 and X11449757 and their conjugates are not considered to be of toxicological concern or a risk in terms of potential dietary exposure, and should not be included in the residue definition for XDE-729 methyl. The dietary risk assessment submitted in the XDE-729 methyl dossier (showing predicted exposure to XDE-729 methyl and XDE-729 acid is at a maximum of 1% of the ADI) does not need updating as the assumptions the assessment is based on (i.e. the residue definition) are considered to remain valid.

## XDE 729 Methyl (Halauxifen-methyl)

## Volume 3, Annex B.7

Table B.7.16.4-1 TTC Tier II assessment – Estimated dietary intake as a percentage of TTC value (TTC = 90 µg/person per day)

XDE-729 metabolites '790 and '757 TTC assessment									
Status of the active substance:		New Active		Code no.					
LOQ (mg/kg bw):		0.01		proposed LOQ:					
Toxicological end points									
TTC (mg/kg bw/day):		0.0015		ARfD (mg/kg bw):		n.n.			
Source of TTC:		EFSA		Source of ARfD:					
Year of evaluation:		-		Year of evaluation:					
<p>Explain choice of toxicological reference values.</p> <p>The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL). The pTMRLs have been submitted to EFSA in September 2006.</p>									
Chronic risk assessment									
TMDI (range) in % of ADI minimum - maximum									
No of diets exceeding ADI: ---									
Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)	
2.6	DK child	1.5	Wheat	1.2	Rye		FRUIT (FRESH OR FROZEN)	2.6	
2.4	WHO Cluster diet B	2.3	Wheat	0.1	Barley	0.0	Rye	2.4	
1.9	WHO cluster diet D	1.7	Wheat	0.1	Rye	0.1	Barley	1.9	
1.8	IT kids/toddler	1.8	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	1.8	
1.4	WHO cluster diet E	1.1	Wheat	0.2	Barley	0.1	Rye	1.4	
1.3	WHO Cluster diet F	1.0	Wheat	0.2	Rye	0.2	Barley	1.3	
1.3	NL child	1.3	Wheat	0.0	Rye	0.0	Barley	1.3	
1.3	DE child	1.1	Wheat	0.2	Rye	0.0	Barley	1.3	
1.2	ES child	1.2	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	1.2	
1.1	IT adult	1.1	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	1.1	
1.1	PT General population	1.0	Wheat	0.0	Rye	0.0	Barley	1.1	
1.1	UK Toddler	1.0	Wheat	0.0	Barley	0.0	Rye	1.1	
1.0	IE adult	0.6	Wheat	0.3	Barley	0.0	Rye	1.0	
0.9	SE general population 90th percentile	0.9	Wheat	0.1	Rye		FRUIT (FRESH OR FROZEN)	0.9	
0.9	WHO regional European diet	0.8	Wheat	0.1	Barley	0.0	Rye	0.9	
0.9	FR all population	0.9	Wheat	0.0	Barley		FRUIT (FRESH OR FROZEN)	0.9	
0.8	ES adult	0.6	Wheat	0.1	Barley		FRUIT (FRESH OR FROZEN)	0.8	
0.7	DK adult	0.5	Wheat	0.2	Rye		FRUIT (FRESH OR FROZEN)	0.7	
0.7	FR toddler	0.7	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	0.7	
0.7	UK Infant	0.7	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	0.7	
0.7	NL general	0.6	Wheat	0.1	Barley	0.0	Rye	0.7	
0.6	LT adult	0.3	Rye	0.3	Wheat	0.0	Barley	0.6	
0.6	UK vegetarian	0.5	Wheat	0.0	Barley	0.0	Barley	0.6	
0.5	UK Adult	0.4	Wheat	0.0	Barley	0.0	Rye	0.5	
0.5	FI adult	0.3	Wheat	0.2	Rye	0.0	Barley	0.5	
0.2	FR infant	0.2	Wheat		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	0.2	
	PL general population		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		
<p><b>Conclusion:</b></p> <p>The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.</p> <p>A long-term intake of residues of XDE-729 metabolites '790 and '757 TTC assessment is unlikely to present a public health concern.</p>									

Prepare workbook for refined calculations

Undo refined calculations

WARNING: This document forms part of an EFSA evaluation data package and should not be used for registration. Registration must not be granted on the basis of this document.

**B.7.17 Summary and evaluation of residue behaviour (Annex II 6.9, Annex IIIA 8.6)**

A summary of the evaluation of residue behaviour is presented in Section 2.4 of Volume 1, Level 2 of the DAR.

**B.7.18 References relied on**

<b>Annex Point/ Reference Number</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not</b>	<b>Data Protection claimed (Y/N)</b>	<b>Owner</b>
KIIA 6.1.1/01	Devine, H. C.	2012a	X11393728 (XDE 729-methyl) and X11393729 (XDE 729): Residue Stability Study in Crops under Freezer Storage Conditions (INTERIM REPORT NUMBER: 1) CEM Analytical Services (CEMAS) DAS Report No.: 110563, CEMS-4957 (Accession Number) 2013696 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.1.1/02	Devine, H. C.	2012b	Cloquintocet-mexyl and Cloquintocet-acid: Residue Stability Study in Crops under Freezer Storage Conditions (INTERIM REPORT NUMBER: 1) CEM Analytical Services (CEMAS) DAS Report No.: 110564, CEMS-4958 (Accession Number) 2013697 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.1.1/03	██████████	2012	Frozen Storage Stability of Residues of XDE-729 Methyl Ester, XDE-729 Acid and X11449757 in Animal Matrices Five Months Stability Data for XDE-729 Methyl Ester and XDE-729 Acid and One Month Stability Data for X11449757 ██████████ <b>DAS Report No.: 110768, ████████-5255</b> (Accession Number) 2013913 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.1.1/04	Lindner, M.	2012	Storage Stability of Residues of XDE 729 Methyl Ester, XDE 729 Acid, and the Metabolite X11449757 in Soil Eurofins Analytical Services DAS Report No.: 110565 , S11-03037 (Accession Number) 2014276 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.1.1/05	Devine, H. C.	2013	X11393728 (XDE 729 methyl) and X11393729 (XDE 729): Residue Stability Study in Crops under Freezer Storage Conditions ((INTERIM REPORT NUMBER: 2) 16 months) CEM Analytical Services (CEMAS) DAS Report No.: 110563, CEMS-4957 (Accession Number) 2016722 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS



Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.1.1/06	[REDACTED]	2013	Frozen Storage Stability of Residues of XDE-729 Methyl Ester, XDE-729 Acid and X11449757 in Animal Matrices Twelve Months Stability Data for XDE-729 Methyl Ester and XDE-729 Acid and Six Month Stability Data for X11449757 - 2nd INTERIM REPORT [REDACTED] DAS Report No.: 110768, [REDACTED] 5255 (Accession Number) 2016872 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.1.1/07	Lindner, M.	2013	Storage Stability of Residues of XDE 729 Methyl Ester, XDE 729 Acid, and the Metabolite X11449757 in Soil. 2nd INTERIM REPORT Eurofins Analytical Services DAS Report No.: 110565 , S11-03037 (Accession Number) 2016872 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.2.1/01	Ma, M., Smith, K.P., Jackson, A.U.	2012	A Nature of the Residue Study with [14C]-XR-729 Methyl Applied to Wheat with and without the Safener Cloquintocet Mexyl (Amended Report) Research for Hire DAS Report No.: 101080 (Amended report) (Accession Number) 2010731 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.2.1/02	Rotondaro, S. L. And el	2012	A Nature of the Residue Study with [14C]-XDE-729 Methyl Applied to Turnips Dow AgroSciences LLC and AgChem Product Development 7528 Auburn Road Concord, OH 44077 DAS Report No.: 110413 (Accession Number) 2013862 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.2.2/01	[REDACTED]	2011a	A Nature of the Residue Study in the Laying Hen with [14C]-XR-729 Methyl Ester [REDACTED] DAS Report No.: 101390 (Accession Number) 2010732 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.2.3/01	[REDACTED]	2011b	A Nature of the Residue Study in the Ruminant with [14C]-XR-729 Methyl Ester [REDACTED] DAS Report No.: 101389 (Accession Number) 2010655 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.3.1/01	Rawle, N.W.	2011a	Residues of XDE-729 and Cloquintocet-mexyl in Winter Wheat at Intervals and Harvest Following Multiple Applications of GF-2573 - Northern and Southern Europe - 2009 to 2010. CEM Analytical Services (CEMAS) DAS Report No.: 090118, CEMR-4552 (Accession Number) 2009526 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.3.1/02	Devine, H. C.	2012c	Residues of XDE-729 and Cloquintocet-Mexyl in Winter Wheat at Intervals and Harvest Following Applications of GF-2573 or GF-2685 – Northern and Southern Europe – 2010 to 2011 CEM Analytical Services (CEMAS) DAS Report No.: 102082, CEMS-4889 (Accession Number) 201338 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.3.2/01	██████ ██████	2011a	Residues of XDE-729 in Spring Wheat at Intervals and Harvest Following Single Applications of GF-2573 - Northern and Southern Europe - 2010 ██ DAS Report No.: 101589, ██████ - 4719 (Accession Number) 2010734 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.3.2/02	Devine, H. C.	2012d	Residues of XDE-729, Cloquintocet and Florasulam in Spring Wheat at Intervals and Harvest Following Applications of GF-2573, GF-2685 or GF-2644 – Northern and Southern Europe – 2011 CEM Analytical Services (CEMAS) DAS Report No.: 110411, CEMS-5001 (Accession Number) 2013384 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.3.3/01	Rawle, N.W.	2011b	Residues of XDE-729 and Cloquintocet-mexyl in Winter Barley at Intervals and Harvest Following Multiple Applications of GF-2573 - Northern and Southern Europe – 2009 to 2010. CEM Analytical Services (CEMAS) DAS Report No.: 090119, CEMR-4553 (Accession Number) 2009527 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.3.3/02	Devine, H. C.	2012e	Residues of XDE-729 and Cloquintocet-mexyl in Winter Barley at Intervals and Harvest Following Applications of GF-2573 or GF-2685 – Northern and Southern Europe – 2010 to 2011 CEM Analytical Services (CEMAS) DAS Report No.: 102083, CEMS-4890 (Accession Number) 2013383 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.3.4/01	Devine, H.C.	2011b	Residues of XDE-729 in Spring Barley at Intervals and Harvest Following Applications of GF-2573 - Northern and Southern Europe - 2010 CEM Analytical Services (CEMAS) DAS Report No.: 101590, CEMR-4720 (Accession Number) 2010735 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.3.4/02	Devine, H. C.	2012f	Residues of XDE-729, Cloquintocet and Florasulam in Spring Barley at Intervals and Harvest Following Applications of GF-2573, GF-2685 or GF-2644 – Northern and Southern Europe – 2011 CEM Analytical Services (CEMAS) DAS Report No.: 110412, CEMS-5002 (Accession Number) 2013385 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.4.2/01	Rawle, N. W.	2012	XDE-729 Livestock Feeding Study: Magnitude of Residue in Milk, Muscle, Fat, Liver and Kidney of Lactating Dairy Cattle CEM Analytical Services (CEMAS) DAS Report No.: 120077, CEMS 5266 (Accession Number) 2013500 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Owner
KIIA 6.5.1/01	Ma, M., Balcer, J.L.	2011	Processing Study to Determine the Nature of Residues of 14C-XDE-729 Methyl and 14C-X11393729 Following Industrial or Household Preparation Dow AgroSciences LLC DAS Report No.: 110369 (Accession Number) 2010766 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.5.3/01	Devine, H. C.	2012g	Residues of XDE-729 in Spring Wheat Grain and Process Fractions at Harvest Following a Single Application of GF-2573 – Northern and Southern Europe – 2011 CEM Analytical Services (CEMAS) DAS Report No.: 110435, CEMS 5003 (Accession Number) 2013589 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS
KIIA 6.5.3/02	Devine, H. C.	2012h	Residues of XDE-729 in Spring Barley Grain and Process Fractions at Harvest Following a Single Application of GF-2573 – Northern and Southern Europe – 2011 CEM Analytical Services (CEMAS) DAS Report No.: 110436, CEMS 5004 (Accession Number) 2013590 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

<b>Annex Point/ Reference Number</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not</b>	<b>Data Protection claimed (Y/N)</b>	<b>Owner</b>
KIIA 6.6.2/01	Rotondaro, S.L.	2011	A Confined Rotational Crop Study with [14C]-XDE-729 Methyl Ester Ricerca DAS Report No.: 101635, 026108 (Accession Number) 2010765 GLP/GEP (Y/N): Y Published (Y/N): N	Y	DAS

#### **B.7.19 References used in assessment of data**

1. Gregory, J., Foster, K., Tyler, H. and Wiseman, M. (1990). The Dietary and Nutritional Survey of British Adults. HMSO.
2. Report on Health and Social Subjects, No. 36 : 'The Diets of British Schoolchildren'. HMSO.
3. Mills, A and Tyler, H. (1992). Food and Nutrient Intakes of British Infants Aged 6-12 months. HMSO.
4. Rees, N and Harris, C. (1995). UK Methods for the Estimation of Dietary Intakes of Pesticide Residues (unpublished)