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Fenoxaprop-P-ethyl

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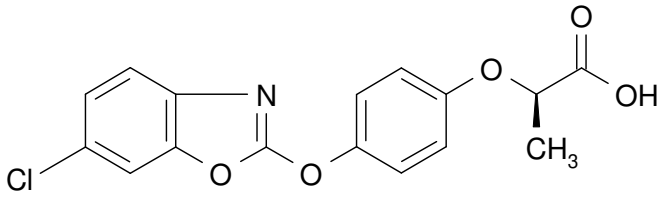
B.7. RESIDUE DATA

This renewal assessment report (DRAR) summarises and evaluates new information which is relevant for the renewal of the approval of **Fenoxaprop-P-ethyl** under Regulation (EC) 1107/2009.

Fenoxaprop-P-ethyl was included in Annex I of Council Directive 91/414/EEC (Commission Directive 2008/66/EC of 30 June 2008). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011.

Figure 7.1 Fenoxaprop-P-Ethyl (Hoe 046360)



Molecular mass: 361.8 g/mol Molecular formula: $C_{18}H_{16}ClNO_5$

Fenoxaprop-P-ethyl is the herbicidal effective R-enantiomer of the racemic substance fenoxaprop-ethyl. It is a herbicide from the chemical class of aryloxyphenoxy-propionates which is especially effective against annual grass weeds from the two-leaf stage up to full tillering, for use in spring and winter cereals, rice, turf and broadleaf crops. Fenoxaprop-P-ethyl is rapidly taken up via the leaves and stems and transported to the sites of action. Within the plant, the active ingredient is very rapidly split to the free acid, which is the compound with the main herbicidal efficacy. The product was originally developed as racemic mixture fenoxaprop-ethyl. In the EU review process it could be demonstrated that studies done with the racemic mixture are also valid to describe the behaviour of fenoxaprop-p-ethyl.

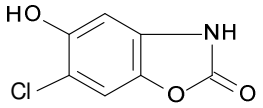
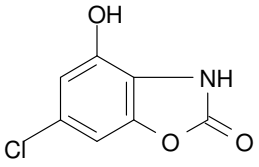
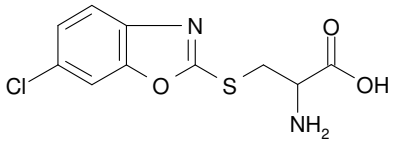
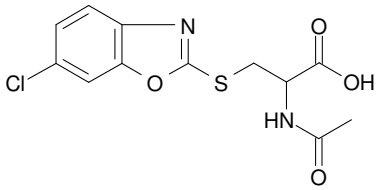
FPP+MPR EW 144 (69+75 g/L) (Bayer CropScience) and CHA 4960 (Fenoxaprop-P-ethyl 69 g/l EW) (Cheminova) are the representative formulations used for re-approval of fenoxaprop-P-ethyl.
The formulation FPP+MPR EW 144 (69+75 g/L) contains the safener Mefenpyr-diethyl (Hoe 107892), which increases the crop tolerance of the active ingredient and maintains at the same time the high level of grass weed control.

The GAP proposed to support the **re-approval of fenoxaprop-P-ethyl on cereals** is the same as the GAP previously used to support first Annex I inclusion in terms of **application rate of 1x 0.083 kg** as/ha, but with an extended growth stage **at BBCH 11-39** (for wheat, durum wheat, rye, tritcale) and at **BBCH 12-32** (barley), respectively.

Bayer CropScience and Cheminova formed a task force to co-operate in generating regulatory data required to maintain registration of the active ingredients and to respond to regulatory queries on the active ingredients. As a result of this sequence, fenoxaprop-P-ethyl and its metabolites have a number of different codes/names associated with them. The key codes and standardized names for fenoxaprop-P-ethyl and its plant or animal metabolites are summarised in the table below. For the full list of structures, synonyms, code numbers and occurrences please refer to chapter B.7.9

Table 7.2.1.1-1 Substances and metabolites: structures, codes, synonyms

Code	Other codes	Name(s) IUPAC name	Structure Molecular formula Molar mass
AE F046360 (parent)	Hoe 046360 BCS-AI29180	**Fenoxaprop-P-ethyl (D-enatiomer)** Ethyl (2R)-2-{4-[(6-chloro-1,3-benzoxazol-2-yl) oxy] phenoxy} propanoate	$C_{18}H_{16}ClNO_5$ 361.8 g/mol
AE F033171	Hoe 033171 BCS-AF52457	**Fenoxaprop-ethyl (Racemat)**	
AE F054014 (Metabolite)	Hoe 054014 RP 011881 RPA 722144 RP 011811 BCS-AC79872	**Benzoxazolone** Chlorobenzoxazolone 6-chloro-1,3-benzoxazol-2(3H)-one	$C_7H_4ClNO_2$ 169.57 g/mol
AE F088406 (Metabolite)	Hoe 088406 BCS-BQ23896	**Fenoxaprop-P-acid (D-Enantiomer)** 2R)-2-{4-[(6-chloro-1,3-benzoxazol-2-yl) oxy] phenoxy}propanoic acid	$C_{16}H_{12}ClNO_5$ 333.7 g/mol
AE F053022	Hoe 53022 BCS-AK65133	**Fenoxaprop-acid (Racemat)**	
AE F096918 (Metabolite)	BCS-CA37065	**HOPP-acid (D-Enantiomer)** (2R)-2-(4-hydroxyphenoxy)propanoic acid	$C_9H_{10}O_4$ 182.2 g/mol
AE F020686 (Metabolite)	Hoe 20686 BCS-AB96029	**HOPP-acid (Racemat)**	
AE F087795 (Metabolite)	BCS-CA37046	**HOPP-acid ester (D-Enantiomer)** ethyl (2R)-2-(4-hydroxyphenoxy)propanoate	$C_{11}H_{14}O_4$ 210.2 g/mol
AE F029062	Hoe 29062 BCS-AA45136	**HOPP-acid ester (Racemat)**	

Code	Other codes	Name(s) IUPAC name	Structure Molecular formula Molar mass
AE F064124 (Metabolite)	BCS-AU56480	**3-Hydroxychloro-benzoxazolone** 6-chloro-5-hydroxy-1,3-benzoxazol-2(3H)-one	 $C_7H_4ClNO_3$ 185.6 g/mol
AE F067978 (Metabolite)	BCS-BB23347	**4-Hydroxychloro-benzoxazolone** 6-chloro-4-hydroxy-1,3-benzoxazol-2(3H)-one	 C_7 H_4 Cl N O_3 185.6 g/mol
AE F0417066	Hoe 0417066 BCS-AX19709 (Racemate)	**benzoxalone-cysteine conjugate** S-(6-chloro-1,3-benzoxazol-2-yl)cysteine	 $C_{10}H_9ClN_2O_3S$ 272.71 g/mol
AE F069225	BCS-BB24444	N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine	 C_{12} H_{11} Cl N_2 O_3 S 298.8 g/mol

All studies already submitted for the Annex I inclusion under Directive 91/414/EEC are contained in the Monograph (DAR Fenoxaprop-P-ethyl, 2005). However to increase the comprehensibility of the present renewal assessment for fenoxaprop-P-ethyl main data and additional details of the previously evaluated studies are included (grey study header) in view of presenting an adequate level of detail.

B.7.1. STORAGE STABILITY OF RESIDUES

No new storage stability study has been submitted for the purpose of renewal of the active substance approval.

Storage stability of fenoxaprop-P-ethyl in cereal matrices has previously been included in the submission for Annex I inclusion under 91/414/EEC and was deemed acceptable following evaluation and peer review at EU level. A summary of the originally submitted data which were considered for the purpose of renewal is presented in the following table.

Crop	Analyte	Fortification level	Duration (month)	Reference in the dossier for renewal of the a.s. (Reference in the RAR)	
Originally submitted and evaluated studies (DAR, 2005) to be considered for purpose of renewal					
Wheat grain	Hoe 046360 Hoe 088406 Hoe 054104	0.2 mg/kg	4, 8, 12, 24	Fuchsbichler G. 1993b	KCA 6.1/01 (7.1.1)
Barley grain, straw	Hoe 046360 Hoe 033171 Hoe 053022 Hoe 054104	0.2 mg/kg	0, 6, 14	Ver Hey Margaret E.; 1992a	KCA 6.1/03 (7.1.2)
Poultry muscle, liver, eggs	Hoe 033171 Hoe 053022 Hoe 054104	0.25 mg/kg	0, 1, 3, 12	Kulkarni, T.S.; Winkler, D.A..; 1995	KCA 6.1/05 (7.1.3)

B.7.1.1. Storage stability in wheat

Reference:	KCA 6.1/01 Hoe 046360, Hoe 088406 and Hoe 054014 Storage stability in wheat and validation of analytical method AL 58/86
Author(s), year:	Fuchsbichler G. 1993b
Report/ Doc. Number:	Document No: A51681
Guideline(s):	Not specified
GLP:	Yes
Previous evaluation:	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 506	-
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

For the investigation of the storage stability in wheat grain, samples were spiked with 0.2 mg/kg Hoe 046360, 0.2 mg/kg Hoe 088406 and 0.2 mg/kg Hoe 054104 (corresponding 0.493 mg Hoe 083312 equivalents/kg) and stored deep frozen in screw-top flasks at -20°C. Untreated blank samples were prepared simultaneously. One blank and two spiked samples were analysed on DAA 0 (day of application) and after 4, 8, 12 and 24 month. Hoe 046360 and its main metabolites are extracted by boiling to reflux with a mixture of acetonitrile and hydrochloric acid. During this process Hoe 046360 and Hoe 088406 are transformed to Hoe 054014, which was then acetylated to obtain the derivate Hoe 083312. Thus Hoe 046360, Hoe 088406 and Hoe 054014 were determined together as Hoe 083312. Final determination was performed by GC with ECD (electronic capture detector) by external standard procedure. There is no correction against recoveries.

Method Validation:

The wheat grain analyses were carried out with 1 control sample, 2 samples spiked with 0.02 mg/kg Hoe 046360 and 2 samples spiked with 0.05 mg/kg Hoe 046360. No residues above the LOQ of 0.02 mg/kg were detected in the control samples. The results are summarized in the table below.

Crop	Portion analyzed	Analyte	n	Fortification level (mg/kg)	Recovery			
					Individual recoveries		Mean	RSD
					mg/kg	%	%	%
Wheat	grain	Hoe 046360	2	0.02	0.014, 0.016	71, 80	76	
			2	0.05	0.042, 0.038	85, 76	81	
						overall	**78**	**7.6**

The results of the method validation are in accordance with the general requirements for residue analytical methods, the method was validated successfully.

Findings:

To obtain the recoveries for the storage stability tests, Hoe 046360, Hoe 088406 and Hoe 054014 were added together to the control sample and analysed. The recoveries were calculated as Hoe 083312. The recovery for the control samples (freshly spiked) ranged from 72 % to 99 %, the mean recovery in stored wheat grain samples ranged from 83 % to 103 %. The results are summarized in the tables below.

Table 7.2.1.1-1 Storage stability of Hoe 046360, Hoe 088406 and Hoe 054014 residues calculated as Hoe 083312

Commodity	Level (mg/kg)	Storage interval (months)	Fresh recovery (mean, %)	residues after storage (mg/kg)		Recovery (% day 0)	Recovery (% nominal content*)
				Individual values	mean		
Wheat grain	0.493	0	75	0.366, 0.376	0.371	-	-
		4	72	0.533, 0.483	0.508	137	103
		8	99	0.383, 0.450	0.417	112	85
		12	97	0.394, 0.426	0.410	111	83
		24	87	0.459, 0.389	0.424	114	86

*...Not corrected for procedural recoveries

Conclusion:

The study demonstrated that fenoxaprop-P-ethyl (AE F046360) and its main metabolites fenoxaprop-P-acid (AE F088406) and bezoxazolone (AE F054014) determined as derivate Hoe 083312 were stable for up to 24 months in cereal grain when stored at -20°C.

B.7.1.2. Storage stability in Barley

Reference:	KCA 6.1/03 *Determination of the residues of Hoe 033171 or Hoe 046360 and their metabolites Hoe 053022 and Hoe 054014 in Barley Grain and Straw: Storage Stability*
Author(s), year:	Ver Hey Margaret E.; 1992a
Report/ Doc. Number:	A49224, Hoechst Report No 1130BSS
Guideline(s):	Residue Chemistry Data Requirements 40 CFR 158.125 Guideline Numbers 171-4(e)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 506	No 10x LOQ spiking level (0.2 mg/kg instead of 0.5 mg/kg)
Comment (RMS):	However the study is considered applicable to provide the required information.

Material and Methods:

Each composite sample of 25 g barley grain and 10g barley straw was fortified separately with 0.2 mg/kg of Hoe 033171 (Fenoxaprop-ethyl), Hoe 053022 (Fenoxaprop), Hoe 046360 (Fenoxaprop-P-ethyl) and the chlorobenzoxazolone metabolite Hoe 054014. The samples were stored at about - 30°C. Residue analysis was conducted immediately after preparation (0 DAA) and after 6 and 14 month (two spiked samples and one control sample per storage interval). The sample material was refluxed for 6 hours with concentrate hydrochloric acid in 90 ml acetonitrile, water was added and the undissolved material removed by filtration. The filtrate was then applied to an Extrelute column and eluated with hexan and ether. The eluate was evaporated and acetylated with acetic anhydride. The derivate was purified and the final determination was performed by GC with ECD (electronic capture detector) using an external standard procedure. Procedural recoveries were run with each analytical set for quality control purposes parallel to the stored sample analysis for all four substances at a level of 0.2 mg/kg.

Findings:

The overall procedural recoveries analyzed concurrently with the stored fortification samples on Day 0 and after 6-month and 14-month for all matrices ranged from 80% to 97% in Hoe 033171, 67% to 100% in Hoe 046360, 63% to 98% in Hoe 053022 and 72% to 108% in Hoe 054014. The LOQ (limit of quantification) was set at 0.05 mg/kg (Hoe 033171 and Hoe 046360 equivalents respectively). No residues above the LOQ of 0.05 mg/kg were detected in the control samples. The detailed results are summarized in the tables below.

Table 7.2.1.1-1 Storage stability of Hoe 033171, Hoe 046360, Hoe 053022 and Hoe 054014 residues in barley grain

Analyte	**Fortifi-cation level** (mg/kg)	**Storage interval** (months)	**Recovery freshly spiked sample** (%)	**residues after storage** (mg/kg)		**Recovery** (% day 0)	**Recovery** (% nominal spinking level)
				Individual values	mean		
Hoe 033171	0.2	0	80,83	0.160, 0.169	0.165	-	-
		6	88	0.187, 0.190	0.189	112	95
		14	83	0.163, 0.169	0.166	101	83
Hoe 046360	0.2	0	77,69	0.153, 0.139	0.146	-	-
		6	100	0.193, 0.184	0.189	129	95
		14	84	0,161, 0.206	0.184	126	92
Hoe 053022	0.2	0	63,71	0.127, 0.142	0.135	-	-
		6	98	0.179, 0.191	0.185	137	93
		14	81	0.143, 0.166	0.155	115	78
Hoe 054014	0.2	0	72,74	0.143, 0.149	0.146	-	-
		6	89	0.190, 0.192	0.191	131	96
		14	108	0.215, 0.186	0.201	138	101

Table 7.2.1.1-2 Storage stability of Hoe 033171, Hoe 046360, Hoe 053022 and Hoe 054014 residues in barley straw

Analyte	Fortification level (mg/kg)	Storage interval (months)	Recovery freshly spiked sample (%)	residues after storage (mg/kg)		Recovery (% day 0)	Recovery (% nominal spinking level)
				Individual values	mean		
Hoe 033171	0.2	0 6 14	82, 92 97 83	0.163, 0.183 0.192, 0.192 0.139, 0.142	0.173 0.192 0.141	- 111 82	- 96 70
Hoe 046360	0.2	0 6 14	83, 71 92 67	0.166, 0.141 0.192, 0.195 0.146, 0.162	0.154 0.194 0.154	- 126 100	- 95 75
Hoe 053022	0.2	0 6 14	77, 66 94 85	0154, 0.132 0.173, 0.175 0.155, 0.170	0.143 0.174 0.163	- 122 114	- 87 82
Hoe 054014	0.2	0 6 14	97, 95 93 92	0.194, 0.190 0.186, 0.192 0.152, 0.145	0.192 0.189 0.149	- 98 78	- 95 75

Conclusion:

The study demonstrated that residues of Hoe 033171 (Fenoxaprop-ethyl), Hoe 046360 (Fenoxaprop-P-ethyl), Hoe 053022 (Fenoxaprop acid) and Hoe 054014 (benzoxazolone) are stable in barley grain and straw over a period of 14 month when stored at -30°C.

B.7.1.3. Storage stability in Poultry tissues and eggs

Storage stability in animal commodities was not deemed necessary for Annex I conclusion under 91/414/EEC. For the purpose of renewal of a.s. approval the GAP was extended to BBCH 39 and therefore the potential transfer of residues into food of animal origin is considered relevant.

Reference:	KCA 6.1/05 *Freezer Stability of Fenoxaprop-ethyl (HOE-033171) and Related Metabolites in Poultry Tissues and Eggs*
Author(s), year:	Kulkarni, T.S.; Winkler, D.A..; 1995
Report/ Doc. Number:	A55153, EN-CAS Analytical Laboratories, Winston-Salem, NC, USA
Guideline(s):	Residue Chemistry Data Requirements 40 CFR 158.240 Guideline Numbers 171-4
GLP:	Yes
Previous evaluation :	**Not deemed necessary in the DAR (2005)** Assessed for the purpose of renewal of a.s. approval.
Deviations from OECD Guideline 506	-
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

The purpose of this study was to determine the freezer storage stability of fenoxaprop-ethyl (Hoe 033171) and its metabolites in poultry tissues (muscle and liver) and eggs.

Poultry muscle and poultry liver control samples were homogenized by mixing with dry ice, egg samples did not require grinding but were thoroughly mixed by either stirring or blending prior to subsampling and stored frozen at approximately -23°C to -27°C. On Day 0, one unfortified control and duplicate samples, freshly fortified at

0.25 ppm with fenoxaprop-ethyl (Hoe 033171) and its metabolites, Hoe 053022 and Hoe 054014, were analyzed for each of the three poultry matrices. For the 1- and 3- and 12-month intervals, one unfortified control, duplicate freshly fortified control samples per analyte (individually fortified at 0.25 ppm with each analyte), and duplicate freezer-stored stability samples per analyte (previously fortified individually at 0.25 ppm with each analyte) were analyzed.
Residues of fenoxaprop-ethyl and its major metabolites were extracted from poultry muscle, eggs and liver matrices by refluxing the sample in a mixture of acetonitrile (ACN):HC1:H2O (90:10:50) for 6 hours. During this process, fenoxaprop-ethyl Hoe 033171 and fenoxaprop acid Hoe 053022 are converted to Hoe 054014.
After reflux, the extraction solution was diluted with distilled water. Any undissolved material was removed by filtration. An aliquot of the filtrate was added to an Extrelut column. Co-extracted substances were then eluted with hexane. The hydrolysis product resulting from the reflux Hoe 054014 was subsequently eluted with diethyl ether in hexanes. The eluate (containing Hoe 054014) was concentrated to dryness, redissolved in ethyl acetate and derivatized for GC analysis using a mixture of acetic anhydride and pyridine, which required heating of the reaction mixture for 2.5 - 3.0 hours at 130°C. The resultant derivative Hoe 083312 was analysed with GC- ECD (electron capture detector).

Findings:

The overall procedural recoveries analyzed concurrently with the stored fortification samples on Day 0 and after 1-month, 3-month and 12-month for all matrices ranged from 78% to 94% in Hoe 033171, 68% to 94% in Hoe 053022 and 77% to 106% in Hoe 054014. The LOQ (limit of quantification) was set at 0.05 mg/kg (Hoe 033171 and Hoe 046360 equivalents respectively).

Recoveries of Hoe 033171, Hoe 053022 and Hoe 054014 in poultry muscle fortified with 0.25 mg/kg ranged from 82-103%, in poultry liver from 84-109% and in eggs from 80-97% from the nominal spiking level. No residues above the LOQ of 0.05 mg/kg were detected in the control samples. The results are summarized in the tables below.

Table 7.2.1.1-1 Storage stability of Hoe 033171, Hoe 046360, Hoe 053022 and Hoe 054014 residues in poultry muscle

Analyte	**Level** (mg/kg)	**Storage interval** (months)	**Recovery freshly spiked sample** (%)	**residues after storage** (mg/kg)		**Recovery** (% day 0)	**Recovery** (% nominal spinking level)
				Individual values	mean		
Hoe 033171	0.25	0	79, 88	0.199, 0.220	0.210	-	-
		1	86, 84	0.196, 0.212	0.204	97	82
		3	79, 82	0.197, 0.210	0.204	97	82
		12	85, 88	0.235, 0.246	0.241	115	96
Hoe 053022	0.25	0	68, 73	0.169, 0.184	0.177	-	-
		1	82, 83	0.195, 0.202	0.199	112	80
		3	78, 77	0.207, 0.203	0.205	116	82
		12	72, 84	0.228, 0.235	0.232	131	93
Hoe 054014	0.25	0	78, 85	0.195, 0.211	0.203	-	-
		1	93, 97	0.244, 0.233	0.239	118	96
		3	86, 90	0.225, 0.217	0.221	109	88
		12	106, 92	0.258, 0.255	0.257	127	103

Table 7.2.1.1-2 Storage stability of Hoe 033171, Hoe 046360, Hoe 053022 and Hoe 054014 residues in poultry liver

Analyte	Level (mg/kg)	Storage interval (months)	Recovery freshly spiked sample (%)	residues after storage (mg/kg)		Recovery (% day 0)	Recovery (% nominal spinking level)
				Individual values	mean		
Hoe 033171	0.25	0	79, 80	0.199, 0.200	0.200	-	-
		1	87, 89	0.217, 0.211	0.214	107	86
		3	85, 83	0.222, 0.236	0.228	114	91
		12	86, 78	0.231, 0.216	0.224	112	90
Hoe 053022	0.25	0	78, 77	0.196, 0.193	0.195	-	-
		1	87, 85	0.211, 0.207	0.209	107	84
		3	83, 82	0.221, 0.204	0.213	109	85
		12	94, 92	0.245, 0.234	0.240	123	96
Hoe 054014	0.25	0	84, 83	0.209, 0.208	0.209	-	-
		1	92, 96	0.249, 0.233	0.241	115	96
		3	95, 99	0.227, 0.228	0.228	109	91
		12	100, 96	0.274, 0.271	0.273	131	109

Table 7.2.1.1-3 Storage stability of Hoe 033171, Hoe 046360, Hoe 053022 and Hoe 054014 residues in eggs

Analyte	Level (mg/kg)	Storage interval (months)	Recovery freshly spiked sample (%)	residues after storage (mg/kg)		Recovery (% day 0)	Recovery (% nominal spinking level)
				Individual values	mean		
Hoe 033171	0.25	0	79, 79	0.197, 0.197	0.197	-	-
		1	92, 80	0.224, 0.208	0.216	110	86
		3	89, 90	0.213, 0.214	0.214	109	86
		12	94, 89	0.171, 0.226	0.199	101	80
Hoe 053022	0.25	0	81, 81	0.203, 0.203	0.203	-	-
		1	84, 80	0.220, 0.222	0.221	109	88
		3	80, 79	0.212, 0.212	0.212	104	85
		12	81, 91	0.206, 0.190	0.198	98	79
Hoe 054014	0.25	0	78, 77	0.195, 0.194	0.195	-	-
		1	93, 98	0.246, 0.238	0.242	124	97
		3	91, 93	0.240, 0.241	0.241	124	96
		12	97, 93	0.243, 0.242	0.243	125	97

Conclusion:

The study demonstrated that Hoe 033171 and its metabolites, Hoe 053022 and Hoe 054014, are stable for at least 12 months in poultry muscle, liver and eggs under freezer storage conditions of approximately -23°C to -27°C. The study is considered suitable to cover the storage periods in the animal feeding study.

B.7.2. METABOLISM, DISTRIBUTION AND EXPRESSION OF RESIDUES

B.7.2.1. Plants

One new metabolism study in spring wheat conducted with [^{14}C]-Fenoxaprop-P-ethyl has been submitted for the purpose of renewal of the active substance approval. The study was commissioned by Cheminova. The study provides more up to date data while confirming the metabolic profile observed and reported in the DAR (2005).

Studies in wheat, barley, soybean and rice have previously been included in the submission for Annex I inclusion under 91/414/EEC to elucidate the **metabolism of fenoxaprop-P-ethyl in plants.** The studies were deemed acceptable following evaluation and peer review at EU level. A summary of the new data and the original submitted data which were considered for the purpose of renewal is presented in the following table.

Crop/ crop group	Active substance	Label	Application rate	Sampling intervals	Reference in the dossier for renewal of the a.s. (Reference in the RAR)	
New submitted study for the purpose of renewal of the active substance approval.						
Wheat/ Cereals	Hoe 046360	Chlorophenyl-^{14}C	1x 143 g as/ha BBCH 23-24	29 DAT (forage) 106 DAT (grain, straw)	Oddy, A. M.; 2012	KCA 6.2.1/13 (B.7.2.1.1)
		dioxyphenyl-1-^{14}C	1x 149 g as/ha BBCH 23-24			
Originally submitted and evaluated studies (DAR, 2005) to be considered for purpose of renewal						
Wheat/ Cereals	Hoe 046360	Chlorophenyl-^{14}C	1x 110 g as/ha, early tillering	0, 15, 30, 60, 109 DAT	Wink O., Kuenzler K., Lemke G.; 1987a	KCA 6.2.1/04 (B.7.2.1.2)
Wheat/ Cereals	Hoe 046360	Chlorophenyl-^{14}C	1x 90 g as/ha, 3-leaf stage	1, 7 DAT	Buerkle L.W.; 2000e	KCA 6.2.1/12 (B.7.2.1.3)
Wheat/ Cereals	Hoe 033171	Chlorophenyl-^{14}C	1x 183 g as/ha, early tillering	0, 10, 37, 59, 93, 109 DAT	Schwalbe-Fehl M., Schmidt E., Koecher H.; 1986a	KCA 6.2.1/08 (B.7.2.1.4)
Wheat/ Cereals	Hoe 033171	Chlorophenyl-^{14}C	1x 180 g as/ha, early tillering	2, 4, 21, 27, 96 hours 10 DAT	Schwalbe-Fehl M., Schmidt E., Koecher H.; 1987b	KCA 6.2.1/03 6.2.1/10 (B.7.2.1.5)
					Wink O., Kuenzler K., Wuerz S.; 1987a[#]	KCA 6.2.1/09 (B.7.2.1.5)
Barley/ Cereals	Hoe 046360	Chlorophenyl-^{14}C	2- leaf stage (nutrient solution)	2, 4, 6, 24, 48, 72, 144 hours	Buerkle W.L., Becker A.; 1997a	KCA 6.2.1/02 (B.7.2.1.6)
			1x 90 g as/ha 2-3 leaf stage	3, 23, 47, 71, 141 hours		
Rice/ Cereals	Hoe 046360	Chlorophenyl-^{14}C	1x 90 g as/ha 5-6 leaf stage	2, 6, 7, 9, 13, 17, 22, 36, 63, 84, 112 DAT	Wink O., Kuenzler K., Lemke G., Haberkorn B., Mueller H.J.; 1988a	KCA 6.2.1/01 (B.7.2.1.7)
Rice/ Cereals	Hoe 046360	dioxyphenyl-1-^{14}C	1x 90 g as/ha 5-6 leaf stage	2, 6, 7, 9, 13, 17, 22, 36, 63, 84, 112 DAT	Buettner B., Kuenzler K., Lemke G., Mueller H.J.; 1988a	KCA 6.2.1/11 (B.7.2.1.8)
Soya bean/ wheat	Hoe 046360	Chlorophenyl-^{14}C	1x 110 g as/ha 1st leaflet developed 2-3 leaf stage	5, 12 DAT	Wink O., Kuenzler K., Lemke G., Koecher H.; 1986a	KCA 6.2.1/05 (B.7.2.1.9)

DAT= days after treatement

[#]..Identification and characterization of the water soluble conjugates in wheat

The metabolism of fenoxaprop-P-ethyl in plants was elucidated in the DAR (2005) using the enantiomer fenoxaprop-P-ethyl (AE F046360) or the racemate fenoxaprop-ethyl (AE F033171). No differences in the metabolic behaviour of the racemic mixture and the P-enantiomer could be observed. Reference material labelled in the chlorophenyl- as well as in the 1-dioxyphenyl position was used. The influence of the safener Hoe 107892 (Mefenpyr-diethyl, Figure 7.2.1.1-4) on the metabolism of fenoxaprop-P-ethyl was investigated on barley. The new plant metabolism study on spring wheat provided for purpose of renewal of the active substance approval was conducted in the presence of the safener cloquintocet-mexyl.

Figure 7.2.1.1-1 Chlorophenyl-^{14}C-labeled Fenoxaprop-P-ethyl (Hoe 046360)

IUPAC: (D+)-ethyl-2-(4-(6-chloro-2-benzoxazolyloxy)-phenoxy)-propanoate
Molecular formula: $C_{18}H_{16}ClNO_5$
M= 361.8 g/mol

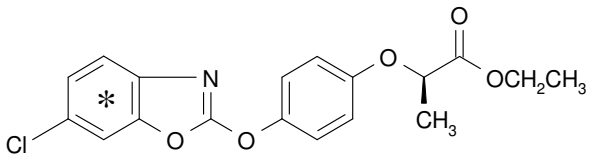


Figure 7.2.1.1-2 Dioxyphenyl-^{14}C- or phenoxy-^{14}C-labeled Fenoxaprop-P-ethyl (Hoe 046360)

IUPAC: (D+)-ethyl-2-(4-(6-chloro-2-benzoxazolyloxy)-phenoxy)-propanoate
Molecular formula: $C_{18}H_{16}ClNO_5$
M= 361.8 g/mol

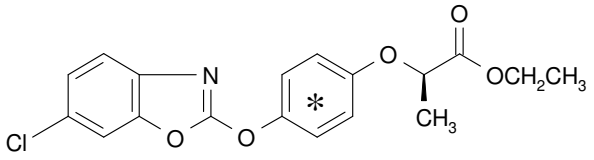


Figure 7.2.1.1-3 Chlorophenyl-^{14}C-labeled Fenoxaprop-ethyl (Hoe 033171)

IUPAC: ethyl-2-(4-(6-chloro-2-benzoxazolyloxy)-phenoxy)-propanoate
Molecular formula: $C_{18}H_{16}ClNO_5$
M= 361.8 g/mol

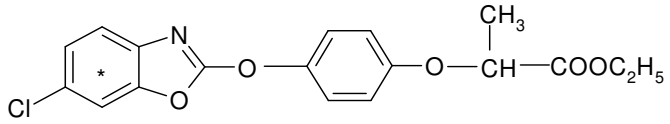


Figure 7.2.1.1-4 Mefenpyr-diethyl (Hoe 107892), safener

IUPAC: diethyl-1-(2, 4-dichlorophenyl)-5-methyl-2-pyrazoline-3,5-dicarboxylate
Molecular formula: $C_{16}H_{18}Cl_2N_2O_4$
M= 373.26 g/mol

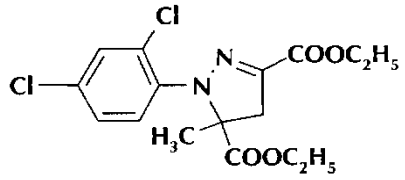
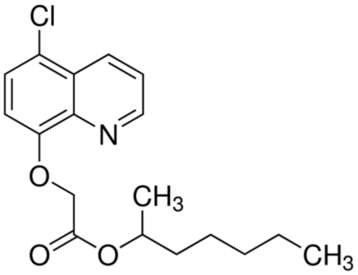


Figure 7.2.1.1-5 Cloquintocet-mexyl, safener

IUPAC: heptan-2-yl 2-(5-chloroquinolin-8-yl)oxyacetate
Molecular formula: $C_{18}H_{22}ClNO_3$
M= 335.83 g/mol



B.7.2.1.1. ***Metabolism in Wheat - study 1***

Reference:	KCA 6.2.1/13 **[^{14}C]-Fenoxaprop-P-Ethyl:** **Metabolism in Spring Wheat Following Post-emergence Application**
Author(s), year:	Oddy, A.M..; 2012
Report/ Doc. Number:	CHA Doc.No. 469 FPE/M-548283-01-1
Guideline(s):	• Regulation (EU) 544/2011 (Part A, Section 6.1) implementing Regulation (EC) 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EC and 91/414/EEC • OECD Guideline 501 for the Testing of Chemicals, January 2007 • EU Commission Working Document 7028/VI/95 rev.3: Appendix A - Metabolism and Distribution in Plants, July 1997
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable

The present study was commissioned by Cheminova. Substance/ metabolite names used in the study are different to those used during Annex I inclusion. The following table shows the different designations opposed to each other.

Designations during Annex I inclusion	**Cheminova designations**
Fenoxaprop-P-ethyl AE F046360	Fenoxaprop-P-ethyl
Fenoxaprop-P-acid AE F088406	FOP-Acid
Benzoxazolone AE F054014	6-Cl-Box
HOPP-acid AE F096918	HPPA

However the study designations were switched to the known designations used during Annex I inclusion for consistency.

This study was designed to provide information on the metabolism of ^{14}C-radiolabelled fenoxaprop-P-ethyl in spring wheat following post-emergence application in the presence of the safener cloquintocet-mexyl (

Figure **7.2.1.1-5**), to assess the nature of residues. In order to fully elucidate the metabolic pathway two separately labelled forms of the test item, [chlorophenyl-U-^{14}C]- and [phenoxy-U-^{14}C]-fenoxaprop-P-ethyl, were used**.**

Test Material

Common Name:	Fenoxaprop-P-ethyl
Name (IUPAC):	Ethyl (R)-2-[4-(6-chloro-1,3-benzoxazol-2-y)oxy)phenoxy]-propionate
Molecular Weight:	361.8
Molecular Formula:	$C_{18}H_{16}ClNO_5$
CAS No.:	71283-80-2
Solubility:	61 g/L in water (pH 7.0) at 20°C
Radiolabel position (specific activity) :	[Chlorophenyl-^{14}C]-Fenoxaprop-P-ethyl (69.45 mCi/mmol)
	[Phenoxy-^{14}C]-Fenoxaprop-P-ethyl (52.19 mCi/mmol)

Material and Methods

Wheat seeds (Variety *Paragon*) were sown into six cylindrical plastic pots (80 cm in diameter, ca 55 cm deep) with sealed bases, filled with a sandy loam soil and sunk in the ground. Each pot was fitted with a 60 cm long plastic tube connected to a layer of drainage material at its base to facilitate drainage and leachate removal. Pots 1-3 were reserved for the application of [chlorophenyl-U-^{14}C]-fenoxaprop-P-ethyl and pots 4-6 were reserved for the application of [phenoxy-U-^{14}C]-fenoxaprop-P-ethyl. The plants were grown outdoors and exposed to normal climatic conditions. Untreated control samples were grown in the native soil surrounding the treated pots provide untreated control samples if required. The plots were enclosed in a wire mesh cage to prevent entry of wildlife.

Fenoxaprop-P-ethyl was applied once, in the presence of the safener cloquintocet-mexyl, as an EW (oil in water emulsion) formulation, post-emergence onto the spring wheat plants at a **nominal rate of 138 g a.i./ha** (~1.7N). The treatment solution was applied to the plants in each pot using a customised sprayer and spray chamber (a separate system was used for the application of each radiolabel) at growth stage BBCH 23-24, forty eight days after sowing, a time representative of commercial usage. Three pots were treated with chlorophenyl labelled fenoxaprop-P-ethyl and a further three pots were treated with phenoxy labelled fenoxaprop-P-ethyl. The achieved application rates were determined to be 143.3 g a.i./ha for the chlorophenyl label and 149.3 g ai/ha for the phenoxy label. A summary is given in the table below.

Table 7.2.1.1-1 Application details

Application number		**Application details**			
		Label	**Application rate**	**Date of application**	**Growth stage at application**
Group I	Plot 1-3	[chlorophenyl-^{14}C] Fenoxaprop-P-ethyl	143.3 g as/ha	11th May 2010	BBCH 23-24
Group II	Plot 4-6	[phenoxy-^{14}C] Fenoxaprop-P-ethyl	149.3 g as/ha	11th May 2010	BBCH 23-24

A first harvest took place 14 days after application on 25th May 2010 (62 days after sowing) at around growth stage BBCH 31-32 (stem elongation). The plants were cut with scissors a few centimetres above the ground, placed into labelled, pre-weighed bags and stored frozen, reserved for later analysis if required. Ultimately these samples were not analysed.

Plants from each of the different label treatments were harvested at two intervals representative of forage and final mature harvest. The **harvest of the forage samples** took place 29 days after application at BBCH 39 (flag leaf stage, flag leaf fully unrolled). The plants were cut with scissors a few centimetres above the ground and placed into labelled, pre-weighed bags. The weight of each harvest sample (fresh weight) was recorded and the samples were then stored in a freezer at < -15°C until further processing.

The final **harvest of straw and grain** took place 106 days after application at BBCH 89 (fully ripening). The plants were cut approximately 2 cm above the ground with scissors. The harvested plants from each pot were put into separate labelled, pre-weighed bags, the weight of each harvest sample (fresh weight) was recorded and the samples were then stored in a freezer at < -15°C until further processing. At final harvest the grains were

removed from the ears of wheat and the remaining stalks, chaff and husks were combined with the appropriate straw sample.
At each harvest interval the samples from pots 1, 2 and 3 (chlorophenyl label) and those from pots 4, 5 and 6 (phenoxy label) were combined prior to homogenisation. Samples of the untreated control plants were harvested in an identical manner on the same days as the test plants. No soil samples were taken.
Table 7.2.1.1-2 Sampling details

Plant matrices sampled	Growth stage at sampling	Time interval from last application	Harvesting method	Plant samples
1st harvest (62 days after sowing)	BBCH 31-32	14 days	cutting the plants a few cm above the soil line	Not analysed, reserved for later analysis if required
Forage samples (77 days after sowing)	BBCH 39	29 days	cutting the plants a few cm above the soil line; samples from the pots (1-3, 4-6) were combined	Cut into 4-6 cm long pieces
Final harvest samples (154 days after sowing)	BBCH 89	106 days		Straw (including chaff, husk) Grain

Forage samples were cut into 4 to 6 cm long pieces using scissors and then homogenised to a fine, uniform particle size in the presence of solid carbon dioxide using a Robot Coupe commercial macerator. A portion (300 to 400 g) of **grain** was homogenised to a fine powder using a 'Waring' spice grinder (without solid carbon dioxide). **Straw samples** (including the chaff and husks) were cut into 4 to 10 cm long pieces using scissors and homogenised to a fine, uniform particle size in the presence of solid carbon dioxide using a Robot Coupe commercial macerator. All samples were placed in appropriately labelled plastic bags and stored at < -15°C to allow the solid carbon dioxide to sublime.

Total radioactive residues (TRR) values were initially determined by combustion of ten replicate (ca 0.3g) aliquots of the frozen homogenised plant material using a Packard 387 oxidiser.

Extraction procedure (Extract 1-7)

The homogenised plant tissue was soaked in acetonitrile for 3 minutes followed by macerating (ultra-turrax) for 3 minutes keeping the sample cool in an ice bath. The extract was separated by centrifugation and decantation. The sample extract was diluted to 250 mL in a volumetric flask with acetonitrile and aliquots (0.1 mL) were assayed for radioactivity by LSC (Extract 1).
The solid residue was re-extracted four times by maceration as above with acetonitrile:water (80:20 v/v) and the sample separated by centrifugation and decantation. The sample extract was diluted with acetonitrile:water (80:20 v/v) and aliquots (0.1 mL) were assayed for radioactivity by LSC (Extract 2-5).
Subsequently the solid residue was transferred to a soxhlet thimble and further extracted with acetonitrile/water 80:20 v/v for ca 4 hours. On cooling, the solvent extract was diluted with acetonitrile:water 80:20 v/v and aliquots (1.0 mL) were assayed for radioactivity by LSC (Extract 6).
The macerator head was rinsed with acetonitrile:water (80:20 v/v) and the sample separated by decantation. The sample extract was with acetonitrile:water 80:20 v/v and aliquots (0.25 mL) were assayed for radioactivity by LSC (Extract 7).

Half of each of the first seven extracts were combined, the volume recorded and aliquots (0.25 mL) were assayed for radioactivity by LSC. The combined sample was concentrated using a rotary evaporator with the water bath set at 30ºC and then reconstituted, with aid of an ultrasonic bath, to a total volume of 100 mL, using 1 mL portions of water followed by portions of acetonitrile. Following the quantitative transfer, the volumetric flask was made up to the final volume with acetonitrile /water (30:70v/v) for forage samples and in water with a small proportion of acetonitrile for straw samples. Aliquots of the concentrated extracts were assayed for total radioactivity by LSC. An additional aliquot was also analysed by HPLC.

Enzyme Hydrolysis (β-glucosidase)

The concentrated forage extracts (from Extracts 1-7) from each label were subjected to enzyme hydrolysis using β-glucosidase (from almonds; purchased from Sigma Aldrich). This enzyme has an optimal activity at pH 5.0 and an optimum temperature of 37°C. A citrate buffer at pH 5.0 was prepared by combining 35 mL of 0.1M citric acid and 65 mL of 0.1 M trisodium citrate. An aliquot of the concentrated forage extract (from Extracts 1-7) was transferred into a glass vial and 2 mL of the buffer solution was added, followed by approximately 2 mg of the β-glucosidase enzyme. The vial was then shaken to mix and placed in an aluminium dri-block heater and incubated at 37°C for six days. After the incubation process the enzyme extracts were analysed by HPLC.

Liquid/liquid Partitioning

An aliquot of the combined, concentrated forage extracts (from Extracts 1-7) from each label was taken and any acetonitrile present removed by rotary evaporation. The remaining aqueous portion was then partitioned three times with ethyl acetate (40 mL). The ethyl acetate fractions were combined and the total volume recorded. The volume of the aqueous remainder was also taken. Aliquots of both partitioned extracts were assayed for total radioactivity by LSC. The ethyl acetate fraction was evaporated to near dryness using turbovap evaporation and the residue re-dissolved in acetonitrile:water (ca 50:50 v/v). An additional aliquot of each partitioned phase was analysed by HPLC.

Acid hydrolysis

To the aqueous fraction post partitioning, from both labels 2M HCl was added and the extracts were heated for 4 hours in a water bath at 80°C. The extracts were then cooled and extracted three times with ethyl acetate. The ethyl acetate fractions were combined and the total volume recorded. The volume of the remaining aqueous phase was also recorded. Aliquots from both phases were assayed for total radioactivity by LSC. The ethyl acetate fraction was evaporated to near dryness using turbovap evaporation and the residue was re-dissolved in acetonitrile:water (ca 50:50 v/v). An additional aliquot of each partitioned phase was also analysed by HPLC.

Extraction procedure (Extract 8-10)

Forage

The solid residue was re-extracted by refluxing for six hours with hydrochloric acid (0.5M HCl). On cooling, the volume of the extract was recorded and aliquots (1.0 mL) were assayed for radioactivity by LSC (Extract 8).

Straw

The air dried solid residue, post extraction, was re-extracted by refluxing for six hours with 0.5M hydrochloric acid (HCl). Upon cooling, the volume of the sample extract was recorded and aliquots (1.0 mL) were assayed for radioactivity by LSC (Extract 8).

A further extraction of the air dried residue was carried out by refluxing for six hours with 6M hydrochloric acid (HCl). Upon cooling, the volume of the sample extract was recorded and aliquots (1.0 mL) were assayed for radioactivity by LSC (Extract 9).

A further harsh extract was subsequently performed by refluxing for six hours with sodium hydroxide (6M NaOH). Upon cooling, the volume of the sample extract was recorded and aliquots were combusted on a Packard Oxidiser and assayed for radioactivity by LSC (Extract 10).

Post extract solids (PES)

The residue remaining after extract 7 (forage) or extract 9 (straw) was air dried and aliquots were analysed by combustion / LSC to determine the amount of unextracted radioactive residue. These post-extraction solids (PES) plus the total radioactivity in the extracts to this point were summarized and defined as the TRR of the sample.

Plant samples were stored frozen at approximately -20°C. All sample extracts were refrigerated at 4°C between handling steps. All samples were extracted within 1 month of sampling and chromatographic profiles were generated within ca 4 months of extraction. From all of the data available, it was concluded that the results of the study were not influenced by storage effects.

Table 7.2.1.1-3 Distribution of [^{14}C]-Fenoxaprop-P-ethyl residues in spring wheat samples

	Fraction		**Total Radioactive Residue**			
			[chlorophenyl-^{14}C] Fenoxaprop-P-ethyl		**[phenoxy-^{14}C] Fenoxaprop-P-ethyl**	
			% TRR	mg/kg	% TRR	mg/kg
Forage PHI 29 days	**Total Radioactive Residue (TRR)**		**100**	**0.657**	**100**	**0.899**
	Extract 1	ACN	20.3	0.134	16.9	0.152
	Extract 2	ACN/Water (80/20)	22.2	0.146	21.8	0.196
	Extract 3	ACN/Water (80/20)	11.8	0.078	10.6	0.095
	Extract 4	ACN/Water (80/20)	6.0	0.039	5.7	0.051
	Extract 5	ACN/Water (30/70)	9.5	0.062	9.1	0.082
	Extract 6	ACN/Water (80/20) Soxhlet	5.6	0.037	5.4	0.048

	Fraction		Total Radioactive Residue			
			[chlorophenyl-^{14}C] Fenoxaprop-P-ethyl		[phenoxy-^{14}C] Fenoxaprop-P-ethyl	
			% TRR	mg/kg	% TRR	mg/kg
	Extract 7	ACN/Water (80/20) rinsed	2.5	0.016	1.2	0.011
		Sum of organic extracts	77.9	0.512	70.7	0.636
	Extract 8	0.5M HCL acidic Hydrolysis	8.0	0.052	12.8	0.115
	Total extracted		**85.8**	**0.564**	**83.6**	**0.751**
	PES (post extraction solids)[#]		14.2	0.093	16.4	0.148
Straw PHI 106 days	**Total Radioactive Residue (TRR)**		**100**	**0.181**	**100**	**0.202**
	Extract 1	H_2O soak ACN/Water (80/20)	10.5	0.019	13.5	0.027
	Extract 2	ACN/Water (80/20)	5.1	0.009	4.5	0.009
	Extract 3	ACN/Water (80/20)	6.1	0.011	4.6	0.009
	Extract 4	ACN/Water (80/20)	3.3	0.006	2.1	0.004
	Extract 5	ACN/Water (30/70)	2.2	0.004	2.2	0.005
	Extract 6	ACN/Water (80/20) Soxhlet	3.4	0.006	1.4	0.003
	Extract 7	ACN/Water (80/20) rinsed	0.8	0.001	1.3	0.003
		Sum of organic extracts	31.3	0.057	29.6	0.06
	Extract 8	0.5M HCL acidic Hydrolysis	12.3	0.022	16.1	0.033
	Extract 9	6M HCL acidic Hydrolysis	4.8	0.009	3.4	0.007
	Extract 10[##]	6M NaOH Reflux/post combustion	30.8	0.056	33.0	0.067
	Total extracted		**79.2**	**0.143**	**82.1**	**0.166**
	PES (post extraction solids)		20.8	0.038	17.9	0.036

[#].....after 0.5N HCL acid reflux (Forage)

[##].....not chromatografically analysed

Quantitative and chromatographic analysis

➢ Combustion/LSC

Quantitative measurement of radioactivity was carried out by liquid scintillation counting (LSC) following solubilisation of the samples in an LSC cocktail. Samples were counted for 10 minutes or until 40,000 counts were accrued, whichever occurred first. Sample counts were automatically corrected for background from the scintillant and solvents present, and for quenching using pre-calibrated quench correction curves to convert cpm to quench-corrected dpm. Sub-samples of homogenised solid samples were combusted using a Packard 387 Oxidiser with automated combustion system. Sample aliquots of approximately 0.1-0.3 g were combusted in oxygen, producing radioactive carbon dioxide which was trapped in a convoluted reaction column filled with Carbosorb ® E and flushed into a scintillation vial with Permafluor® E+ (both supplied by Packard Instruments). The radioactivity in solution was then quantified by LSC.

The limit of quantification (LOQ) for the determination of plant residues by combustion was calculated based on the specific activity of the radiolabelled compound, the amount of plant material combusted and the background of the liquid scintillation counter. As approximately 0.2 g of plant material was generally combusted the LOD was calculated to be 50 dpm/g or 0.00012 µg /g for [chlorophenyl-U-^{14}C] fenoxaprop-P-ethyl samples and 50 dpm/g or 0.00016 µg/g for [phenoxy-U-^{14}C]-fenoxaprop-P-ethyl samples. Thus a LOQ of 0.00024 µg /g (0.2 ppb) has been assigned for [chlorophenyl-U-^{14}C]- fenoxaprop-P-ethyl and an LOQ of 0.00032 µg/g (0.3 ppb) has been assigned for [phenoxy- U-^{14}C]-fenoxaprop-P-ethyl.

➢ High Performance Liquid Chromatography (HPLC)

High performance liquid chromatography was used for determination of the radiopurity of the test materials and for the chromatographic examination of sample extracts. The system and methods are described below.

Apparatus: Jasco PU-980 Intelligent Pump, Jasco AS 950 Intelligent, Autosampler, Gastor GT-103 Degasser

Column: Kromasil 100 C8 (5µm, 250 x 4.6 mm id) for radiopurity and sample analysis
Detector: Jasco UV-975 Intelligent UV/VIS Detector set at 290 nm Packard Radiomatic 525 TR radiodetector
Scintillant: FloLogic 1.5 mL min-1
Mobile Phase: A) 0.3 g sulphuric acid in 1 L of water plus 10 mL acetonitrile B) acetonitrile
Flow Rate: 1mL min-1
*Temperature: A*mbient

Gradient table 1 (Radiopurity):

Time (min)	% A	% B
0	100	0
5	100	0
25	0	100
30	0	100
35	100	0
40	100	0

Gradient table 2 (forage and straw sample extracts):

Time (min)	% A	% B
0	100	0
5	100	0
36	0	100
40	0	100
50	100	0
55	100	0

To verify that all of the radioactive material injected onto the HPLC column was eluted, column recoveries were carried out on selected samples. Representative injections were made onto the HPLC column for each radiolabel and the eluate was collected for 40 minutes, the volume was measured and aliquots were taken for liquid scintillation counting (post column). Duplicate injections were also performed for each label without the HPLC column attached. The pre-column eluate was collected directly and Lumasafe scintillation cocktail added. The total radioactivity in each sample was determined by LSC. The HPLC column recovery was calculated by comparison of the results obtained pre- and post-column.

➢ Liquid Chromatography Mass Spectrometry

To confirm the presence of fenoxaprop-P-ethyl and its major metabolites in the concentrated plant extracts, the samples were analysed by liquid chromatography mass spectrometry in electrospray ionisation mode on a QUATTRO-LC mass spectrometer. A mixed standard was also analysed for comparison chromatographic purposes. For confirmation analyses of fenoxaprop-P-ethyl and its metabolites the standard and samples were analysed using the LC-MS/MS conditions given below.

Mass Spectrometer General Instrument Conditions		
Instrument	MICROMASS QUATTRO-LC Triple Quadrupole	
Ion Source	Negative Ion Electrospray Ionisation (ESP-)	Positive Ion Electrospray Ionisation (ESP+)
Capillary Voltage	3.5 – 3.75 kV	3.5 kV
RF Lens	0.1 V	0.1 V
Source Temp.	120°C	
Desolvation Temp.	220°C	
Multiplier Voltage	650 V	
Nebuliser Gas	*ca* 62 – 86 L/hr N_2	
Desolvation Gas	*ca* 956 – 1173 L/hr N_2	

LC-MS/MS Mass Spectrometric Conditions				
Gas Cell Pressure	Between 1e-3 mBar and 6e-4 mBar Ar			
Compound	Benzoxazolone (AE F054014)	HOPP-Acid (AE F096918)	Fenoxaprop-P-acid (AE F088406)	Fenoxaprop-P-ethyl (AE F046360)
Ion Mode	ESP-	ESP-	ESP-	ESP+
Cone Voltage	16 V	16 V	16 V	16 V
Collision Energy	15 eV	15 eV	15 eV	15 eV
Precursor Ion	168 $[M-H]^-$	181 $[M-H]^-$	332 $[M-H]^-$	362 $[M-H]^+$
Daughter Ion	35 $[Cl]^-$	109 $[HO.C_6H_4.O]^-$	152 $[Ci.C_6H_3NCO]^-$	288 $[M-CO.OCH_2CH_3]^+$
MRM Transition	168>35	181>109	332>152	362>288

The analogue data from the [^{14}C] detector was captured to the mass spectrometer data system. Due to the large internal volume of the [^{14}C] detector flow cell, a lag time of ca-0.65 min. was observed between the events in the ion source and the events in the radio detector cell. All data were aligned to allow for this lag time. The following, modified HPLC methods were used during experiments to identify conjugates in the chlorophenyl and phenoxy forage extracts, respectively.

Instrument	Jasco 900 Series consisting of two PU-980 Intelligent HPLC pumps and a UV-975 UV/Vis Detector and CTC Analytics HTS PAL Autosampler		
Column	Kromasil C18 5µm (250 x 4.6mm)		
Mobile Phase A	100:0.5 v/v water:formic acid		
Mobile Phase B	100:0.5 v/v acetonitrile:formic acid		
Gradient	Time (min)	%A	%B
	0	95	5
	5	95	5
	30	85	15
	40	85	15
	60	0	100
	65	0	100
	65.1	95	5
	70	95	5
Flow Rate	1 mL/min with *ca* 100 µL/min into MS ion source.		
Injection Volume	250 µL		
[^{14}C]-Detection	LabLogic β-Ram Model 3 Radiodetector fitted with a 0.5mL Liquid cell using 1.5 mL/min Flo Logic scintillant		

Instrument	Jasco 900 Series consisting of two PU-980 Intelligent HPLC pumps and a UV-975 UV/Vis Detector and CTC Analytics HTS PAL Autosampler		
Column	Kromasil C18 5µm (250 x 4.6mm)		
Mobile Phase A	100:0.5 v/v water:formic acid		
Mobile Phase B	100:0.5 v/v acetonitrile:formic acid		
Gradient	Time (min)	%A	%B
	0	95	5
	5	95	5
	35	0	100
	40	0	100
	40.1	95	5
	45	95	5
Flow Rate	1 mL/min with *ca* 100 µL/min into MS ion source.		
Injection Volume	250 µL		
[^{14}C]-Detection	LabLogic β-Ram Model 3 Radiodetector fitted with a 0.5mL Liquid cell using 1.5 mL/min Flo Logic scintillant		

Characterisation and identification of residues

The combined organic extracts (extracts 1-7) from both labels were concentrated and analysed by high performance liquid chromatography (HPLC). These samples were subsequently partitioned between organic (ethyl acetate) and aqueous phases with, in all cases, the majority of the radioactive residue remaining in the aqueous phase. Aliquots of both the organic and aqueous phases were assayed for total radioactivity by LSC and analysed by HPLC. The aqueous fractions post partitioning from both labels were subjected to acid hydrolysis (2 M HCl, 80°C), with the resultant solution again partitioned between organic (ethyl acetate) and aqueous phases and with both phases then analysed by HPLC. The nature of the conjugates in the forage samples were also investigated by treatment with β-glucosidase enzyme.

The 0.5 M HCl forage extracts (extract 8) were neutralised and analysed by HPLC. For the phenoxy label straw samples, both the 0.5 M HCl (extract 8) and 6 M HCl extracts (extract 9) were partitioned with ethyl acetate. The organic partitions were concentrated and analysed by HPLC.

Due to the higher residue levels and with the sample extracts being more amenable to chromategraphic analysis, most of the analyses were focused on the forage sample extracts. No chromatographic analysis was performed on the 6 M NaOH extracts (extract 10).

Table 7.2.1.1-4 Overview on the extraction efficiencies

Extract	**Chlorophenyl Label**				**Phenoxy Label**			
	Forage		**Straw**		**Forage**		**Straw**	
	% TRR	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Organic extracts (1-7)	77.9	0.512	31.3	0.057	70.7	0.636	29.6	0.060
Acid extracts (8-9)*	8.0	0.052	17.1	0.031	12.8	0.115	19.5	0.040
Base extract (10)	---	---	30.8	0.056	---	---	33.0	0.067
Total extracted	**85.8**	**0.564**	**79.2**	**0.143**	**83.6**	**0.751**	**82.1**	**0.166**
Unextracted (PES)	14.2#	0.093	20.8	0.038	16.4#	0.148	17.9	0.036
Total	100.0	0.657	100.0	0.181	100.0	0.899	100.0	0.202

* extract 8 for forage; extracts 8+9 for straw # after acid hydrolysis

➢ Forage (chlorophenyl label)

A total of 85.8% (0.564 mg/kg) of the TRR was extracted from the chlorophenyl forage sample including the harsh 0.5 M HCl reflux extraction (Extract 8). The unextracted portion of the residue represented 14.2% (0.093 mg/kg) (see Table 7.2.1.1-3).

HPLC analysis of the initial forage extracts (Extract 1-7) representing 0.512 mg/kg (77.9 % TRR) showed a number of regions of radioactivity. The largest components were represented by two relatively polar peaks designated “conjugate 1” (0.147 mg/kg, 22.4% TRR) and “conjugate 2” (0.109 mg/kg, 16.6% TRR). Other

components present were identified as parent fenoxaprop-P-ethyl (0.023 mg/kg, 3.5% TRR) and benzoxazolone metabolite AE F054014 (0.012 mg/kg, 1.8% TRR). The remainder of the radioactivity eluted as a diffuse, probably multi-component, region between 16-22min (Table 7.2.1.1-5). HPLC analysis of the β-glucosidase treated sample showed little effect, inferring that no glucoside conjugates were present.

Upon partitioning the majority of the radioactivity remained in the aqueous fraction (61.5% TRR, 0.404 mg/kg). HPLC analysis of the concentrated organic partition (16.4% TRR, 0.108 mg/kg) confirmed the presence of the parent fenoxaprop-P-ethyl and AE F054014 with the quantification being in good agreement with the figures from the raw extract. A very small amount of fenoxaprop-P-acid (AE F088406) was also detected (0.005 mg/kg, 0.5% TRR). A portion of the diffuse region of radioactivity and small amounts of "conjugate 2" also appeared in the organic partition. The aqueous partition contained the majority of the "conjugate 1" (16.8 % TRR, 0.111 mg/kg) and "conjugate 2" (13.3 % TRR, 0.087 mg/kg). HPLC analysis of the acidic reflux Extract 8 (8.0% TRR, 0.052 mg/kg) showed that this process had released more benzoxazolone (2.5% TRR, 0.016 mg/kg) along with more polar components including "conjugate 2" (0.013 mg/kg, 2.0% TRR) (Table 7.2.1.1-6).

Following acid hydrolysis of the aqueous phase, the sample was again partitioned. With this partition about half of the radioactivity now transferred to the organic phase (29.3% TRR, 0.192 mg/kg). The organic phase was found to contain some benzoxazolone (AE F054014) with 0.052 mg/kg and 7.9% TRR which had been released by the acid hydrolysis. The remainder of the radioactivity comprised residual "conjugate 2" (9.3 % TRR, 0.061 mg/kg) plus some minor unknown (12.0 % TRR, 0.079 mg/kg). The aqueous phase contained the two "conjugate" peaks, "conjugate 1" (9.1 % TRR, 0.060 mg/kg) and "conjugate 2" (16.7 % TRR, 0.109 mg/kg) (Table 7.2.1.1-7)

In total, following acid hydrolysis of the neutral extracts and including the results for the acid extracts of the plant tissue (Extracts 8 and 9) 12.5% of the TRR (0.076 mg/kg) in the forage sample was accounted for as benzoxazolone AE F054014 (free plus conjugated).

Straw (chlorophenyl label)

A total of 79.2% (0.143 mg/kg) of the TRR was extracted from the chlorophenyl label straw sample. The unextracted portion of the residue represented 20.8% (0.038 mg/kg). Further harsh extractions (reflux) using 6 M HCl and 6 M NaOH extracted a further 4.8% (0.009 mg/kg) and 30.8% (0.056 mg/kg) of the TRR but these extracts were not chromatographically analysed (see Table 7.2.1.1-3).

HPLC analysis of the initial straw extracts (Extract 1-7) representing 0.057 mg/kg (31.3% TRR) showed that the majority of the radioactivity eluted as the diffuse, probably multi-component, region between 14 and 23 min that had been seen in the forage extracts (Table 7.2.1.1-5).

Upon partitioning the majority of the radioactivity remained in the aqueous fraction (21.5 % TRR, 0.039 mg/kg). HPLC analysis of the concentrated organic partition (9.9% TRR, 0.018 mg/kg) confirmed the presence of small amounts benzoxazolone AE F054014 (1.5% TRR, 0.003 mg/kg) and fenoxaprop-P-acid AE F088406 (3.2% TRR, 0.006 mg/kg) but no parent fenoxaprop-P-ethyl. The majority of the radioactivity in the aqueous partition still consisted of the diffuse region (Table 7.2.1.1-6).

Following acid hydrolysis of the aqueous partition, the sample was again partitioned with two thirds of the radioactivity now transferred to the organic phase (14.3% TRR, 0.03 mg/kg) (Table 7.2.1.1-7).

Table 7.2.1.1-5 Identification and characterisation of residues in wheat samples after application of [chlorophenyl-^{14}C]Fenoxaprop-P-ethyl in % TRR and mg as eq/kg (combined extracts 1-7)

	Wheat Forage 1 x 143.3g/ha		**Wheat straw** 1x 143.3 g/ha	
Time interval from last application	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
TRR – Total Radioactive residues	**100**	**0.657**	**100**	**0.181**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.4 min)	3.5	0.023	n.d.	n.d.
Conjugate 1 (RT 14.7 min)	22.4	0.147	n.d.	n.d.
Conjugate 2 (RT 15.9 min)	16.6	0.109	n.d.	n.d.
Benzoxazolone (AE F054014) (RT 24.2 min)	1.8	0.012	0.7	0.001
Fenoxaprop-P-acid (AE F088406) (RT 31 min)	n.d.	n.d.	1.2	0.002
Total identified	**44.3**	**0.291**	**1.9**	**0.003**

Time interval from last application	Wheat Forage 1 x 143.3g/ha		Wheat straw 1x 143.3 g/ha	
	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Unknown (RT= 4 min)	-	-	2.0	0.004
Unknown (RT= 15 min)	-	-	1.6	0.003
Unknown (RT= 15.7 min)			1.7	0.003
Unknown (RT= 16.6 min)	4.0	0.026	2.3	0.004
Unknown (RT= 17.5 min)	-	-	5.5	0.010
Unknown (RT= 17.9 min)	3.2	0.021	4.5	0.008
Unknown (RT= 18.5 min)	3.5	0.023	1.3	0.002
Unknown (RT= 19 min)	3.6	0.023	1.9	0.003
Unknown (RT= 19.6 min)	2.6	0.017	3.4	0.006
Unknown (RT= 20.3 min)	3.0	0.019	1.3	0.002
Unknown (RT= 21.2 min)	4.0	0.027	-	-
Unknown (RT= 20.6 min)	2.1	0.014	-	-
Unknown (RT= 22 min)	1.7	0.011	-	-
Unknown (RT= 22.4 min)	1.9	0.012	-	-
Sum of Unknown[1]	4.0	0.026	4.2	0.008
Total characterized	**33.6**	**0.219**	**29.5**	**0.054**
ERR - Extracted Radioactive Residues	**77.9**	**0.512**	**31.3**	**0.057**
URR – Unextracted Radioactive Residues	22.1	0.145	68.6	0.124

[1] Individual peaks all less than 1% TRR or 0.01 mg/kg

Table 7.2.1.1-6 Identification and characterisation of residues in wheat samples in aqueous and organic phases post partitioning of combined Extracts 1-7 and Extract 8 &9 in % TRR and mg as eq/kg [chlorophenyl-^{14}C label]

Time interval from last application	Wheat Forage 1 x 143.3g/ha		Wheat straw 1x 143.3 g/ha	
	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Organic fraction (extract 1-7)	**16.4**	**0.108**	**9.9**	**0.018**
Fenoxaprop-P-ethyl (AE F046360) (RT 35 min)	3.4	0.023	n.d.	n.d.
Conjugate 1 (RT 16 min)	1.6	0.010	n.d.	n.d.
Conjugate 2 (RT 17 min)	1.2	0.008	n.d.	n.d.
Benzoxazolone (AE F054014) (RT 24.2 min)	2.1	0.014	1.5	0.003
Fenoxaprop-P-acid (AE F088406) (RT 31 min)	0.5	0.005	3.2	0.006
Sum of minor unknown	7.5	0.049	5.2	0.009
Aqueous fraction (extract 1-7)	**61.5**	**0.404**	**21.5**	**0.039**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.4 min)	n.d.	n.d.-	n.d.	n.d.
Conjugate 1 (RT 14.7 min)	16.8	0.111	n.d.	n.d.
Conjugate 2 (RT 15.9 min)	13.3	0.087	n.d.	n.d.
Benzoxazolone (AE F054014) (RT 24.2 min)	n.d.	n.d.	n.d.	n.d.
Fenoxaprop-P-acid (AE F088406) (RT 31 min)	n.d.	n.d.	n.d.	n.d.
Sum of minor unknown	31.4	0.206	21.5	0.039
0.5M HCL Extract 8 (forage)/Extracts 8+9 (straw)	**8.0**	**0.052**	**17.1[#]**	**0.031[#]**

Time interval from last application	**Wheat Forage** 1 x 143.3g/ha		**Wheat straw** 1x 143.3 g/ha	
	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Fenoxaprop-P-ethyl (AE F046360) (RT 34.4 min)	n.d.	n.d.	n.a.	n.a.
Conjugate 1 (RT 14.7 min)	n.d.	n.d.	n.a.	n.a.
Conjugate 2 (RT 15.9 min)	2.0	0.013	n.a.	n.a.
Benzoxazolone (AE F054014) (RT 24.2 min)	2.5	0.016	n.a.	n.a.
Fenoxaprop-P-acid (AE F088406) (RT 31 min)	n.d.	n.d.	n.a.	n.a.
Sum of minor unknown	3.5	0.023	n.a.	n.a.
ERR - Extracted Radioactive Residues	**85.8**	**0.564**	**48.5**	**0.088**
URR – Unextracted Radioactive Residues	14.2	0.093	51.6	0.093
TRR – Total Radioactive residues	100	0.657	100	0.181

[#] extracted, but not analysed (Extract 8+9)
n.d. not detected
n.a. not analysed

Table 7.2.1.1-7 Identification and characterisation of residues in wheat samples after partitioning of the acid hydrolysed aqueous fraction (extract 1-7) in % TRR and mg as eq/kg [chlorophenyl-^{14}C label]

Time interval from last application	**Wheat Forage** 1 x 143.3g/ha		**Wheat straw** 1x 143.3 g/ha	
	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Organic fraction	**29.3**	**0.192**	**14.3**	**0.026**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.4 min)	n.d.	n.d.	n.d.	n.d.
Conjugate 1 (RT 14.7 min)	n.d.	n.d.	n.d.	n.d.
Conjugate 2 (RT 15.9 min)	9.3	0.061	n.d.	n.d.
Benzoxazolone (AE F054014) (RT 24.2 min)	7.9	0.052	n.d.	n.d.
Sum of minor unknown	12.0	0.079	14.3	0.026
Aqueous fraction	**32.2**	**0.212**	**7.2**	**0.013**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.4 min)	n.d.	n.d.	n.d.	n.d.
Conjugate 1 (RT 14.7 min)	9.1	0.060	n.d.	n.d.
Conjugate 2 (RT 15.9 min)	16.7	0.109	n.d.	n.d.
Benzoxazolone (AE F054014) (RT 24.2 min)	n.d.	n.d.	n.d.	n.d.
Sum of minor unknown	6.4	0.042	7.2	0.013
ERR - Extracted Radioactive Residues	**61.5**	**0.404**	**21.5**	**0.039**

Table 7.2.1.1-8 Identification and characterisation of residues in wheat forage samples following ß-glucosidase treatment for combined extracts 1-7 in % TRR and mg as eq/kg [chlorophenyl-^{14}C label]

Time interval from last application	**Wheat Forage** 1 x 143.3g/ha	
	29 days	
	TRR (%)	mg/kg
Fenoxaprop-P-ethyl (AE F046360) (RT 35 min)	1.2	0.008
Conjugate 1 (RT 15 min)	21.5	0.141
Conjugate 2 (RT 16 min)	14.2	0.093
Benzoxazolone (AE F054014) (RT 25 min)	5.9	0.038
Sum of minor unknown	35.2	0.231
ERR - Extracted Radioactive Residues	**77.9**	**0.512**

➢ Forage (phenoxy label)

A total of 83.6% (0.751 mg/kg) of the TRR was extracted from the [phenoxy-U-^{14}C] fenoxaprop-P-ethyl forage sample including the harsh 0.5 M HCl reflux extraction (Extract 8). The unextracted portion of the residue represented 16.4% (0.148 mg/kg) (see Table 7.2.1.1-3).

HPLC analysis of the initial forage extracts (Extract 1-7) representing 70.7% TRR (0.636 mg/kg) showed a number of regions of radioactivity. The largest component was represented by a relatively polar peak subsequently designated "HOPP acid conjugate" (26.4% TRR, 0.238 mg/kg). Other components present were identified as parent fenoxaprop-P-ethyl (3.9% TRR, 0.035 mg/kg), fenoxaprop-P acid (0.7% TRR, 0.006 mg/kg) and HOPP acid AE F096918 (5.6% TRR, 0.051 mg/kg). The remainder of the radioactivity mainly eluted as a diffuse, probably multi-component, region between 26 and 23 min (see Table 7.2.1.1-9).

Upon partitioning the majority of the radioactivity remained in the aqueous phase (56.7% TR, 0.509 mg/kg). HPLC analysis of the concentrated organic partition (14.1% TRR, 0.127 mg/kg) confirmed the presence of the parent fenoxaprop-P-ethyl, fenoxaprop-P acid (AE F088406) and HOPP acid (AE F096918) with the quantification being in good agreement with the figures from the raw extract. The "HOPP acid conjugate" was mainly present in the aqueous partition (25.7% TRR, 0.23 mg/kg) (see Table 7.2.1.1-10).

Following acid hydrolysis of the aqueous partition, the sample was again partitioned with ethylactetate, the majority of the radioactivity now transferred to the organic phase (53.7% TRR, 0.483 mg/kg). The organic phase was found to contain mainly HOPP acid conjugate (44% TRR, 0.396 mg/kg) which had been released by the acid hydrolysis. The remainder of the radioactivity comprised the diffuse region. The aqueous phase (3% TRR, 0.03 mg/kg) contained a very small amount of the diffuse region (see Table 7.2.1.1-11).

HPLC analysis of the β-glucosidase treated sample showed a reduction in the signal for the "HOPP acid conjugate", peak whilst there was an increase in the signal for HOPP acid. This data suggests that the conjugate was a glucoside conjugate of HOPP acid (AE F096918). Confirmatory data for this assignment was obtained by mass spectroscopy. HPLC analysis of the acidic reflux extract Extract 8 (12.8% TRR, 0.115 mg/kg) showed that this process had released more (10.6% TRR, 0.096 mg/kg) (see Table 7.2.1.1-12)

In total, following acid hydrolysis of the neutral extracts and including the results for the acid extracts of the plant tissue (Extracts 8 and 9), 56.4% of the TRR (0.509 mg/kg) in the forage sample was accounted for as HOPP acid (free plus conjugated).

➢ Straw (phenoxy label)

A total of 82.1% (0.166 mg/kg) of the TRR was extracted from the phenoxy label straw sample. 29.6% (0.060 mg/kg) was extracted in the standard solvent extracts (Extracts 1 to 7) and 16.1% (0.033 mg/kg) in Extract 8 (0.5 M HCl reflux). The unextracted portion of the residue represented 17.9 % (0.036 mg/kg). Further extractions using 6 M HCl reflux (Extract 9) and 6 M NaOH reflux (Extract 10) extracted a further 3.4% (0.007 mg/kg) and 33.0% (0.067 mg/kg) of the TRR (see Table 7.2.1.1-3). Of these harsh extracts only the acid extract (Extract 9) was analysed by HPLC.

HPLC analysis of the initial straw extracts (Extract 1-7) representing 29.6% TRR (0.060 mg/kg) showed the majority of the radioactivity eluted as the diffuse, probably multi-component, region between 14 and 23 min that

had been seen in the forage extracts. Upon partitioning the majority of the radioactivity remained in the aqueous fraction (24.4% TRR, 0.049 mg/kg), containing HOPP acid AE F096918 (5.5% TRR, 0.011 mg/kg) and a small amount of the diffuse region. HPLC analysis of the concentrated organic partition (5.2% TRR, 0.011 mg/kg) confirmed the presence of fenoxaprop-P-acid AE F088406 (2% TRR, 0.004 mg/kg) and some minor unknowns.
HPLC analysis of the acidic reflux extracts (organic partition) of Extract 8 (9.2% TRR, 0.019 mg/kg) and Extract 9 (2.2% TRR, 0.004 mg/kg) showed that these processes released more HOPP-acid (AE F096918 (in total 7.8% TRR, 0.016 mg/kg) along with very minor components (see Table 7.2.1.1-10).
Following acid hydrolysis of the aqueous partition, the sample was again partitioned with approximately half of the radioactivity now transferred to the organic phase. The organic phase (12.7% TRR, 0.026 mg/kg) was found to contain a significant quantity of HOPP-acid AE F096918 (5.7% TRR, 0.012 mg/kg) which had been released by the acid hydrolysis again suggesting the presence of HOPP-acid conjugates in the extractable residue. The remainder of the radioactivity still comprised the diffuse region. The aqueous phase (11.6% TRR, 0.024 mg/kg) contained the remaining diffuse region (see Table 7.2.1.1-11).

Table 7.2.1.1-9 Identification and characterisation of residues in wheat samples after application of [phenoxy-^{14}C] Fenoxaprop-P-ethyl in % TRR and mg as eq/kg (combined extracts 1-7)

	Wheat Forage 1 x 149.3g/ha		**Wheat straw** 1x 149.3 g/ha	
Time interval from last application	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
TRR – Total Radioactive residues	**100**	**0.899**	**100**	**0.202**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	3.87	0.035	n.d.	n.d.
HOPP acid conjugate (RT 14.7 min)	26.4	0.238	n.d.	n.d.
HOPP acid (AE F096918) (RT 29.9 min)	5.61	0.051	3.3	0.007
Fenoxaprop-P-acid (AE F088406) (RT 30.2 min)	0.69	0.006	1.2	0.002
Total identified	**36.6**	**0.33**	**4.5**	**0.009**
Unknown (RT= 3-4 min)	4.61	0.041	2.9	0.005
Unknown (RT= 13.7 min)	1.92	0.017	2.2	0.005
Unknown (RT= 14.9 min)	-	-	2.1	0.004
Unknown (RT= 15.5 min)	3.98	0.036	3.0	0.006
Unknown (RT= 16.2 min)	1.75	0.016	1.8	0.004
Unknown (RT= 17.0 min)	2.63	0.024	2.5	0.005
Unknown (RT= 17.2 min)	2.84	0.026	-	-
Unknown (RT= 17.5 min)	1.89	0.017	5.5	0.011
Unknown (RT= 18.0 min)	2.82	0.025	-	-
Unknown (RT= 19.3 min)	1.31	0.012	1.9	0.004
Unknown (RT= 20.1 min)	3.13	0.028	1.2	0.002
Unknown (RT= 20.4 min)	1.0	0.009	-	-
Unknown (RT= 21.1 min)	1.11	0.010	-	-
Unknown (RT= 22.1 min)	1.06	0.010	-	-
Sum of Unknown[1]	4.09	0.037	1.9	0.002
Total characterized	**34.1**	**0.308**	**25.1**	**0.048**
ERR - Extracted Radioactive Residues	**70.7**	**0.636**	**29.6**	**0.057**
URR – Unextracted Radioactive Residues	29.3	0.263	70.4	0.145

[1] Individual peaks all less than 1% TRR or 0.01 mg/kg

Table 7.2.1.1-10 Identification and characterisation of residues in wheat samples in aqueous and organic phases post partitioning of combined Extracts 1-7 and Extract 8 &9 in % TRR and mg as eq/kg [phenoxy-^{14}C label]

	Wheat Forage 1 x 149.3g/ha		**Wheat straw** 1x 149.3 g/ha	
Time interval from last application	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Organic fraction (extract 1-7)	**14.1**	**0.127**	**5.2**	**0.011**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	3.09	0.028	n.d.	n.d.
HOPP acid conjugate (RT 16.1 min)	3.17	0,029	n.d.	n.d.
HOPP acid (AE F096918) (RT 19.3 min)	1.21	0.011	2.0	0.004
Fenoxaprop-P-acid (AE F088406) (RT 30.7 min)	0.58	0.005	n.d.	n.d.
Sum of unknown	6.03	0.055	3.2	0.006
Aqueous fraction (extract 1-7)	**56.7**	**0.509**	**24.4**	**0.049**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	n.d.	n.d.	n.d.	n.d.
HOPP acid conjugate (RT 16.2 min)	25.7	0.231	n.d.	n.d.
HOPP acid (AE F096918) (RT 19.4 min)	4.0	0.036	5.5	0.011
Fenoxaprop-P-acid (AE F088406) (RT 30.7 min)	n.d.	n.d.	n.d.	n.d.
Sum of unknown	27.0	0.242	18.9	0.038
0.5M HCL Extract 8 (forage)/Extracts 8+9 (straw)	**12.8**	**0.115**	**11.4[#]**	**0.023[#]**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	n.d.	n.d.	n.d.	n.d.
HOPP acid conjugate (RT 16 min)	0.43	0.004	n.d.	n.d.
HOPP acid (AE F096918) (RT 29.9 min)	10.6	0.096	7.8	0.016
Fenoxaprop-P-acid (AE F088406) (RT 30.2 min)	n.d.	n.d.	n.d.	n.d.
Sum of unknown	1.77	0.015	3.6	0.007
Extracted, but not analysed (Extract 8+9)	n.a.	n.a	8.1	0.016
ERR - Extracted Radioactive Residues	**83.6**	**0.751**	**49.1**	**0.099**
URR – Unextracted Radioactive Residues	16.4	0.148	**50.9**	**0.103**
TRR – Total Radioactive residues	100	0.899	100	0.202

[#] sum of Extract 8 (9.2% TRR, 0.019 mg/kg) + Extract 9 (2.2% TRR, 0.004 mg/kg)
n.d. not detected
n.a. not applicable

Table 7.2.1.1-11 Identification and characterisation of residues in wheat samples after partitioning of the acid hydrolysed aqueous fraction (extract 1-7) in % TRR and mg as eq/kg [phenoxy-^{14}C label]

	Wheat Forage 1 x 149.3g/ha		**Wheat straw** 1x 149.3 g/ha	
Time interval from last application	29 days		106 days	
	TRR (%)	mg/kg	TRR (%)	mg/kg
Organic fraction	**53.7**	**0.48**	**12.7**	**0.026**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	n.d.	n.d.	n.d.	n.d.
HOPP acid conjugate (RT 16.1 min)	44.02	0.396	n.d.	n.d.
HOPP acid (AE F096918) (RT 19.3 min)	n.d.	n.d.	5.7	0.012
Fenoxaprop-P-acid (AE F088406) (RT 30.7 min)	n.d.	n.d.	n.d.	n.d.
Sum of unknown	9.7	0.086	7.1	0.015
Aqueous fraction	**3.0**	**0.027**	**11.6**	**0.024**
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	n.d.	n.d.	n.d.	n.d.
HOPP acid conjugate (RT 16.1 min)	0.82	0.007	n.d.	n.d.
HOPP acid (AE F096918) (RT 19.3 min)	0.64	0.006	n.d.	n.d.
Fenoxaprop-P-acid (AE F088406) (RT 30.7 min)	n.d.	n.d.	n.d.	n.d.
Sum of unknown	1.5	0.013	11.6	0.024
ERR - Extracted Radioactive Residues	**56.7**	**0.51**	**24.3**	**0.05**

Table 7.2.1.1-12 Identification and characterisation of residues in wheat forage samples following ß-glucosidase treatment for combined extracts 1-7 in % TRR and mg as eq/kg [phenoxy-^{14}C label]

	Wheat Forage 1 x 149.3g/ha	
Time interval from last application	29 days	
	TRR (%)	mg/kg
Fenoxaprop-P-ethyl (AE F046360) (RT 34.3 min)	1.9	0.017
HOPP acid conjugate (RT 16.1 min)	11.6	0.104
HOPP acid (AE F096918) (RT 19.3 min)	30.7	0.276
Fenoxaprop-P-acid (AE F088406) (RT 30.7 min)	n.d.	n.d.
Sum of unknown	26.6	0.239
ERR - Extracted Radioactive Residues	**70.7**	**0.636**

- Grain (chlorophenyl- and phenoxy label)

Residues in grain, resulting from post-emergence application of fenoxaprop-P-ethyl (using two radio labels) in the presence of the safener cloquintocet-mexyl to spring wheat at a nominal rate of 138 g a.i./ha were low, being 0.002 and 0.004 mg/kg, respectively, for chlorophenyl and phenoxy label samples. Due to the low total residue (<< 0.01 mg/kg) no further analysis of the grain samples was necessary.

Conclusion

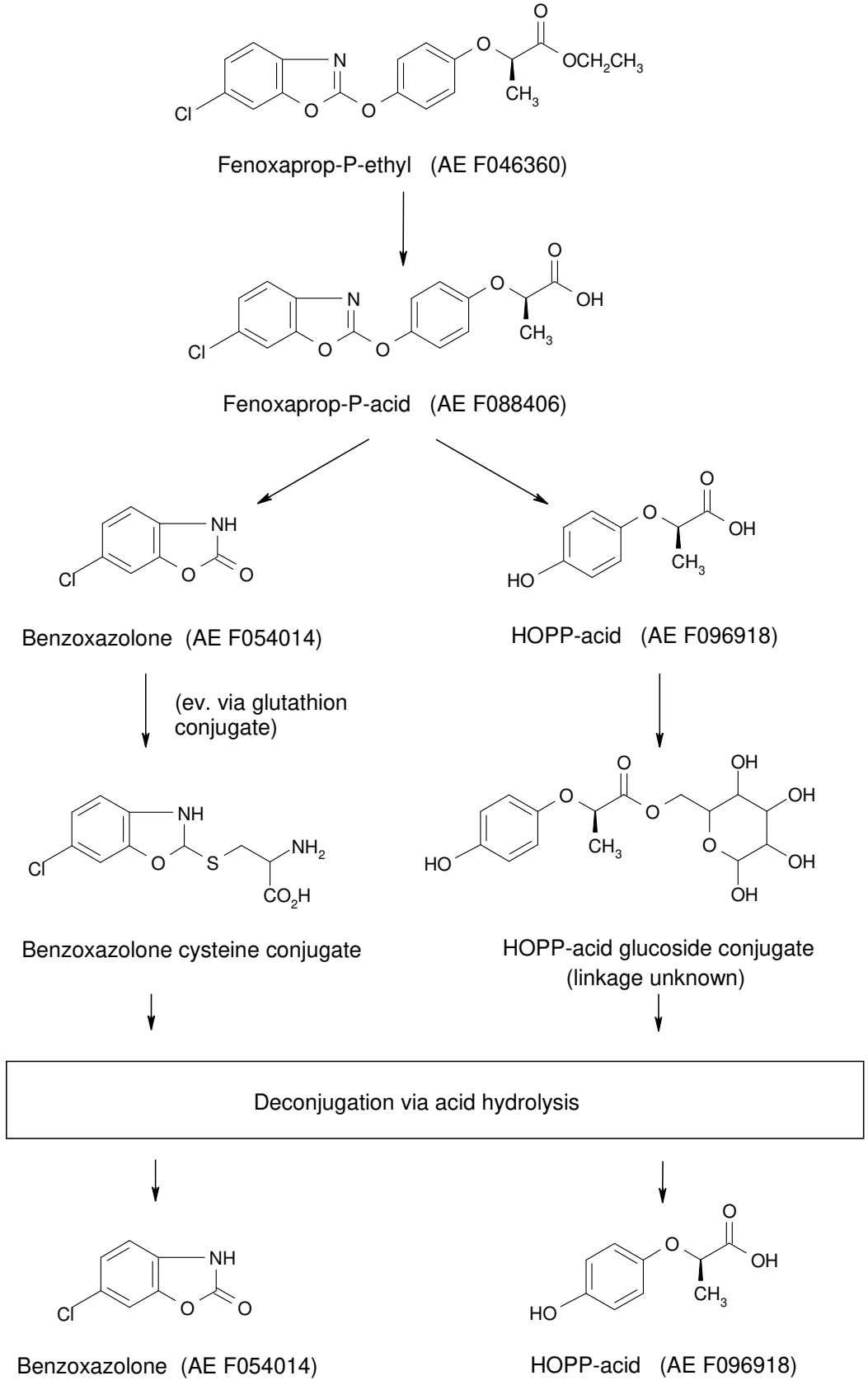
The present study elucidates the metabolism of fenoxaprop-P-ethyl in spring wheat following post-emergence application of 143.3 g as/ha (chlorophenyl label) and 149.3 g as/ha (phenoxy-label) in the presence of the safener cloquintocet-mexyl. Plants from each label treatments were harvested at two intervals representative of forage and final mature harvest. The harvest of the forage samples (BBCH 39) took place 29 days after application. The final harvest sampling of straw and grain (BBCH 89) took place 106 days after application. Due to the low total residue (<< 0.01 mg/kg) in grain samples no further analysis was necessary.

The total residues in interim forage and final harvest straw samples were low at 0.657 and 0.899 mg/kg (forage) and 0.181 and 0.202 mg/kg (straw) for chlorophenyl and phenoxy labels, respectively.
The major components of the extractable residue for both the forage and straw samples were HOPP-acid AE F096918 with the phenoxy label and benzoxazolone AE F054014 with the chlorophenyl label, both metabolites being present in free and conjugated forms. Smaller quantities of fenoxaprop-P-ethyl (AE F046360) and fenoxaprop-P-acid (AE F088406) were also detected in the forage samples of both labels, the chlorophenyl label and the phenoxy-label.
The metabolic pathway for fenoxaprop-P-ethyl as proposed in the first evaluation in the DAR (2005) was confirmed straight as well as in presence of other safeners. The present study therefore also confirms the postulated independency of the route of metabolisation from the presence of a safener.
Foliar applied residues of fenoxaprop-P-ethyl on cereals in the presence of the safener cloquintocet-mexyl can be readily metabolised such that no significant residues of fenoxaprop-P-ethyl remain in forage, straw or grain following an application at BBCH 23-29 with the major components of the extractable residue being HOPP-acid AE F096918 and benzoxazolone AE F054014, both present in free and conjugated forms. The route of metabolism of fenoxaprop-P-ethyl in wheat following post-emergence application in the presence of the safener cloquintocet-mexyl was therefore shown to be similar to its metabolism in wheat in the presence of other chemical safeners. A summary of the identified components in wheat matrices and a proposed metabolic pathway is shown below.

Table 7.2.1.1-13 Summary of components in wheat matrices treated with Fenoxaprop-P-ethyl

Crop	**Wheat (outdoor)**									
Year (Author)	**2012 (Oddy, A.M.)**									
Rate (actual)	**143.3 g a.s./ha**					**149.3 g a.s./ha**				
Label	**[chlorophenyl-^{14}C]**					**[phenoxy-^{14}C]**				
Crop part	**Forage**		**Straw**		**Grain**	**Forage**		**Straw**		**Grain**
PHI (d)	29		106		106	50		134		134
TRR (mg/kg)	**0.657**		**0.181**			**0.899**		**0.202**		
	%	**mg/kg**	**%**	**mg/kg**	Not analysed	**%**	**mg/kg**	**%**	**mg/kg**	Not analysed
Fenoxaprop-P-ethyl (AE F046360)	3.5	0.023	n.d.	n.d.		3.9	0.035	n.d.	n.d.	
Fenoxaprop-P-aicd (AE F088406)	n.d.	n.d.	1.2	0.002		0.7	0.006	1.2	0.002	
Benzoxazolone (AE F054014)	1.8	0.012	0.7	0.001		-	-	-	-	
Conjuagte 1	22.4	0.147	n.d.	n.d.		-	-	-	-	
Conjuagte 2	16.6	0.109	n.d.	n.d.		-	-	-	-	
HOPP acid (AE F096918)	-	-	-	-		5.6	0.051	3.3	0.007	
HOPP acid conjugate	-	-	-	-		26.4	0.238	n.d.	n.d.	
Total identified	**44.3**	**0.291**	**1.9**	**0.003**		**36.6**	**0.33**	**4.5**	**0.009**	
unknown metabolites (characterised by retention times)	-	-	2.0	0.004		4.61	0.041	2.9	0.005	
	-	-	1.6	0.003		1.92	0.017	2.2	0.005	
	-		1.7	0.003		-	-	2.1	0.004	
	4.0	0.026	2.3	0.004		3.98	0.036	3.0	0.006	
	-	-	5.5	0.010		1.75	0.016	1.8	0.004	
	3.2	0.021	4.5	0.008		2.63	0.024	2.5	0.005	
	3.5	0.023	1.3	0.002		2.84	0.026	-	-	
	3.6	0.023	1.9	0.003		1.89	0.017	5.5	0.011	
	2.6	0.017	3.4	0.006		2.82	0.025	-	-	
	3.0	0.019	1.3	0.002		1.31	0.012	1.9	0.004	
	4.0	0.027	-	-		3.13	0.028	1.2	0.002	
	2.1	0.014	-	-		1.0	0.009	-	-	
	1.7	0.011	-	-		1.11	0.010	-	-	
	1.9	0.012	-	-		1.06	0.010	-	-	
	4.0	0.026	4.2	0.008		4.09	0.037	1.9	0.002	
Total characterised	**33.6**	**0.219**	**29.5**	**0.054**		**34.1**	**0.308**	**25.1**	**0.048**	
ERR- Extracted Radioactive Residues	**77.9**	**0.512**	**31.3**	**0.057**		**70.7**	**0.636**	**29.6**	**0.057**	
PES- Post extraction solid	22.1	0.145	68.6	0.124		29.3	0.263	70.4	0.145	

Figure 7.2.1.1-1 **Proposed metabolism pathway of fenoxaprop-P-ethyl in cereals**



B.7.2.1.2. *Metabolism in Wheat - study 2*

Reference:	KCA 6.2.1/04 *Hoe 046360-chlorophenyl-U-^{14}C, Residue Determination in Wheat (triticum aestivum var. Schirokko) after Application of 110g Active Ingredient/ha*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	Wink O., Kuenzler K., Lemke G.; 1987a CMO29/86 / A35778 EPA, 171-4 (October 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

Wheat was treated under outdoor conditions with formulated Hoe 046360-^{14}C (emulsifiable concentrate, EC) by spraying at early tillering stage with **an application rate equivalent to 110 g active ingredient/ha** (~1.3N). Plant samples were taken directly after application and 15, 30, 60 and 109 days after treatment (DAT). In addition, soil samples are taken up to a depth of 25 cm from the plant container at the same dates (except day 60). With sampling at day 60, the wheat plants were separated into shoots and ears and on sampling day 109 also in grain and husks. The fresh weight of the different plant parts was determined directly after sampling. Additional control plants for background determination were kept outside the controlled area but under the same climatic conditions.

Soil samples were taken with the aid of plastic tubes and kept deep frozen until analysis. They were sawn into different sections, which were separately analysed for total radioactivity (TRR) by combustion and liquid scintillation counting (LSC).

Soil samples of one sampling day were pooled, homogenized and then filled in a glass column and extracted with a mixture of acetonitrile:water (8:2, v/v). The extract was then concentrated to near dryness and re-dissolved in methanol. The solution was used for radioactivity measurements (as mentioned above) and for HPLC-analysis.

Findings:

The total radioactive residues (TRR) in wheat decreased from 7.96 mg as equ /kg fresh material directly after spraying (0 DAT) to 0.424 mg as equ /kg fresh material after a month (30 DAT) and to 0.011 mg as equ /kg fresh material (= LOQ) in the straw at harvest (109 DAT); shoots, ears, straw, grains and husks were separately analysed. In all samples the radioactive residues were below the corresponding limits of quantification (LOQ), which extended from 0.011 mg as /kg fresh material in straw to 0.004 mg as/kg in grains. The radioactive concentrations in the control samples were always below the LOQ indicating that no radioactivity was taken up from the air.

In soil samples only the upper 5cm layer contained significant radioactive residues. Directly after treatment an initial radioactivity concentration of 0.078mg as /kg dry soil (0 DAT) was found, which remained nearly constant during the whole testing period up to the day of harvest (DAT 109 = 0.074 mg as /kg dry soil). In the lower layers of soil no radioactivity above the LOQ (0.004 mg as /kg) was found.

Figure 7.2.1.2-1 Total radioactive residues (TRR) in wheat and soil treated with ^{14}C-chlorophenyl-labeled Hoe 046360

Days after treatment (DAT)	Wheat	Total radioactive residue (TRR) mg a.s. equiv./kg	Soil (cm)	Total radioactive residue (TRR) mg a.s. equiv./kg dry soil
0	Whole plant	7.96	0-5	0.078
			5-10	< LOQ
			10-15	< LOQ
			15-19	< LOQ

Days after treatment (DAT)	Wheat	Total radioactive residue (TRR) mg a.s. equiv./kg	Soil (cm)	Total radioactive residue (TRR) mg a.s. equiv./kg dry soil
15	Whole plant	1.11	0-5	0.061
			5-10	< LOQ
			10-15	< LOQ
			15-19	< LOQ
30	Whole plant	0.424	0-5	0.050
			5-10	< LOQ
			10-15	< LOQ
			15-19	< LOQ
60	Shoots Ears	< LOQ < LOQ	n.a.	n.a.
109	Straw Husks Grains	< LOQ < LOQ < LOQ	0-5	0.074
			5-10	< LOQ
			10-15	< LOQ
			15-19	< LOQ

LOQ (wheat plants) : ≤ 0.01 mg/kg DAT= days after treatment n.a. not analysed
LOQ (soil) : < 0.004 mg/kg

Conclusion:

No significant radioactive residues are expected in any part of mature wheat plants after the treatment with Fenoxaprop-P-ethyl (Hoe 046360) at an application rate of 110 g ai/ha.
In soil the application of Hoe 046360 according to agricultural practice showed that in the upper layers (0-5cm) radioactive residues < 0.1 mg as /kg dry soil were determined at a nearly constant level at all sampling times. In lower soil layers no radioactivity above the LOQ (0.004 mg/kg) was determined. Consequently, application of Hoe 046360 in wheat according to agricultural practice does not lead to soil-residues above 0.1 mg/kg even directly after spraying.

B.7.2.1.3. *Metabolism in Wheat - study 3*

Reference:	KCA 6.2.1/12 *Identification of Residues in Wheat (triticum aestivum var. Ralle) Following Treatment with ^{14}C-Fenoxaprop-P-ethyl (Hoe 046360-chlorophenyl-U-^{14}C) at a Rate of 90 g as /ha*
Author(s), year:	Buerkle L.W.; 2000e
Report/ Doc. Number:	CM96/137/ C009798
Guideline(s):	Not reported
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study only developed qualitative results. No quantitation. However the study is considered applicable to provide the required information.

As residues at regular harvest samples were determined to be extremely low and exaggerated rates to produce higher residues are not possible (because of the phytotoxicity of the compound) this short term study was performed to determine the nature of residues in young cereals in the presence of the safener mefenpyr-diethyl and to identify an additional hydrolysis product.

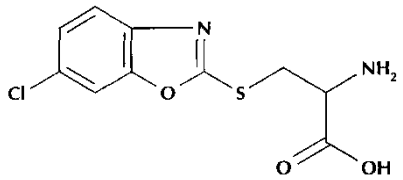
Material and Methods:

Young wheat plants, were treated at the three leaf growth stage by spraying the formulated (oil-in-water, EW) ^{14}C-labeled Hoe 046360 (Figure 7.2.1.1-1) at an **application rate of 90 g as/ha** (~1N) in the presence of the non labeled safener Mefenpyr-diethyl (Hoe 107892, Figure 7.2.1.1-4), which protects the crop against phytotoxic effects of the herbicide. The ratio of active substance to safener was 1:1 (w/w).
One day and seven days after growth in a greenhouse, the plants were harvested and extracted with a mixture of acetonitrile/water (4/1, v/v), 95 - 98 % of the total radioactive residues (TRR) could be extracted indicating an almost complete extraction efficiency and an acceptable repeatability in parallel extractions. After a solid phase extraction (using a SePak-C18 cartridge), the purified extracts were hydrolysed with 12N hydrochloric acid (4 hr, 70°C) followed by a partition between ethyl acetate and the acidified water. The resulting fractions were analysed for composition by HPLC using UV- and flow-through radio-detection techniques. In addition, HPLC/MS coupling techniques were applied to identify the major components formed after acidic hydrolysis. Co-elution of authentic reference standard material was used for the identification of the components however no quantification of the identified metabolites was reported. The measurements of ^{14}C- total radioactivity in the different fractions were carried out by LSC (liquid scintillation counting).

Findings:

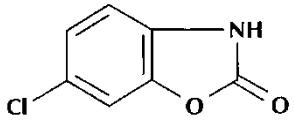
Approximately 36 % of the radioactivity in the original extract could be recovered in the organic phase and 56 % in the aqueous phase resulting in a total recovery of 92 %. Radio-HPLC analysis showed one predominant residue peak in each of the two phases, respectively. The peak in the organic phase was identified as 6-chloro-2,3-dihydro-benzoxazol-2-one (AE F054014). The peak in the aqueous phase was identified by HPLC/MS/MS and chromatographic and mass spectroscopic comparison of the reference standard AE 0417066 as a hydrolytically stable conjugate between AE F054014 and cysteine, i.e. 2-amino-3-(6-chlorobenzoxazol-2-ylthio)propionic acid (= AE 0417066). Residues in the original extract, before hydrolysis, were tentatively identified as complexer conjugates consisting of AE 0417066 and endogenic plant compounds, e.g. glucose.

Figure 7.2.1.3-1 Benzoxalone-cystein conjugate (AE 0417066)



$C_{10}H_9ClN_2O_3S$ MW= 272.71 g/ml

Figure 7.2.1.3-2 Chlorobenzoxazolone (AE F054014)



$C_7H_4Cl\ NO_2$ MW= 169.57 g/ml

The cysteine conjugates were formed by conjugation of fenoxaprop-ethyl with glutathione (GSH). The benzoxazole-cysteine conjugate appeared as main metabolite in the rat in its acetylated form as mercapturic acid AE F069225. It was thus toxicologically evaluated within toxicological studies in rats with administration of the parent substance.

Conclusion:

Young wheat plants were treated with formulated ^{14}C- labeled Fenoxaprop-P-ethyl at a nominal application rate of 90 g as/ha in combination with the non-labeled safener Mefenpyr-diethyl (Hoe 107892, Figure 7.2.1.1-4). Fenoxaprop-P-ethyl (Hoe 046360,) is quickly metabolised in wheat plants to the Fenoxaprop-P (Hoe 088406). Already one day after treatment a qualitative metabolite pattern in the HPLC-chromatograms (using UV- and ^{14}C-detection) was observed showing amounts of the active substance Hoe 046360 without any further identification of the other components. Seven days after treatment, there was a tendency to a simpler residue pattern showing only a small amount of Hoe 046360 and two major metabolites, which were not identified within the chromatograms. Acidic hydrolysis delivered the metabolites chlorobenzoxazolone (Hoe 054014),

formed by phenyl ether cleavage, and a conjugate between the benzoxazolone and cystein identified as Hoe 0417066. No quantification was performed.

B.7.2.1.4. *Metabolism in Wheat - study 4*

Reference:	KCA 6.2.1/08 *Hoe 33171-^{14}C (Fenoxaprop-ethyl), Residue Determination in Wheat (triticum aestivum) after Application of 183 g Active Ingredient/ha in presence of Hoe 070542*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	Schwalbe-Fehl M., Schmidt E., Koecher H.; 1986a CM032/86 I/A34525 EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

Wheat plants were treated under outdoor conditions with formulated Hoe 033171-^{14}C (oil-in water-emulsion) by spraying at early tillering stage with **an application rate equivalent to 183 g as/ha** (~2.2N) in combination with the non-labeled safener fenchlorazol-ethyl Hoe 070542 (46 g/ha). Plant samples were taken directly after spraying and 10, 37, 59, 83 and 91 days after treatment (DAT). In addition, soil samples were taken up to a depth of 25 cm from the plant container on day 0, 37, 38, 59 and 91 days after treatment. With sampling day 59 the wheat plants were separated into shoots and ears. On day 83 and 91 after treatment the plants were divided into straw, grain and husk. The fresh weight of the different plant parts was determined directly after sampling. Additional control plants for background determination were kept outside the controlled area but in the same soil and under the same climatic conditions.
Samples of wheat straw at harvest (91 DAT) were used for the characterisation of the radioactive residues. The samples were refluxed using a mixture of ethanol/hydrochloric acid or acetonitrile/hydrochloric acid, respectively. After filtration and clean-up steps followed a derivatisation to the acetylated derivate of Hoe 054014, which then could be quantified by GC. For determination of the radioactivity distribution throughout the soil depth, soil samples were taken with the aid of plastic tubes and kept deep frozen until analysis. They were sawn into different sections and separately analysed for total radioactivity (TRR) by combustion and liquid scintillation counting (LSC).

Findings:

Radioactivity concentrations in the whole wheat plants decreased from 20.9 mg as-equ/kg fresh weight on day 0 to 0.052 mg as-equ/kg on day 37 after treatment. At harvest (91 DAT), for straw a value of 0.087mg as-equ/kg was determined, whereas the radioactive concentration in wheat grain was below the LOQ (0.001 mg as-equ/kg). In soil samples only the upper 5 cm layer contained significant radioactive residues. Directly after treatment an initial radioactivity concentration of 0.091 mg as-equ/kg on day 0 was found, which decreased to 0.035 mg as-equ/kg at harvest (91 DAT). In the lower layers of soil no radioactivity above the LOQ (0.004 mg as /kg) was found. Therefore Hoe 033171 and its degradation products are considered to be immobile and not to leach to soil layers deeper than 5 cm. The results are summarised in the table below.

Table 7.2.1.4-1 Total radioactive residues (TRR) in wheat and soil treated with ^{14}C-chlorophenyl-labeled Hoe 033171. Values are given as mg a.s. equivalents in the fresh weight and dry soil, respectively

Total radioactive residues	0 DAT mg/kg	10 DAT mg/kg	37 DAT mg/kg	59 DAT mg/kg	83 DAT mg/kg	91 DAT mg/kg
Whole plant	20.9	2.5	0.052	n.a.	n.a.	n.a.
Shoots				0.007	0.029	n.a.
Ears				< LOQ	n.a.	n.a.
Husk					< LOQ	< LOQ
Straw					**n.a.**	**0.087**
Grain					**< LOQ**	**< LOQ**

Total radioactive residues	0 DAT mg/kg	10 DAT mg/kg	37 DAT mg/kg	59 DAT mg/kg	83 DAT mg/kg	91 DAT mg/kg
Soil 0-5 cm	0.091		0.086	0.076		0.035
Soil 5-10 cm	< LOQ		< LOQ	< LOQ		< LOQ
Soil 10-15 cm	< LOQ		< LOQ	< LOQ		< LOQ
Soil 15-20 cm	< LOQ		< LOQ	< LOQ		< LOQ
Soil 20-25 cm	< LOQ		< LOQ	< LOQ		< LOQ

LOQ < 0.004 mg/kg

Conclusion:

The study should provide data concerning the estimate of total residues of Hoe 033171-^{14}C in treated wheat plants and the distribution of radioactive residues in the different plant parts and in soil. Wheat plants were treated at an application rate of 183 g ai/ha in combination with the safener Hoe 070542 (fenchlorazol-ethyl). Most varities of wheat are susceptible to the herbicide Hoe 033171 (fenoxaprop ethyl), therefore the addition of the safener Hoe 070542 is necessary to achieve better crop tolerance. The influence of the safener was not elucidated. The radioactive residues in harvest crops were low (grains <0.001 mg active ingredient equivalents/kg; husks 0.003 mg a. i.equiv./kg; straw 0.087 mg a.i. equiv./kg), so no metabolite identification was possible. Metabolism was therefore investigated in separate studies in which immature wheat shoots with higher radioactive residues were sampled and processed (see B.7.2.1.5).

In soil the application of Hoe 033171 showed residues < 0.1 mg ai/kg dry soil at all sampling dates in the upper layers (0-5 cm). In lower soil layers no radioactivity above the LOQ (0.004 mg/kg) was determined. Thus the active substance Hoe 033171 and its metabolites are regarded as immobile with no tendency to leach in deeper soil layers.

B.7.2.1.5. *Metabolism in Wheat - study 5*

Reference:	KCA 6.2.1/03 *Hoe 033171-^{14}C, Metabolism and Degradation Kinetics in Wheat (triticum aestivum var. Schirokko)* KCA 6.2.1/10 *Hoe 033171-^{14}C, Metabolism and Degradation Kinetics in Wheat (triticum aestivum var. Schirokko) in presence of Hoe 070542*
Author(s), year: Report/ Doc. Number:	Schwalbe-Fehl M., Schmidt E., Koecher H.; 1987b CM033/86 I/A36855 CM033/86 II/A37400
Guideline(s): GLP:	EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	the study is considered applicable to provide the required information.

Material and Methods:

Wheat shoots were treated under outdoor conditions with Hoe 033171-^{14}C (Fenoxaprop-ethyl) formulated as emulsifiable concentrate by spraying at **an application rate equivalent to 180 g as/ha** (~2.2N) at early tillering stage in absence and in presence of the non-labeled safener Hoe 07542 (fenchlorazole-ethyl). Aliquots of the treated shoots were taken 2, 4, 21, 27 and 96 hours (Part II) and 10 days (Part I) after treatment. Part II is a study conducted in order to support and validate the results of the study Part I (which took place previously). The plants were treated in the same way but sampled at earlier sampling times. The sample workup started first by a rinse of the shoots surface (**fraction A**) with diethylether followed by several extraction procedures with acetonitril/water (80:20) resulting in **fraction B** (rinsed shoots). Aliquots of the extracted solid residue (fraction C) were used for the remaining "bound" radioactivity. The crude extracts (fraction D) were concentrated and partitioned between ethylacetate and water resulting in an aqueous extract (**fraction E**) and an organic extract (fraction F). Radioactive compounds present in the surface rinses, organic extracts and aqueous fractions were separated and identified by radio-HPLC with two different systems as well as by TLC by using authentic reference compounds for identification of the metabolites.

Additionally aliquots of the extracted solid residue (**Fraction C**) of the 96hours and 10-day samples were hydrolysed with hydrochloric acid (conc. hydrochloric acid/water 1:1, v/v) for 4 hours under reflux and analysed by HPLC.

Aliquots of fraction E (aqueous extract) and fraction F (organic extract) of the 27-hours and 10-days samples were also hydrolysed with hydrochloric acid (conc HC1/water 1:1, v/v) for 2 hours under reflux. The resulting solution was diluted with a mixture of acetonitrile/water (80:20, v/v) and directly analysed by HPLC (Fraction E). Fractions F were extracted three times with acetic acid ethylester after hydrolysis; the organic extract was afterwards concentrated and investigated by HPLC.

Findings without safener

Total radioactive concentration in the intact wheat shoots was 20.7 mg a.i. equiv./kg directly after application (day 0) decreasing within 96 hours to 11.3 mg a.i. equiv./kg. Total radioactive concentration 10 days after application was 9.7 mg a.i. equiv./kg.

In the **rinse of plant surfaces** (Fraction A) Hoe 033171 was the only significant component, the amount decreased from 56.2 % of TRR after 2 hours to 6.8 % after 96 hours. More than 95 % of the total radioactivity of Fraction A consisted of Hoe 033171. After 10 days, under the test conditions of part I of the study, 36.3 % Hoe 033171 were detected in the rinse Fraction A. This indicated a lower uptake and metabolisation. The significant difference between part I and part II was considered to be caused by a different metabolic activity in the wheat plants due to the lower temperature (19°C) during the course of part I.

In the **aqueous fractions (Fraction E)** the chlorobenzoxazolone (Hoe 054014) and three additional polar metabolites (M1, M2, M3) were detected. The presence of Hoe 054014 in the aqueous extract, which is

extractable with acetic acid ethylester and therefore should only be found in the organic extract, must be considered as the result of partial degradation of polar metabolites. One of them (M2) was present up to 11.2 % after 96 hours.

In the **organic extracts (Fraction F)** the free acid Hoe 053022 (Fenoxaprop) and Hoe 054014 (chlorobenzoxazolone) have been identified as the main degradation products, which were formed after the cleavage of heterocyclic ether bond. The amount of the free acid Hoe 053022 decreased from 28.8 % of TRR after two hours to 13.3 % after 96 hours, at this time only 0.3 % of intact Hoe 033171 could be detected. The amount of Hoe 054014 was low at the beginning with 5.9 % of TRR after 2 hours, reaching a maximum after 27 hours with 24.2 % of TRR. The results of the distribution of the radioactive residues in different fractions are summarized in the table below.

Table 7.2.1.5-1 Distribution and of radioactive residues in wheat shoots treated with ^{14}C-chlorophenyl-labeled Hoe 033171. Values are given as mg a.s. equivalents in the fresh weight and % of TRR (without safener).

	2 hours		4 hours		21 hours		27 hours		96 hours		10 days#	
	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg
Total radioactive residue	**100**	15.3	**100**	17.3	**100**	13.5	**100**	14.7	**100**	11.3	**100**	9.7
Fraction A (surface rinse)	**56.2**	8.6	**48.1**	8.3	**23.1**	3.1	**18.1**	2.7	**7.9**	0.9	**37.8**	3.6
Hoe 033171(parent)	56.2	8.6	47.6	8.2	22.4	3.0	16.7	2.5	6.8	0.8	36.3	3.5
Fraction B (rinsed shoots)	**43.8**	6.7	**51.9**	9.0	**76.9**	10.4	**81.9**	12.0	**92.1**	10.4	**62.2**	6.0
Fraction E (aqueous extract)	**0.5**	0.08	**0.8**	0.1	**7.8**	1.1	**12.6**	1.8	**30.4**	3.4	**21.2**	2.0
M1	n.d.	n.d.	n.d.	n.d.	1.8	0.25	2.8	0.4	6.4	0.7	3.0	0.3
M2	n.d.	n.d.	0.1	0.01	3.0	0.4	4.1	0.6	11.2	1.3	11.8	1.1
M3	0.5	0.08	0.6	0.08	1.2	0.2	2.3	0.3	4.2	0.5	3.4	0.3
Hoe 054014 (benzoxazole)	n.d.	n.d.	0.1	0.01	1.8	0.25	3.4	0.5	8.6	1.0	3.0	0.3
Fraction F (organic extract)	**41.8**	6.4	**44.1**	7.6	**54.6**	7.4	**44.8**	6.6	**24.9**	2.8	**21.5**	2.1
Hoe 033171(parent)	7.1	1.1	4.5	0.8	2.3	0.3	2.1	0.3	0.3	0.03	9.0	0.9
Hoe 053022 (acid)	28.8	4.4	24.3	4.2	31.4	4.3	18.4	2.7	13.3	1.5	7.9	0.8
Hoe 054014 (benzoxazole)	5.9	0.9	15.3	2.6	20.9	2.8	24.2	3.6	11.3	1.3	4.6	0.4
Non extractable residues	0.7	0.1	1.4	0.2	5.8	0.8	6.8	1.0	15.3	1.7	2.4	0.2
Recovery	**99.2**	15.2	**93.9**	16.1	**90.6**	12.2	**80.8**	11.9	**77.4**	8.7	**81.4**	7.9

#...values of a previously conducted study (Part I)

Characterization of the radioactive residues after acidic hydrolysis

The amount of the **non extractable residues** was low at the beginning (0.7 %), but increased up to 15.3 % after 96 hours. These residues could partially be released by acidic hydrolysis with hydrochloric acid. The main product of hydrolysis was Hoe 054014.

After hydrolysis 64.1% and 68.4% of the radioactivity was released for the 96 hour sample and the 10-day sample, respectively. Characterisation by HPLC showed 66% Hoe 054014 in the 96-hour sample and 39% in 10-day sample. A second radioactive peak showed the same chromatographic behaviour as Hoe 064124, a hydroxylated chlorobenzoxazolone, but was not definitely identified.

The amount of Hoe 054014 (benzoxazolone) increased after hydrolysis of the aqueous extract (fraction E) from 28% in the 27 hour sample to 52% and from 14% in the 10-days sample to 40%. The amount of Hoe 054014 after hydrolysis, however, could not be explained only by a cleavage of Ml, because the sum of Ml and Hoe 054014 prior to hydrolysis was smaller than the amount of Hoe 054014 after hydrolysis. Partial degradation of M2 and/or M3 to Hoe 054014 was therefore assumed.

Hoe 054014 (benzoxazolone) was the only detectable radioactive compound in the organic extract (fraction F) after hydrolysis. Recoveries amounted to 87 % (27 hours sample) and 90 % (10 days sample), respectively. Consequently, the radioactivity of the organic extract can be converted almost quantitatively to Hoe 054014 after acidic hydrolysis.

Findings in presence of the safener Hoe 07542 (fenchlorazole-ethyl)

Total radioactive concentration in the intact wheat shoots was 26.0 mg a.i. equiv./kg directly after application (day 0) decreasing within 96 hours to 14.2 mg a.i. equiv./kg. Total radioactive concentration 10 days after application was 6.3 mg a.i. equiv./kg.

In the **rinse of plant surfaces** (Fraction A) Hoe 033171 was the only significant component, the amount decreased from 42.2 % of TRR after 2 hours to 2.9 % after 96 hours. These results indicate a rapid penetration of Hoe 033171 into the wheat shoots. The amount of penetrated parent compound seemed to be dependent on the climatic conditions and the overall metabolic activity, because the 10 days sample which was taken in a separate part of the study (Part I) at lower temperatures (19°C) showed considerably lower uptake and metabolization of Hoe 033171 (11% TRR).

In the **aqueous fractions (Fraction E)** the chlorobenzoxazolone (Hoe 054014) and three additional polar metabolites (M1, M2, M3) were detected. The presence of Hoe 054014 in the aqueous extract, which is extractable with acetic acid ethylester and therefore should only be found in the organic extract, must be considered as the result of partial degradation of polar metabolites. One of them (M2) was present up to 16 % after 96 hours.

In the **organic extracts (Fraction F)** the free acid Hoe 053022 (Fenoxaprop) and Hoe 054014 (chlorobenzoxazolone) have been identified as the main degradation products, which were formed after the cleavage of heterocyclic ether bond. This was proved by two different HPLC systems as well as by the use of TLC with three different developing systems. In every case, the fortifications with the authentic reference compounds confirmed the identity of the determined metabolite.

The amount of the free acid Hoe 053022 decreased from 26.3 % of TRR after 2 hours to 5.5 % after 96 hours, at this time 1.5 % of intact Hoe 033171 could be detected. The amount of Hoe 054014 reached a maximum of 27.2 % TRR after 4 hours. The results of the distribution of the radioactive residues in different fractions are summarized in the table below.

Table 7.2.1.5-2 Distribution and of radioactive residues in wheat shoots treated with ^{14}C-chlorophenyl-labeled Hoe 033171. Values are given as mg a.s. equivalents in the fresh weight and % of TRR (with safener).

	2 hours		4 hours		21 hours		27 hours		96 hours		10 days#	
	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg	TRR (%)	mg/ kg
Total radioactive residue	**100**	24.6	**100**	19.6	**100**	19.0	**100**	17.4	**100**	14.2	**100**	6.3
Fraction A (surface rinse)	**44.1**	10.8	**35.7**	7.0	**14.7**	2.8	**12.0**	2.1	**3.1**	0.4	**11.8**	0.7
Hoe 033171(parent)	42.0	10.3	34.5	6.8	13.8	2.6	12.0	2.1	2.9	0.4	11.1	0.7
Fraction B (rinsed shoots)	**55.9**	13.8	**64.3**	12.6	**85.3**	16.2	**88.0**	15.3	**96.9**	13.8	**88.2**	5.6
Fraction E (aqueous extract)	**0.7**	0.2	**3.6**	0.7	**22.6**	4.3	**24.8**	4.3	**36.3**	5.2	**49.0**	3.1
M1	n.d.	n.d.	0.5	0.1	4.0	0.8	3.3	0.6	8.4	1.2	14.6	0.9
M2	n.d.	n.d.	0.4	0.1	10.0	1.9	11.5	2.0	16.0	2.3	22.6	1.4
M3	0.7	0.2	2.4	0.5	4.8	0.9	6.0	1.0	4.6	0.7	5.2	0.3
Hoe 054014 (benzoxazole)	n.d.	n.d.	0.3	0.1	3.8	0.7	4.0	0.7	7.3	0.1	6.6	0.4
Fraction F (organic extract)	**48.1**	11.8	**49.6**	9.7	**28.0**	5.3	**29.5**	5.1	**14.4**	2.0	**10.5**	0.7
Hoe 033171(parent)	4.0	1.0	4.8	0.9	1.4	0.3	0.8	0.1	1.5	0.2	3.2	0.2
Hoe 053022 (acid)	26.3	6.5	17.6	3.4	21.6	4.1	14.9	2.6	5.5	0.8	3.2	0.2
Hoe 054014 (benzoxazole)	17.9	4.4	27.2	5.3	5.0	1.0	13.8	2.4	7.4	1.1	4.0	0.3
Non extractable residues	1.5	0.4	2.5	0.5	12.6	2.4	14.6	2.5	25.3	3.6	11.4	0.7
Recovery	**92.4**	22.7	**90.2**	17.7	**77.0**	14.6	**80.9**	14.1	**78.9**	11.2	**81.9**	5.2

#...values of a previously conducted study (Part I)

Characterization of the radioactive residues after acidic hydrolysis

The amount of the **non extractable residues** was low at the beginning (1.5 %), but increased up to 25.3 % after 96 hours and could partially be released by acidic hydrolysis. The main product of hydrolysis was Hoe 054014.

After hydrolysis of solid residues a radioacticty of 33.7 % (corresponding to 8.5% of the total radioactivity) and 17.2 % (corresponding to 2% of the total radioactivity), respectively was released for the 96 hour sample and the 10-day sample, respectively. Characterisation by HPLC showed 82 % Hoe 054014 in the 96-hour sample and 50 % in 10-day sample. A second radioactive peak showed the same chromatographic behaviour as Hoe 064124, a hydroxylated chlorobenzoxazolone, but was not definitely identified.
Hoe 054014 (benzoxazolone) was the only detectable radioactive compound in the organic extract (fraction F) after hydrolysis. Recoveries amounted to 96 % (27 hours sample) and 93 % (10 days sample), respectively. Consequently, the radioactivity of the organic extract can be converted almost quantitatively to Hoe 054014 after acidic hydrolysis.
The amount of Hoe 054014 (benzoxazolone) increased after hydrolysis of the aqueous extract (fraction E) in the 27 hour sample from 16 % to 35 % and in the 10-days sample from 13 % to 35 %. The identity of Hoe 054014 was confirmed by spiking the original sample with the non-labeled reference compound and subsequent HPLC analyses. The rest of the radioactivity in the hydrolyzed fractions was present as several additional peaks. No radioactivity corresponding to Ml could be detected. The amount of Hoe 054014 after hydrolysis, however, could not be explained only by a cleavage of Ml, because the sum of Ml and Hoe 054014 prior to hydrolysis was smaller than the amount of Hoe 054014 after hydrolysis. Partial degradation of M2 and/or M3 to Hoe 054014 was therefore assumed.

Conclusion:

No metabolite identification was possible due to the low radioactive residues at harvest in grain with < 0.001 mg ai-equiv/kg, husks with 0.003 mg ai-equ /kg and in straw with 0.087 mg ai-equ /kg (see B.7.2.1.4).
Therefore a metabolism study investigating immature wheat shoots was provided. The results showed that the racemic compound Hoe 033171 is rapidly metabolized within a few days after treatment via ester hydrolysis to the free Fenoxaprop Hoe 053022. Subsequent cleavage of the benzoxazolyloxy-linkage resulted in forming Hoe 054014, which is the basic structure to be determined in the routine analytical analysis. The metabolic behaviour of ^{14}C- Hoe 033171 (fenoxaprop ethyl) in wheat was shown to be independent from the presence of a safener. Non extractable residues in the extracted wheat shoots were low in the beginning (0.7 % TRR and 1.5% TRR, respectively) but increased up to 15.3 % and 25.3%, respectively after 96 hours and could partially be released by acidic hydrolysis mainly as Hoe 054014. The aqueous fractions contained Hoe 054014 and three different polar degradation products (M1, M2, M3). These products remained unidentified due to their polar character and due to the limited amounts available. Characterisation attempts of the degradation products by means of Thermos-spray-HPLC are elucidated in a separate study following below.

Reference:	KCA 6.2.1/09 *Identification and characterisation of the water-soluble conjugates in wheat*
Author(s), year:	Wink, O., Kuenzler K., Wuerz S.; 1987a
Report/Doc. Number:	(B) 150/87 / A36657
Guideline(s):	EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)**
Deviations from OECD Guideline 501	The study is a special study and supplements additional information to the aqueous metabolites M1 M2 and M3 found with study CM033/86 I. The study is strongly connected to study CM033/86 I and guideline EPA Pesticide Assessment Guidelines, Subdivision 0: Residue Chemistry, reference number § 171-4 (October 1982) does also apply to this part of the investigations.
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

Shoots were excised from wheat plants at the three leaf stage, incubated with Hoe 033171-^{14}C for 2 days and extracted with acetonitrile/water (80:20, v/v). The extract was concentrated and following by extraction with acetic ethylester. The organic phase was not further investigated. The aqueous phase was concentrated under reduced pressure and used for the semipreparative isolation of the water-soluble conjugates for structure elucidation. Comparative HPLC-analysis of aqueous extracts from whole plants and from excised shoots showed identical metabolite patterns.

The polar metabolites were separated and concentrated by means of a semi-preparative HPLC. The isolated compounds were subjected to hydrolysis and derivatisation experiments. In addition the separated metabolites and their derivatives were investigated by HPLC/MS coupling using Thermospray techniques. A number of synthetic reference substances were investigated by thermospray under the same conditions to obtain a satisfactory data base for interpretation of the results.

Findings:

For M-1, efforts did not result in interpretable MS-spectra, but data suggested an alteration in benzoxazole moiety.
The structure of M-2 is probably made up by a reduction at the double bond in the heterocyclic ring and was proposed to be conjugated via sulphur bridge to an altered homoglutathione group. In addition the nitrogen of the reduced benzoxazol ring was further conjugated to a cysteine amino acid. M-3 was unequivocally identified to be the gamma-glutamylcysteine conjugat of Hoe 054014. This conjugate was quantitatively cleavable to Hoe 054014 by acidic hydrolysis.

Figure 7.2.1.5-1 Proposed structure of Conjugate M-2

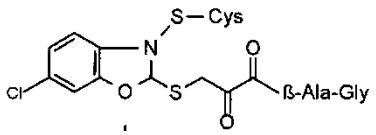
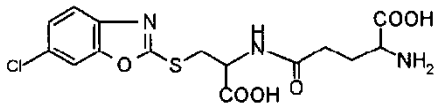


Figure 7.2.1.5-2 Proposed structure of Conjugate M-3



Conclusion:

Besides Fenoxaprop (Hoe 053022) and the chlorobenzoxazolone metabolite Hoe 054014, three further metabolites (M1 to M3) were observed in the study on wheat metabolism before. The objective of this study was the elucidation of the structure of the three polar metabolites M1, M2, M3, identified in the aqueous fraction.
Mass production of the conjugates for structure elucidation was carried out by means of excised wheat shoots which were incubated with Hoe 033171 -^{14}C. For the conjugates M2 and M3 a structure was proposed, for the conjugate M1 no interpretable mass spectrum was obtained, but data suggested an alteration in the benzoxazole moity. The results indicate that the dominant route of detoxification of Hoe 033171 in wheat was via the conjugation with glutathione and subsequent biochemical alterations of the conjugates.

B.7.2.1.6. *Metabolism in Barley*

Reference:	KCA 6.2.1/02 *Influence of the safener Hoe 107982 on the metabolism of the radiolabeled Herbicide Fenoxaprop-P-ethyl, Hoe 046360, in Barley*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	Buerkle W.L., Becker A.; 1997a CM92/102/A58851 EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The lack of quantified results is a deficiency in the study. No quantification of the individual compounds was presented in the report. However the study is considered applicable to provide the required information.

Material and Methods:

One part of the investigations was carried out with a **"bouquet test"**, e.g. freshly cut barley shoots (at 2-leaf stage) were put with their bottom into two nutrient solutions, one contained the herbicide Fenoxaprop-P-ethyl Hoe 046360 (Figure 7.2.1.1-1) only, the other contained the herbicide and the unlabeled safener Mefenpyr-diethyl Hoe 107982 (Figure 7.2.1.1-4). The ratio of active substance to safener was 1:1 by weight. The plants were incubated at room temperature and admission of daylight and analysed after 2, 4, 6, 24, 48, 72 and 144 hours. The shoots were rinsed with water directly after taking out of the nutrient solution, chopped and then extracted with a mixture of acetonitrile/water (4/1, v/v). The concentrated extract as well as the nutrient solution was analysed by radio-HPLC, the radioactivity of the non-extractable residues was determined by combustion and LSC (liquid scintillation counting).
The other part of investigations was carried out with a **"flower-pot test",** where young intact barley shoots at the 2-3 leaf stage were treated with the radiolabeled herbicide at a nominal rate of 90 g as /ha by spraying using a graphic spray gun (Grafo Type IV) in two parallel sets, one in absence and the other in presence of the safener. The plant pots remained in the greenhouse until sampling 3, 23, 47, 71 and 141 hours after spraying. The shoots were cut off directly above ground and shortly dipped into diethylether to remove radioactivity from the surface. After the determination of the fresh weight, the shoots were extracted three times with a mixture of acetonitrile/water (4/1, v/v) and then the phases were separated by centrifugation. The radioactivity of all liquid fractions (rinse liquids, extracts and the combined supernatant solutions) and the remaining solid plant material were analysed for the composition of the radioactive compounds by radio-HPLC and to some extent additionally by radio-TLC.

Findings:

For the **"bouquet test"** the presence of the safener resulted in a higher uptake of the extractable radioactivity within the first two hours but at the end of the incubation time (after 144 hours) approximately the same level as in the set without the safener was reached. After 144 hours, the extractable radioactivity reached a maximum of 41 mg as-equ /kg fresh weight (without safener) and 39.5 mg as-equ /kg (with safener), the non-extractable radioactivity reached values of 3.4 and 3.9 mg as-equ/kg fresh weight, respectively. The results are shown in the tables below.

Table 7.2.1.6-1 Total radioactive residues (TRR) in barley treated with ^{14}C-chlorophenyl-labeled Hoe 046360 (without safener)

Incubation interval	Extracted radioactivity		Non extracted radioactivity	
[h]	[mg equ/kg]	[% of TRR*]	[mg equ/kg]	[% of TRR]
2	6.7	**98.9**	0.1	**1.1**
4	28.1	**99.8**	0.1	**0.2**
6	22.0	**99.2**	0.2	**0.8**
24	20.9	**98.8**	0.3	**1.2**
48	34.6	**98.7**	0.4	**1.3**
72	30.1	**96.7**	1.0	**3.3**
144	41.0	**92.3**	3.4	**7.7**

*…TRR= total radioactive residue (sum of extracted and non-extracted radioactivity)

Table 7.2.1.6-2 Total radioactive residues (TRR) in barley treated with ^{14}C-chlorophenyl-labeled Hoe 046360 with safener Hoe 107892 (Mefenpyr-diethyl)

Incubation interval	Extracted radioactivity		Non extracted radioactivity	
[h]	[mg equ/kg]	[% of TRR*]	[mg equ/kg]	[% of TRR]
2	21.2	**98.4**	0.3	**1.6**
4	49.9	**99.3**	0.4	**0.7**
6	29.9	**99.0**	0.3	**1.0**
24	26.2	**98.7**	0.3	**1.3**
48	40.6	**98.3**	0.7	**1.7**
72	32.1	**96.1**	1.3	**3.9**
144	39.5	**91.0**	3.9	**9.0**

*…TRR= total radioactive residue (sum of extracted and non-extracted radioactivity)

In both sets the active substance decreased with time, but still appeared at the end of the incubation time (after 144 hours) and was gradually hydrolysed to Fenoxaprop-P Hoe 088406. There were also formed three polar metabolites, one of them was assigned by co-elution to a mercapturic acid derivate of chlorobenzoxazolone (Hoe 069225). However, there was no significant difference either in the fractionation of the radioactivity or in the metabolic behaviour between plants treated in the presence of a safener or without.

Additionally a **"flower-pot test"** was subsequently conducted. The plant samples were worked-up by two successive steps consisting of a rinsing and an extraction step with an aqueous organic solvent. The rinsed radioactivity decreased from 4.9 to 0.5 mg equ/kg (without safener) and from 7.9 to 1.2 mg equ/kg (with safener), respectively, 141 hours after treatment (last sampling time). The extractable radioactivity reached values from 10.3 mg equ/kg (without safener) to 8.3 mg equ/kg (with safener) after 23 hours followed by a gradual decrease to 8.9 mg equ/kg (without safener) and 5.5 mg equ/kg (with safener) 141 hours after treatment. In each case more then 60 % of TRR were extractable. The portion of the non-extractable residues slowly increased from 0.2 to 2.2 mg equ/kg (without safener) and from 0.1 to 0.9 mg equ/kg (with safener) corresponding to 18.8 % of the TRR (without safener) and 12.2 % of the TRR (with safener). The results are shown in the tables below.

Table 7.2.1.6-3 Total radioactive residues (TRR) in barley treated with 14C-chlorophenyl-labeled Hoe 046360 without safener

Incubation interval	Rinsed radioactivity	Extracted radioactivity		Non extracted radioactivity	
[h]	[mg equ/kg]	[mg equ/kg]	[% of TRR*]	[mg equ/kg]	[% of TRR]
3	4.9	6.9	**57.9**	0.2	**1.3**
23	1.3	10.3	**83.8**	0.7	**5.8**
47	0.8	10.2	**83.4**	1.2	**9.8**
71	1.0	9.7	**77.9**	1.7	**13.7**
141	0.5	8.9	**76.9**	2.2	**18.8**

*…TRR= total radioactive residue (sum of extracted and non-extracted radioactivity)

Table 7.2.1.6-4 Total radioactive residues (TRR) in barley treated with ^{14}C-chlorophenyl-labeled Hoe 046360 with safener Hoe 107892 (Mefenpyr-diethyl)

Incubation interval	Rinsed radioactivity	Extracted radioactivity		Non extracted radioactivity	
[h]	[mg equ/kg]	[mg equ/kg]	[% of TRR*]	[mg equ/kg]	[% of TRR]
3	7.9	4.4	**35.4**	0.1	**0.6**
23	3.3	8.3	**67.8**	0.7	**5.5**
47	1.7	7.4	**73.9**	0.9	**9.1**
71	1.7	7.3	**72.6**	1.0	**10.4**
141	1.2	5.5	**72.2**	0.9	**12.2**

*…TRR= total radioactive residue (sum of extracted and non-extracted radioactivity)

No difference was observed for the distribution of radioactivity between extractable and non-extractable residues for plants treated with or without safener. A comparison of the metabolic behaviour based on the chromatograms submitted, showed that in the absence of a safener unchanged Hoe 046360 could be still observed after 141 hours (end of the incubation). In presence of a safener, there was no amount of Hoe 046360 in the last sampling portion. In both cases, Hoe 088406 (Fenoxaprop-P) was formed as the main product of conversion of the active substance. In addition further metabolites have been detected, the mercapturic acid derivate Hoe 069225 and other polar metabolites consisting of conjugated material. The major portion of the conjugates could be hydrolysed by aqueous acidic treatment into the chlorobenzoxazolone Hoe 054014.

Conclusion:
Details on the fenoxaprop-ethyl metabolism are expected to be only observed within a relatively short time interval after treatment. Thus short-term model studies, the bouquet test and the flower-pot test, were conducted which more likely allow an insight into the safener's influence on the metabolism of the herbicide Hoe 046360.
The bouquet test consisted of young excised barley shoots which were placed into two beakers containing a nutrient solution and the radiolabelled test substance Hoe 046360. The non-labelled safener Hoe 107892 (Mefenpyr-diethyl) was added to one of two beakers. In the second study design, the flower-pot test, young barley shoots grown in flower-pots were sprayed with test substance, the non-labelled safener was added to one of the two series.
Both tests showed that the metabolic behaviour in barley shoots was independent from the presence or absence of the safener. The identity of the residue components in barley is not changed due to the action of the safener, as the same metabolite peaks were observed in the radio-chromatograms of the plant extracts in presence and absence of the safener. The influence of the safener consisted in an increase of the rate of the fenoxaprop-P-ethyl metabolism in cereals particularly seen in the flower-pot test with intact plants. In presence of the safener the final pattern of metabolites was already reached 141 hours (approx. 6 days) after treatment while without a safener the time for metabolism would be prolonged. The pattern observed without a safener is comparable with the safener pattern detected after 2 days.

The results are confirmed by metabolism studies on wheat conducted with the racemic compound ^{14}C-Hoe 033171 in presence of the non-labeled safener fenchlorazole-ethyl (Hoe 070542) and in absence of the respective safener (refer to B.7.2.1.5). The metabolic behaviour was shown to be independent from the presence of a safener.

B.7.2.1.7. *Metabolism in Rice- Study 1*

Reference:	KCA 6.2.1/01 *Hoe 046360-chlorophenyl-U-14C ,* *Metabolism and Kinetics in Rice Plants (Oryza sativa) under Field Conditions*
Author(s), year:	Wink O., Kuenzler K., Lemke G., Haberkorn B., Mueller H.J.; 1988a
Report/ Doc. Number:	CM29/87/ A38627
Guideline(s):	EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study is not necessary, but with respect to a propably intended use on rice in the future, it has been assessed for Annex I inclusion under 91/414/EEC and was deemed acceptable following peer review at EU level. The study is considered as supplementary information.

Material and Methods:

Rice plants (Oryzy sativa var. Bahia) were cultivated in containers under paddy field conditions in Spain and were treated with chlorophenyl-U-^{14}C -labeled Hoe 046360, formulated as a emulsifiable concentrate (EC) by spraying at the 5-6 leaf stage with **an application rate equivalent to 90 g active ingredient/ha** (~1N). All samples were stored deep frozen until analysis.

Plant samples were taken at different sampling intervals up to 112 days after treatment (DAT). The whole rice plants were cut off above the ground 2, 6, 7, 9, 13, 17 days after treatment. The plant samples 22, 36, 63, 84 and 112 days after treatment were separated into directly affected leaves, newly grown parts, stems, panicles and grains, wrapped up into aluminium foil and stored deep frozen until analysis. The whole rice plants (up to 17 DAT) and directly affected rice leaves/straw (22 DAT and later) were investigated to characterize the nature of the radioactive residues. The intact active substance and possible metabolites were extracted from the plants three times with a mixture of acetonitril/water (7:3, v/v) and subsequently partitioned between ethylacetate and water. The resulting aqueous and organic fractions were separately investigated for characterization of the residues by radio-HPLC using authentic reference material for comparison. Hydrolysis with hydrochloric acid was carried out with the ethylacetate and the aqueous extract as well as with the non-extractable residues. The solid phase remaining after hydrolysis contained the "non extractable residues" which were air-dried and analysed by combustion and subsequent radioassay.

Soil samples were taken pre and post application (0 DAT), prior flooding (6 DAT) and at harvest of the ripe rice (112 DAT) with the aid of plastic tubes and kept deep frozen until analysis. They were sawn into different sections, which were separately analyzed after air-drying for total radioactivity (TRR) by combustion and liquid scintillation counting (LSC).

6 days after treatment (DAT) the containers were flooded with deionizied water (the water depth was kept constant at 7-9 cm). Aliquot samples of the **paddy water** were taken from different sites of the container 3 and 6 hours after flooding as well as 1 (= 7 DAT), 2, 3, 7, 11, 16, 30, 57and 78 days after flooding (= 84 DAT), radioactivity concentration was determined by LSC.

Findings:

Residue concentration in the whole plants and the plant parts which were directly affected by spraying decreased from 12.2 mg as equ/kg fresh material on day 0 after treatment (0 DAT) to 2.8 mg as/kg at 17 DAT and 0.8 mg/kg at harvest (112 DAT). Residue concentrations in the plant parts grown after treatment, were considerably lower (0.02 mg as/kg at 22 DAT and 0.008 mg as/kg at 63 DAT). Hoe 046360 and its degrates were not translocated in the rice plants as residues in newly grown parts after treatment were determined as 0.007 mg as equ /kg in rice grains at harvest (112 DAT) only. The results are summarised in the table below.

Table 7.2.1.7-1 Total radioactive residues and distribution of the radioactivity after extraction of the rice plants. Values are given as mg as-equ/kg fresh material and as percentage of the total radioactivity (TRR) in the respective plant parts

DAT	Sample	Radioactive residue concentration						
			Ethylacetat extract		Aqueous extract		Non extractable residues	
		[mg /kg]	[mg /kg]	[%TRR]	[mg /kg]	[%TRR]	[mg /kg]	[%TRR]
0	Whole plants	12.2	9.0	73.7	3.1	25.6	0.1	0.7
2		11.3	6.5	57.0	3.7	32.4	1.2	10.6
6[1)]		4.01	1.1	26.5	2.0	49.7	0.9	23.5
7		**5.07**	0.9	17.8	2.7	53.3	1.5	28.9
9		6.5	1.0	15.9	3.3	49.9	2.2	33.9
13		2.2	0.4	17.1	0.9	39.5	1.0	43.4
17		**2.8**	0.3	11.0	1.0	34.1	1.5	54.9
22	Leaves (dry)	5.5	0.7	13.2	2.2	39.5	2.6	47.2
	New leaves &stems	0.02	0.01	26.2	0.01	24.0	0.01	49.9
36	Leaves (dry)	1.9	2.0	10.4	0.7	37.5	1.0	52.1
	New leaves &stems	< 0.018[#]	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
63	Leaves (dry)	2.5	0.3	17.0	0.2	4.6	2.1	82.0
	New leaves &stems	0.008						
	panicles	< 0.004[#]						
84	Straw (dry)	1.5	0.3	17.0	0.1	7.0	1.1	76.0
	New leaves &stems	0.008						
	Hulls of panicles	< 0.009[#]						
	grain	0.010						
112	Straw (dry)	0.8	0.1	16.0	0.05	6.0	0.6	78.0
	New straw (dry)	0.007						
	Hulls of panicles	< 0.010[#]						
	grain	0.007						

[#]...LOQ (Limit of quantification) [1)]…prior flooding

Because of the low residues in grain, the metabolic behaviour was investigated in the whole rice plants. The **organic extracts** contained at each sampling day only unchanged Hoe 046360 and Hoe 088406. There was no free compound Hoe 054014 detectable indicating a rapid cleavage of the benzoxazolyloxy linkage and further conjugation to polar and non extractable endproducts.
After acidic hydrolysis of the aqueous extract and subsequent HPLC-analysis, the majority of the residues were detected as the chlorobenzoxazolone Hoe 054014 (36.7 % on day 7 and 15.2 % on day 17). In addition, two further components assigned to an N-glucosid of the Hoe 054014 (16.4 % of TRR on day 7 and 14.8 % of TRR on day 17) and a hydroxylated chlorobenzoxazolone Hoe 064124 were found (4.1 % of TRR on day 17). These compounds were identified by comparison of the relative retention times with those of the authentic references substances. The results are summarised in table below.

Table 7.2.1.7-2 Nature of the total radioactivity in the whole rice plants in the organic and in the aqueous extract (after hydrolysis). Values are given as mg as equivalents/kg fresh material and as percentage of the total radioactivity (TRR) in plants.

	Hoe 046360 *parent*		***Hoe 088406*** *Fenoxaprop-P-acid*		***Hoe 054014*** *Chloro-benzoxazolone*		***Hoe 064124*** *Chrloro-OH-benzoxazolone*		***N-glucoside conjugate of Hoe 054014***	
	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg
Ethylacetate extract										
0 DAT	56.1	6.8	17.6	2.1						
2 DAT	27.3	3.1	29.7	3.4						
6 DAT	14.0	0.56	12.5	0.50						
7 DAT	9.1	0.46	8.7	0.44						
9 DAT	9.7	0.64	6.2	0.41						
13 DAT	17.1	0.38	n.d.	n.d.						
17 DAT	11.0	0.31	n.d.	n.d.						
Aqueous extract (after acidic hydrolysis)										
7 DAT					36.9	1.8	n.d.	n.d.	16.4	0.83
9 DAT					35.5	2.3	n.d.	n.d.	14.4	0.94
13 DAT					19.3	0.43	20.1	7.9	12.3	0.28
17 DAT					15.2	0.42	4.1	0.11	14.8	0.41

For further characterization of the radioactivity the **solid residues** of the days 7, 22, 63, 84 and 112 were hydrolysed with the aid of hydrochloric acid. Aliquots of solid sample and hydrochloric acid were boiled under reflux for 4 - 6 hours. Afterwards the reaction mixture was centrifuged to separate the aqueous phase from the solid residue. Aliquots of liquid fractions were added to the equivalent volume of hydrochloric acid and boiled under reflux for 2 - 4 hours. The cooled solution was used either for HPLC-analysis or partitioning with organic solvents. More than 70 % of the solubilised radioactivity was always found in the organic phase. HPLC-analyses showed that the radioactivity in the ethyl acetate phase consisted exclusively of Hoe 054014. Due to the low radioactivity and the high concentration of hydrolytically released natural products, the water phase was not further investigated by HPLC. The radioactivity in the remaining solid plant matrix after hydrolysis was assumed to be the covalently bound residues. It increased from 1.7 % of the total radioactivity in the whole plants of day 7 up to 32.7 % of the total radioactivity in the straw of day 84.

Table 7.2.1.7-3 Distribution of the readioactivity after acidic hydrolysis of the non-extractable residues. Values are given as percentage of the total radioactivity (TRR) in plants and mg ai equi./kg.

	7 DAT **Whole plant**		**22 DAT** **Directly affected leaves**		**63 DAT** **Directly affected leaves**		**84 DAT** **Directly affected straw**		**112 DAT** **Directly affected straw**	
	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg
non- extractable residue	28.9	1.5	47.2	2.6	82.0	2.1	76.0	1.1	78.0	0.6
Ethylacetat phase	26.0	1.3	35.0	1.9	49.2	1.3	31.9	0.46	50.7	0.39
aqueous phase	1.2	0.06	6.1	0.33	6.6	0.17	11.4	0.17	5.5	0.04
Bound residue	1.7	0.09	6.1	0.33	26.2	0.67	32.7	0.47	21.8	0.17

In the soil samples the radioactivity concentration in the upper soil layer (0-5 cm) remained between 0.047 and 0.058 mg ai-equ/kg dry soil during the course of the study. No significant radioactivity concentrations were detected in soil layers deeper than 5cm (the results are given in the table below).

Table 7.2.1.7-4 Radioactive residues in soil after the treatment of rice plants with ^{14}C -chlorophenyl-labeled Hoe 046360 (mean values mg as-equ/kg dry soil)

Days after treatment (DAT)	Soil depth (cm)	radioactive residue concentration (mg as-equiv/kg)	
		Single values	mean value
0 (pre application)	0-5	< LOQ	
	5-10	< LOQ	
	10-15	< LOQ	
0 (post application)	0-5	0.054, 0.039	0.047
	5-10	< LOQ	
	10-15	< LOQ	
	15-20	< LOQ	
6 (prior to flooding)	0-5	0.069, 0.042	0.056
	5-10	0.006, 0.006	0.006
	10-15	< LOQ	
	15-20	< LOQ	
112 (harvest of ripe rice)	0-5	0.052, 0.064	0.058
	5-10	< LOQ	
	10-15	< LOQ	
	15-20	< LOQ	

LOQ = < 0.006 mg as-equiv/kg (determined with the soil samples of the control container)

Radioactivity in the rice paddy water showed values of 0.008 mg as-equ/kg 3 hours after flooding and a maximum concentration of 0.012 mg as-equ/kg between 6 and 24 hours after flooding. The results are detailed in the table below.

Table 7.2.1.7-5 Radioactive residues in the rice paddy water after the treatment of rice plants with ^{14}C-chlorophenyl-labeled Hoe 046360.

Days after treatment (DAT)	Hours / days after flooding	radioactive residue concentration mg ai-equ/kg
6	3 hr	0.008
	6 hr	0.012
7	1	0.012
8	2	0.009
9	3	0.006
13	7	0.003
17	11	0.002
22	16	0.002
36	30	0.001
63	57	<0.001
84	78	0.002

Conclusion:

The distribution and degradation of Hoe 046360 in rice plants was investigated under field conditions at the 5-6 leaf stage with the radio-labeled compound at an application rate of 90 g as/ha. Radioactivity concentration was periodically determined in the different plant parts. In the **soil samples** the radioactivity concentration in the upper soil layer (0 - 5cm) remained between 0.047 and 0.058 mg as-equ/kg dry soil during the course of the study. There were no significant radioactivity concentrations found deeper than 5 cm. In the **rice paddy water**

no significant radioactive residues were determined (max. 0.012 mg as/kg fresh weight). The total radioactive residues in **rice grain**, 84 and 112 days after application, were at or below 0.01mg ai/kg fresh weight. The results show, that the residues occurred mainly in the directly affected leaves indicating a very low translocation to newly grown leaves and stems.
The total radioactivity in the directly affected plant parts was identified after acidic hydrolysis as Hoe 054014 (62.9 % on day 7 and 50.2 % on day 17), Hoe 064124 (4.1 % at day 17) and the N-glucoside of Hoe 054014 (16.4 % at day 7 and 14.8 % at day 17). With exception of the N-glucoside of Hoe 054014, the above mentioned degradation products were also found (free and conjugated) as important excretion products after dosing Hoe 046360-^{14}C to rats (Wink, O. et al, 1987, A37324).

B.7.2.1.8. *Metabolism in Rice- Study 2*

Reference:	KCA 6.2.1/11 *Hoe 046360-dioxyphenyl-1-^{14}C ,* *Degradation Behaviour in/on Rice Plants (Oryza sativa) under Field Conditions*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	Buettner B., Kuenzler K., Lemke G., Mueller H.J.; 1988a CM030/87/A40366 EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study is not necessary, but with respect to a propably intended use on rice in the future, it has been assessed for Annex I inclusion under 91/414/EEC and was deemed acceptable following peer review at EU level. The study is considered as supplementary information.

Material and Methods:

The metabolism of 1-dioxyphenyl-^{14}C-labeled Hoe 046360 (see Figure 7.2.1.1-2) was investigated again in rice (Oryzy sativa var. Bahia) grown under paddy field conditions in Spain and treated with the emulsifiable concentrate of the parent compound by spraying at the five to six leaf stage at **an application rate of 90 g as/ha** (~1N). At day 6 after treatment, soil was flooded with water, as is normal with rice. Plant-, soil- and paddy water samples were taken at different sampling intervals and periodically analysed for their radioactivity concentrations.
The intact **plants** and later on the different plant parts were homogenized and aliquots (at least 6 replicates) of each sample were taken, air-dried and combusted in order to determine the total radioactivity. Rice plants were extracted three times with a mixture of acetonitril/water (7:3, v/v) and subsequently partitioned between ethylacetate and water. Aliquots of the extracted solid residues were used for the determination of the remaining radioactivity in the plant matrix ("non-extractable residue"). The crude extract was concentrated by means of a rotary evaporator under reduced pressure and the resulting aqueous concentrate (pH adjusted to 4 - 5 with acetic acid) was extracted 3 times with ethyl acetate. The resulting aqueous and organic fractions were separately investigated for the radioactivity concentrations by radio-HPLC, using authentic reference material for comparison. Hydrolysis experiments were carried out with the ethyl acetate extract, the water extract and the non-extractable residues. For this purpose aliquots of the mentioned fraction were refluxed with hydrochloric acid and the hydrolysis mixture of the water extract and the ethyl acetate extract was investigated directly by HPLC. The solid phase remaining after hydrolysis contained the “non extractable residues” which were air-dried and analysed by combustion and subsequent radioassay.
Soil samples were taken at day 0 pre and post application, at day 6 prior to flooding and at day 112 (harvest of ripe rice) from treated container as well as from the control container. The different soil layers (5 cm pieces) were separately analyzed for their radioactivity content after air-drying.

Flooding was performed at day 6 after treatment. Samples from five different sites of the container were taken 3 hours, 6 hours, 1, 2, 3, 7, 11, 16, 30, 57 and 78 days after flooding. Water depth was kept constant (7-9 cm) throughout the flooding period (87 days). The radioactivity concentration in the **rice paddy water** was determined by liquid scintillation counting.

Findings:

Residue concentrations in the whole plants decreased from 20.0 mg as/kg fresh matrial on day 0 to 1.2 mg as/kg on day 17. Later on the different plant parts were analysed separately. The residue concentration in the directly affected leaves (straw) was 2.998 mg as-equ/kg on day 22 and decreased to 0.856 mg as/kg at day 112 (harvest), the values in the panicles were below the LOQ at all sampling days. The radioactive concentrations in the newly-grown leaves and stems decreased from 0.05mg as/kg (22 DAT) to 0.009 mg as/kg on harvest (84 DAT). Thus it can be stated that the Hoe 046360 and its metabolites were not translocated in the plants. The total residues for the rice grain were also low (0.01 mg as/kg at day 84 and 0.006 mg as-equ/kg at harvest= 112DAT). The results are summarised below.

Table 7.2.1.8-1 Total radioactive residues and distribution of the radioactivity after extraction of the rice plants. Values are given as mg as-equ/kg fresh material and as percentage of the total radioactivity (TRR) in the respective plant parts

DAT	Sample	Radioactive residue concentration						
			Ethylacetat extract		Aqueous extract		Non extractable residues	
		[mg /kg]	[mg /kg]	[%TRR]	[mg /kg]	[%TRR]	[mg /kg]	[%TRR]
0	**Whole plants**	20.0	16.6	83.0	3.2	16.1	0.18	0.9
2		10.5	5.5	52.2	4.0	38.5	0.97	9.3
6[1)]		6.0	1.2	19.5	3.3	54.8	1.55	25.7
7		5.7	1.1	18.5	3.1	53.7	1.60	27.8
9		3.6	0.62	17.3	1.4	38.3	1.60	44.4
13		2.2	0.17	8.0	0.97	45.2	1.02	46.8
17		1.2	0.09	7.7	0.38	33.3	0.68	59.0
22	Leaves (dry)	3.0	0.28	9.2	0.97	32.3	1.75	58.5
	New leaves & stems	0.05	0.005	10.6	0.006	12.7	0.036	76.7
36	Leaves (dry)	1.8	0.12	6.8	0.62	35.2	1.02	58.0
	New leaves & stems	0.013	n.d.	n.d.	n.d.	n.d.	0.01	100
63	Leaves (dry)	2.5	0.18	7.4	0.09	3.5	2.2	89.1
	New leaves & stems	0.012	n.d.	n.d.	0.003	20.9	0.009	79.1
	panicles	0.010						
84	Straw (dry)	0.4	0.02	6.2	0.02	5.5	0.32	88.3
	New leaves & stems	0.009						
	Hulls of panicles	0.008[#]						
	Grain	0.010						
112	Straw (dry)	0.86	0.07	7.9	0.03	3.7	0.76	88.4
	New straw (dry)	0.01						
	Hulls of panicles	0.009[#]						
	grain	0.006						

[#]...LOQ (Limit of quantification) [1)]…prior flooding

Because of the low residues in grain, the metabolic behaviour was investigated in the whole rice plants. The **organic extracts** contained at each sampling day only unchanged Hoe 046360 and Hoe 088406. No further degradation product was detected.

Table 7.2.1.8-2 Nature of the total radioactivity in the whole rice plants in the organic extract (before hydrolysis)

	Hoe 046360 parent		***Hoe 088406 Fenoxaprop-P-acid***	
	TRR (%)	**mg as equiv/kg fresh material**	**TRR (%)**	**mg as equiv/kg fresh material**
0 DAT	10.2	2.05	72.8	14.6
2 DAT	24.3	2.54	27.9	2.9
6 DAT	8.4	0.51	11.1	0.67
7 DAT	10.9	0.63	7.6	0.44
9 DAT	9.5	0.34	7.8	0.28
13 DAT	4.4	0.09	3.6	0.08
17 DAT	3.9	0.04	3.8	0.04

In the **aqueous extracts** of the rice plants two radioactive peaks were detectable in the chromatogram indicating highly polar conjugates. In order to identify these compounds, the water extract of day 7 was hydrolysed with hydrochloric acid. Both conjugates were cleavable under these conditions, resulting in two new compounds. By fortification with a mixture of reference compounds, the major peak was clearly identified as 2-(4-hydroxyphenoxy)-propionic acid (HOPP-acid, Hoe 096918) or its racemic mixture Hoe 020686, respectively. The second compound could not be identified up to now, but its retention time proposes an even more polar structure with additional hydroxylic or carboxylic groups.
The **solid residues** of the days 6, 7, 9, 13, 17, 22, 36, 63, 84 and 112 were hydrolysed with the aid of hydrochloric acid by refluxing for 4-6 hours. The major amount of the radioactivity in the nonextractable residues were solubilised and partitioned between water and ethyl acetate. The radioactivity in the remaining solid plant matrix after hydrolysis was assumed to be the covalently bound residues. It increased from 3.1 % of the total radioactivity in the whole plants of day 7 up to 46.9 % of the total radioactivity in the straw of day 112. This increase is partly due to the desiccation of the plant parts until harvest. The results are summarised in the table below.

Table 7.2.1.8-3 Distribution of the readioactivity after acidic hydrolysis of the non-extractable residues. Values are given as percentage of the total radioactivity (TRR) in the investigated plant parts and mg ai equi./kg.

	6 DAT Whole plant		**7DAT Whole plant**		**9 DAT Whole plant**		**13 DAT Whole plant**		**17 DAT Whole plant**	
	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg
non- extractable residue	25.7	1.55	27.8	1.60	44.4	1.60	46.8	1.01	59.0	0.68
Ethylacetat phase	17.5	1.06	19.7	1.13	33.3	1.20	34.6	0.75	39.5	0.46
aqueous phase	3.9	0.24	5.0	0.29	5.3	0.19	4.7	0.10	8.9	0.10
Bound residue	4.4	0.27	3.1	0.18	5.8	0.21	7.5	0.16	10.6	0.12
	22 DAT Directly affected leaves		**36 DAT Directly affected leaves**		**63 DAT Directly affected straw**		**84 DAT Directly affected straw**		**112 DAT Directly affected straw**	
	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg
non- extractable residue	58.5	1.75	58.0	1.02	89.1	2.19	88.3	0.32	88.4	0.76
Ethylacetat phase	35.7	1.07	n.a.	n.a.	43.7	1.07	40.6	0.15	30.9	0.27
aqueous phase	12.3	0.37	n.a.	n.a.	12.5	0.31	6.2	0.02	10.6	0.09
Bound residue	10.5	0.31	n.a.	n.a.	33.0	0.81	41.5	0.15	46.9	0.40

The sample of day 7 was further investigated with regard to the identity of the assigned radioactivity. After hydrolysis with the aid of hydrochloric acid (c=1mol/L), partitioning with organic solvents and subsequent HPLC-analysis, the two polar conjugates in the aqueous extract were cleavable resulting in two new components. One of them was identified as 2-(4-hydroxyphenoxy)-propionic acid (HOPP-acid).The other could not be identified, but its retention time proposes a polar structure. Due to the low radioactivity and the high concentration of hydrolytically released natural products, the water phase could not be further investigated by HPLC. A considerable portion of the non-extractable residues (13.4 %) was also liberated in form of Hoe 096918 (D-enatiomer of the HOPP-acid Hoe 02686) with the aid of hydrochloric acid. The result are summarised below.

Table 7.2.1.8-4 Identification and distribution of the radioactivity in the whole rice plants sampled 7 days after treatment (DAT). Values are mg as- equivalents/kg fresh material and as percentage of the total radioactivity (TRR) in plants.

	% TRR	mg as/kg	Step of workup/fraction
Radioactive concentration on day 7	**100**	**5.74**	-
Fenoxaprop-P-ethyl (Hoe 046360)	10.9	0.63	Ethyl acetate phase
Fenoxprop-P (Hoe 088406)	7.6	0.44	
HOPP-Acid (Hoe 096918 or Hoe 020686[1])	33.8	1.94	After hydrolysis of aqueous extract
HOPP-Acid (Hoe 096918 or Hoe 020686[1])	13.4	0.77	After hydrolysis of non-extractable residues and subsequent ethyl-acetate extraction
Sum of assigned radioactivity	**65.7**	**3.78**	
Sum of unidentified compounds	31.2	1.81	
Non extractable residues (bound residues)	3.1	0.18	

[1]….Hoe 020686 is the racemate of Hoe 096918

In **soil** the initial concentration was 0.040 mg as -equ/kg dry soil in the 0-5cm layer remaining between 0.040 and 0.058 mg as/kg during the course of the study. The residues in the 5-10 cm layer had the low level of 0.008 mg as-equ/kg at DAT 112.The results are summarised below. The results are summarised below.

Table 7.2.1.8-5 Radioactive residues in soil after the treatment of rice plants with Hoe 046360-dioxyphenyl-1-^{14}C labeled. Values are given mg as dry material (mean).

Days after treatment (DAT)	Soil depth (cm)	radioactive residue concentration (mg as-equiv/kg)	
		Single values	mean value
0 (pre application)	0-5	< LOQ	
	5-10	< LOQ	
	10-15	< LOQ	
	15-20	< LOQ	
0 (post application)	0-5	0.079, 0.006	0.040
	5-10	< LOQ	
	10-15	< LOQ	
	15-20	< LOQ	
6 (prior to flooding)	0-5	0.045, 0.047	0.047
	5-10	< LOQ	
	10-15	< LOQ	
	15-20	< LOQ	
112 (harvest of ripe rice)	0-5	0.069, 0.046	0.058
	5-10	0.008, 0.008	0.008
	10-15	< LOQ	
	15-20	< LOQ	

LOQ = < 0.006 mg as-equiv/kg (determined with the soil samples of the control container)

In the **rice paddy water** a maximum concentration of 0.012 mg as -equ/kg was reached three hours after flooding (6 days after treatment) and afterwards the concentration decreased continuously to values below 0.001 mg as/kg.

Table 7.2.1.8-6 Radioactive residues in the rice paddy water after the treatment of rice plants with ^{14}C-dioxyphenyl-1-^{14}C labeled Hoe 046360

Days after treatment (DAT)	Hours / days after flooding	radioactive residue concentration mg ai-equ/kg
6	3 hr	0.012
	6 hr	0.012
7	1	0.009
8	2	0.07
9	3	0.005
13	7	0.002
17	11	0.002
22	16	0.001
36	30	< 0.001
63	57	< 0.001
84	78	< 0.001

Conclusion:

The objective of this study was the clarification of the metabolic fate of the phenoxy-group with the dioxyphenyl-1-^{14}C-labeled Hoe 046360. Rice plants at the 5-6 leaf stage were treated at an application rate equivalent to 90 g active ingredient/ha. At day 6 after treatment, soil was flooded with water to simulate normal agricultural practice rice. The radioactivity concentrations in the **rice paddy water** reached a maximum of 0.012

mg a.i. equiv./kg 3 hours after flooding. 1 day after flooding the concentration had already fallen to 0.009 mg/kg and decreased constantly later on. The results of the **soil** measurements clearly show that radioactivity was detectable only in the upper 0 - 10 cm layer (< 0.06 mg a.i. equiv./kg dry soil) at all sampling dates. Radioactivity concentrations in those **plant** parts which were directly affected by spraying decreased from 20 mg a.i. equiv./kg fresh material at day 0 to 0.86 mg/kg at harvest (day 112 after treatment) whereas concentrations in the plant parts grown after treatment were considerably lower, indicating that Hoe 046360 and its biotransformation products were not translocated in the rice plants. Rice grains at harvest (day 112) contained less than 0.006 mg a.i. equiv./kg dry rice. Consequently, there are no significant residues in the seed at harvest time.
Additionally whole rice plants (up to day 17) and directly affected rice leaves/straw (day 22 and later on) were investigated to characterize the nature of the radioactive residues. Extractable radioactive compounds were separated and identified by radio-HPLC using authentic reference substances for comparison. The organic extracts contained only the unchanged parent compound Hoe 046360 (10.9% TRR) and its free carboxylic acid Hoe 088406 (7.6 % TRR) at each sampling day. The aqueous extracts contained two conjugates, so water extract of day 7 was hydrolysed in acidic medium and both conjugates were cleavable under the used conditions. The major one of the two liberated compounds was identified as HOPP-acid (Hoe 096918 or Hoe 020686) with 33.8 % of TRR. In the non-extractable portion 13.4 % of TRR (on day 7) were identified as HOPP-acid (Hoe 096918 or Hoe 020686) after acidic hydrolysis and subsequent ethyl-acetate extraction.

B.7.2.1.9. *Metabolism in soya bean and wheat*

Reference:	KCA 6.2.1/05 *Studies on the racemization of Hoe 046360-chlorophenyl-U- ^{14}C in soya beans and wheat*
Author(s), year:	Wink O., Kuenzler K., Lemke G., Koecher H.; 1986a
Report/ Doc. Number:	CM34/86/A35943
Guideline(s):	EPA Subdivision O, Residue Chemistry, § 171-4 (Oktober 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 501	-
Comment (RMS):	The study is considered applicable to provide the required information

Material and Methods:

Young soya bean (first leaflet developed) and summer wheat plants (2- to 3- leaf stage) were treated with U-chlorophenyl-^{14}C-Hoe 046360 at **an application rate of 0.11 kg/ha** (ratio of 94 to 6 for D-enantiomer and L-enantiomer, respectively).The plants were grown in pots (9 cm diameter) in the greenhouse and sampled 5 and 12 days after application. Only directly affected leaves were used for the investigations. The plant material was homogenized and extracted twice with acetonitril and water (8:2, v/v). The radioactivity in the nonextractable portion was determined by combustion/LSC. The acetonitrile-water phase was extracted twice with n-hexane each time to separate the active ingredient. After removal of the acetonitrile by the rotary evaporator the aqueous solution was adjusted to pH 5 and extracted twice with diethyl ether each time. The extracted aqueous phase was not investigated further. In the diethyl ether phase the free acid of the active ingredient Hoe 088406 (D-form); Hoe 088405 (L-form) and Hoe 054014 and the other metabolites were separated and quantified by TLC. The silica gel zone containing the free acid was scraped off the glass plate, the free acid was eluted from the silica gel with methyl acetate/methanol (1:1,v/v). After derivatisation of the acid Hoe 088406 with diazomethane, the enantiomers ratio of the resulting methylester Hoe 036036 as well as of Hoe 046360 (in the hexan phases form the prior extraction procedures) was determined by HPLC using chiral phase with UV- and ^{14}C-detection. The free acid is the sole metabolite that contains both the ^{14}C labelling and the optically active centre in the molecule and in which the enantiomer ratio can be determined directly after methylation.

Findings:

A ratio of D-enantiomer and L-enantiomer (94:6) was determined for the ^{14}C-labeled Hoe 046360 and its main metabolite Fenoxaprop-P (Hoe 088460).

Differences in the metabolism of Hoe 046036 in wheat and soya beans can be observed. The proportion of total radioactivity corresponding to the intact active ingredient decreases much faster in wheat than in soya beans. Only 4% free acid was detectable in the wheat on day 5, but 22% in the soya beans. On both days when samples were taken, significantly more polar extractable metabolites were measured in the wheat than in the soya beans. By contrast the amount of non-extractable residues in soya bean plants on both harvest days was 2 to 3 times higher than in wheat. The results are summarised in the table below.

Table 7.2.1.9-1 Residues of active ingredient and metabolites in mg a.i.-equivalents per kg fresh weight and as a percentage of total radioactivity in wheat and soya bean plants.

	5 DAT				12 DAT			
	Wheat		Soya bean		Wheat		Soya bean	
	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg	TRR (%)	mg/kg
Hoe 046360	14	0.84	23	3.24	2	0.05	196	1.80
Hoe 088406	4	0.24	22	3.10		.	6	0.57
Hoe 054014	30	1.79	7	0.99	19	0.50	9	0.85
Polar metabolites	44	2.62	28	3.94	68	1.80	43	4.08
Non extractable residues	5	0.30	17	2.40	11	0.29	24	2.3
Total	97	5.8	97	16.7	100	2.64	101	9.6

Investigation of the enantiomer ratio in the extracted intact active ingredient showed that no change had taken place compared to the applied active ingredient. Nor was any change in the enantiomer ratio observed in the isolated free acid Hoe 088406 (D-form) and Hoe 088405 (L-form).

Table 7.2.1.9-2 Percentages of the enantiomers in the intact active ingredient and in the free acid formed; after treatment of wheat and soya bean plants with Hoe 046360

	Wheat		Soya bean	
	5 DAT	12 DAT	5 DAT	12 DAT
Hoe 046360 parent compound				
D-Form	>90	>90	>95	>95
L-Form	<10	< 10	<5	<5
Hoe 088406 free acid				
D-Form	>90		>95	>90
L-Form	<10		<5	<10

At 5 and 12 days after treatment the D-enantiomer remained greater than 90 % for Hoe 046360 and for the free acid Hoe 088406 in wheat. No results with regard to the optical isomers are reported for the D-form of the free acid at 12 DAT. In soya beans the proportion of Fenoxaprop-P-ethyl was equal to or greater than 95 % on both sampling days.

Conclusion:

The study was regarded as important information to show that on basis of the available data no racemization either of the intact active ingredient or the free acid occurs after application of ^{14}C-labeled Hoe 046360 in soya beans and wheat within the first 12 days.

B.7.2.1.10. *Overall conclusion on the metabolism in plants*

A new study submitted for the purpose of renewal of a.s. approval elucidated the metabolism of fenoxaprop-P-ethyl in wheat following post-emergence application at a nominal rate of 138 g as/ha (~1.7N) in the presence of the safener cloquintocet-mexyl.

Metabolism in plants evaluated in the DAR (2005) was conducted using representative species of wheat (4), barley (1), rice (2) or soybean (1). Metabolism in plants evaluated in the DAR (2005) was conducted on wheat (4), barley (1), rice (2) and soybean (1). The plant metabolism studies were conducted with fenoxaprop-P-ethyl AE F046360 as well as with the racemic substance fenoxaprop-ethyl AE F033171. The substances were labelled either in the chlorophenyl ring or the dioxyphenyl ring to provide complete information on the degradation profile.

Foliar applied residues of fenoxaprop-P-ethyl (AEF 046360) or its racemic compound fenoxaprop-ethyl (AE F033171) on cereals can be readily metabolised such that no significant residues of the respective parent remain in forage, straw or grain. Identification and characterisation of at least 90% of the total radioactive residue (TRR) in each raw agricultural commodity (RAC) of the treated crops was not possible, but adequate attempts were made to present the components and to characterise them. The findings in all studies were consistent.

Shortly after application the parent compound in plant undergoes ester hydrolysis forming the free acid fenoxaprop-P (AE F088406, or AE F053022 for the racemic mixture), which is still herbicidally active. Subsequent cleavage of the ether bond between the benzoxazolone- and the phenoxy- part of the compound leads to the formation of the non chiral chlorobenzoxazolone AE F054014 and glutathionate conjugation of the benzoxazolone. The study with the dioxyphenyl-label on rice (see B.7.2.1.8) showed, that via cleavage of the ether bond also HOPP-acid (AE F096918) was formed.

These metabolic reactions were not influenced by the chirality of the molecule and are therefore identical for the racemat (AE F033171) or its optically active form fenoxaprop-P-ethyl Hoe 046360. To sum up

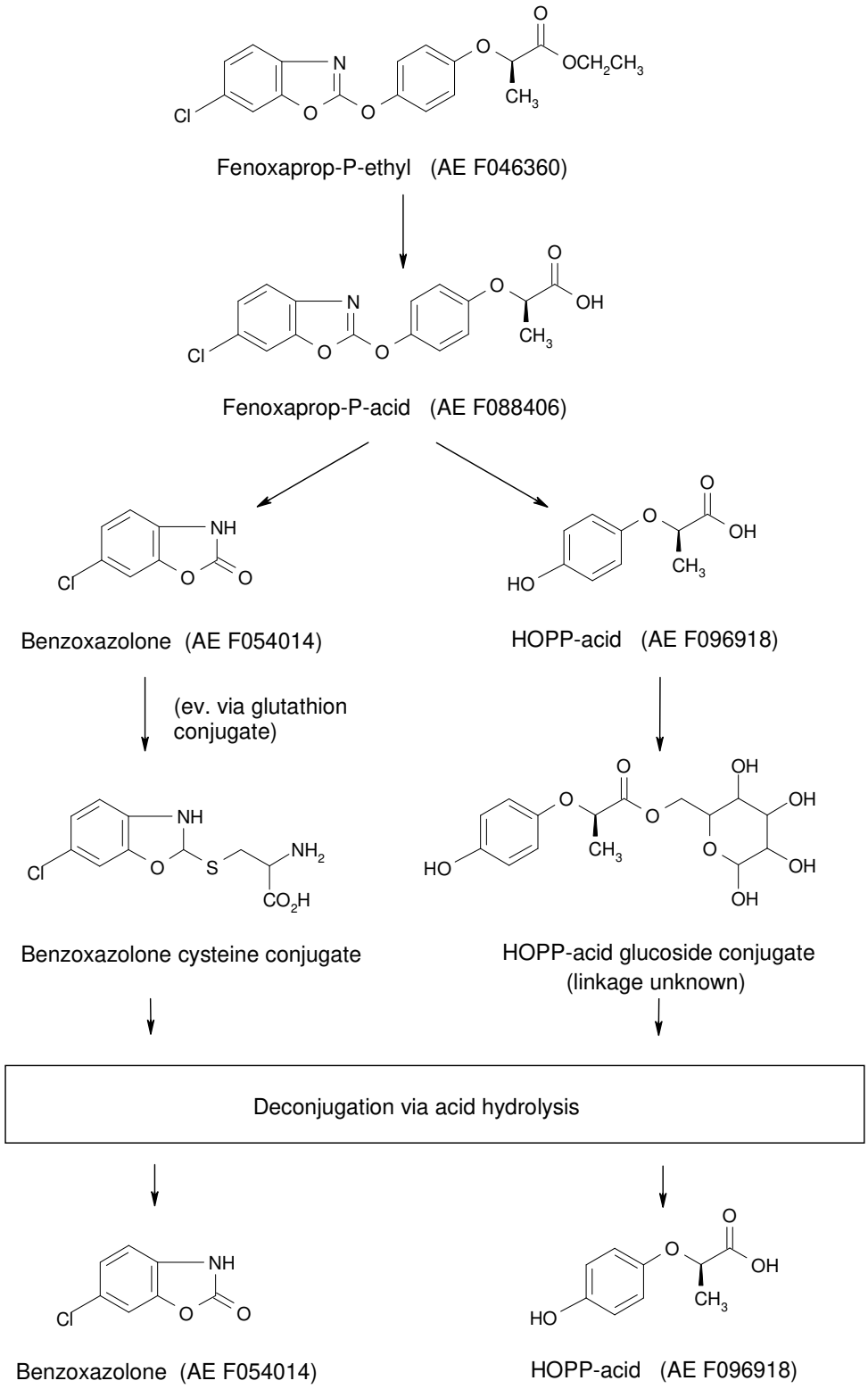
(1) hydrolysis of the ethyl ester group forming the free acid AE F088406, the D(+)- enantiomer of the racemic version AE F053022
(2) phenyl ether cleavage forming AE F054014 [6-chloro-2,3-dihydro-benzoxazol-2- one]
(3) conjugation of AE F054014 by glutathionate and additionally by glycosides.

A study on soya bean and wheat (B.7.2.1.9) demonstrated that there was no racemization observed for the parent compound fenoxaprop-P-ethyl or it's rapidly formed main metabolite fenoxaprop-P acid (AE F088406).

The new metabolism study on wheat (B.7.2.1.1) also confirms the postulated independency of the route of metabolisation from the presence of a safener.

Since the findings in all studies were consistent a common metabolic pathway for all investigated crops can be proposed. The proposed metabolism pathway for cereals is shown below.

Figure 7.2.1.10-1 **Metabolism scheme of fenoxaprop-P-ethyl residues in cereals**



B.7.2.2. Livestock

No new metabolism study in livestock was submitted for the purpose of renewal of the active substance approval.

Studies on laying hens, cow and lactating goats have previously been included in the submission for Annex I inclusion under 91/414/EEC to elucidate the **metabolism of fenoxaprop-P-ethyl in livestock.** The studies were deemed acceptable following evaluation and peer review at EU level. A summary of the original submitted data which were considered for the purpose of renewal is presented in the following table.

Species	Active substance	Label	Dose rate Duration	Matrices	Reference in the dossier for renewal of the a.s. (Reference in the RAR)	
Originally submitted and evaluated studies (DAR, 2005) to be considered for purpose of renewal						
Laying hen	Hoe 033171	Chlorophenyl-^{14}C	0.41 mg/kg bw/day 5 days	Eggs, Liver, Kidney, Muscle, Fat, Stomach, Heart, Brain, Skin, Ovary, Spleen, Blood, Plasma	[redacted] 1989a	KCA 6.2.2/01 (B.7.2.2.1)
Laying hen	Hoe 033171	Chlorophenyl-^{14}C	0.74 mg/kg bw/day 5 days	Egg white, Egg yolk, Liver, Muscle, Fat, Blood, Heart, Kidney, Skin, GI tract	[redacted] 1994a	KCA 6.2.2/02 (B.7.2.2.2)
		dioxyphenyl-1-^{14}C	0.81 mg/kg bw/day 5 days			
Lactating goat	Hoe 033171	Chlorophenyl-^{14}C	5.5 mg/kg bw/day 3 days	Milk, Urine, Liver, Kidney, Muscle, Fat	[redacted] 1989	KCA 6.2.3/01 (B.7.2.2.3)
					[redacted] 1990b	KCA 6.2.3/02 (B.7.2.2.3)
Cow	Hoe 033171	Chlorophenyl-^{14}C	0.1 mg/kg bw/day 3 days	Milk, Urine, Liver, Kidney, Muscle, Fat	[redacted]	KCA 6.2.3/03 (B.7.2.2.4)

Test material used for the livestock metabolism studies was in all cases the chlorophenyl-U-^{14}C labeled compound Hoe 033171 (Fenoxaprop-ethyl, Figure 7.2.1.1-3), which was regarded to be acceptable since metabolism studies in rat (see B.6.1.6) and plants showed no obvious difference in the metabolic behaviour of the racemic compound and the P-enantiomer.

B.7.2.2.1. *Poultry- study 1*

Reference:	KCA 6.2.2/01 *Distribution and excretion of Hoe 033171-^{14}C after repeated oral administration to laying hen*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	[redacted] 1989a RCC Project 071932/A40877 EPA, 171-4 (October 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 503	o 9 birds treated instead of at least 10 birds o Dosing for 5 consecutive days instead of at least 7 days
Comment (RMS):	However, the study is considered applicable to provide the required information.

Animal information:

Species/breed	Laying hens (white leghorn hybrids)
Number of tested animals	12 (out of 18)
Weight (range)	1.6 kg - 2.0 kg
Egg Production	1/per hen/day
Housing	Individually in stainless steel metabolism cages
Acclimatisation period	approximately 14days
Diet	Powdered hen feed *ad libitum*
Water	Fresh tap water *ad libitum*
Feed consumption[1]	0.12-0.16 kg/hen/day
Environmental conditions	
Temperature	20 ±3 C
Humidity	40-70 %
Light exposure	16-hour illumination

[1]….Feed consumption determined for four days prior to the first administration

Material and Methods:

Three groups of 3 laying hens (group 2-4) were orally dosed with ^{14}C Hoe 033171 via crop intubation once daily at a dose level of **0.41mg/kg body weight for 5 consecutive days** after the morning collection of excreta and eggs. One group of 3 hens remained as control (group 1).
Excreta were sampled once prior to dosing and once daily during administration. During depuration, excreta were sampled 4, 8, and 24 hours after the last dose and thereafter once daily up to day 7; they were pooled per sampling interval and group and stored deep frozen at -20°C until analysis. Eggs were collected twice daily during acclimation and before daily administration and 8 hours post. Eggs were pooled (per sampling interval and group) and separated into yolks and whites.
The hens were sacrificed 8 hours (group 2), 72 hours (group 3) and 7 days (group 4, control group 1) after the last treatment. The following organs and tissues were taken from the individual hens: Liver, kidney, muscle (chest and leg), muscle forestomach, heart, brain, fat (stomach and kidney), skin (+ adj. fat), ovaries (including eggs) and spleen. At sacrifice, the weights of the animals as well as of organs and tissues were recorded. Thereafter, aliquots of tissues and organs were taken for measurement of radioactivity and remaining organs and tissues stored at -20 °C until analysis. Blood samples were taken as well and analysed within the following 24 hours; the separated plasma was stored at -20°C. The radioactivity in the cage wash was determined by combustion of the aqueous suspension. All samples were investigated for total radioactivity in duplicate by liquid scintillation counter (LSC) and TLC.
Organs and egg yolk were additionally treated with a mixture of acetonitrile and hydrochloric acid. The analysis was then conducted with GC combined with 63 Ni-ECD.

Findings:

After the last administration of ^{14}C-Hoe 033171 to laying hens 91.3 % of the administered dose (inclusive 2.1 % cage wash) was detected in the excreta 8 hours after the last administration (group 2). 7 days after the last dose (group 4), a mean value of 94.2 % (inclusive 1.2% cage wash) for total radioactivity excreted was determined. Residues in tissue/organs/blood were higher in hens of group 2 (sacrificed 8 hours after the last dose) than in group 3 (sacrificed 72 hours after the last dose) amounting to 2.6 % and 1.0 %, respectively. Almost no radioactivity was found in organs and tissues (0.4 %) 168 hours after the last dose. Residues in eggs found in the respective groups amounted to 0.2 % (group 2), 0.4 % (group 3) and 0.5% after 7 days. The results are summarized in the table below.

Table 7.2.2.1-1 Total radioactive residues in eggs, tissues and excreta following administration of ^{14}C-Hoe 033171 to laying hens with a dose rate of 0.41 mg/kg bw/day

Matrix	I	II	Group 2	Group 3	Group 4
	Hr	hr	% of dose	% of dose	% of dose
Excreta	24		16.9	17.0	16.5
	48		18.8	23.8	17.9
	72		19.1	23.0	17.7
	96		18.6	20.0	18.8
		4	11.0	13.0	10.9
		8	4.8	4.8	4.8
		24		4.0	4.1
		48		1.2	1.1
		72		0.6	0.4
		168		-	0.1
Cage wash			2.1	1.7	1.2
Total excreted			91.3	106.4	94.2
Eggs			0.2	0.4	0.5
Total tissues[#]			2.6	1.4	0.4
Total Recovery			94.1	108.2	95.1

I….time after 1st administration
II…time after last administration
[#].....For the calculation of residual radioactivity 40 % of the body weight in muscle, 12% in fat and 8% in blood were assumed, respectively

Residues in egg white reached a maximum of 0.016 mg as.-equ/kg 24 hours after the last administration and decreased to or below the LOQ (=0.005 mg/kg) during a depuration period of 168 hours. Residue values in egg yolk increased up to 0.19 mg/kg 48 hours after the last administration and decreased thereafter below the LOQ. The results are summarized in the table below.

Radioactivity in eggs following repeated (5x) oral administration of Hoe 033171-^{14}C to laying hens (mean values given as mg as-equ per kg fresh weight).

I (hr)	II (hr)	Dose Number	Group 2 mg as-equiv./kg		Group 3 mg as-equiv./kg		Group 4 mg as-equiv./kg	
			Egg white	Egg york	Egg white	Egg york	Egg white	Egg york
Prior 1st dose			< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
24		2	< LOQ	< LOQ	0.013	< LOQ	< LOQ	< LOQ
48		3	0.012	0.013	0.015	0.02	0.009	0.018
72		4	0.013	0.031	0.014	0.038	0.009	0.051
96		5	0.014	0.075	0.014	0.078	0.011	0.097
	4		0.013	0.121	0.011	0.138	No egg	No egg
	8		No egg	No egg	No egg	No egg	No egg	No egg
	24				0.016	0.123	0.013	0.114
	48				0.006	0.189	0.008	0.178
	72				< LOQ	< LOQ	< LOQ	0.171
	96						< LOQ	< LOQ
	120						< LOQ	< LOQ
	144						< LOQ	< LOQ
	168						< LOQ	< LOQ

LOQ= 0.005 mg/kg I….time after 1st administration II…time after last administration

The radioactivity in liver and kidney accounted for 0.191 mg/kg and 0.743 mg/kg, respectively, 8 hours after the last dosing (group 2) decreasing to 0.014 mg/kg and 0.065 mg/kg, respectively, after 168 hours (group 4). Values for ovaries were 0.169 mg/kg after 8 hours and 0.079 mg/kg following a 72 hours depuration phase. At the end of the depuration period (168 hours after last administration) radioactive residues in most organs and tissues were slightly above or below the LOQ, except for kidney (0.065 mg/kg), fat (0.059 mg/kg), spleen (0.021 mg/kg) and blood (0.062 mg/kg). The results are summarized in the table below.

Table 7.2.2.1-2 Mean Radioactivity values in organs, tissues, blood and plasma following repeated (5x) oral administration of Hoe 033171-^{14}C to laying hens

Matrix	**Group 2** Sacrifce 8 hours after last dose **mg as-equ/kg**	**Group 3** Sacrifce 72 hours after last dose **mg as-equ/kg**	**Group 4** Sacrifce 168 hours after last dose **mg as-equ/kg**	**Group 1 (control)** Sacrifce 168 hours after last dose **mg as-equ/kg**
Liver	0.191	0.035	0.014	< LOQ
Kidney	0.743	0.187	0.065	< LOQ
Muscle (chest) **Muscle (leg)**	0.030 0.028	0.017 0.010	0.009 0.008	< LOQ < LOQ
Stomach	0.043	0.034	< LOQ	< LOQ
Heart	0.069	0.020	0.013	< LOQ
Brain	0.023	< LOQ	<LOQ	< LOQ
Fat (stomach)	0.050	0.042	0.059	< LOQ
Fat (kidney)	0.059	0.037	0.029	< LOQ
Skin (+ adj. fat)	0.047	0.023	0.020	< LOQ
Ovary	0.169	0.079	0.011	< LOQ
Spleen	0.089	0.036	0.021	< LOQ
Blood	0.221	0.089	0.062	< LOQ
Plasma	0.149	0.032	0.015	< LOQ

LOQ= ≤ 0.01 mg/kg

Conclusion:

Radiolabeled Hoe 033171 was administered repeatedly (5x) to laying hens at a **nominal dose of 0.41 mg/kg body weight** and the excretion was followed for 168 hours after the last dose.

The majority of the administered dose was excreted since 86.6% of the total dose was recovered in the excreta 8 hours after the last dose. After seven days (end of the depuration period), excretion was almost completed with 94.2 % (including cage wash).The TRR in tissues/organs and blood accounted for 2.6% of the dose (8 hours after the last dose) and 0.5% of the dose at the end of the depuration period (7 days after the last dose). TRR in eggs accounted for 0.2- 0.5% of the dose during the depuration period.

In **egg whites**, the highest radioactive residues were found 24 hours after the last administration with 0.016 mg/kg. After 72 hours all values were below the limit of quantification (0.005 mg/kg). In **egg yolks**, residual radioactivity was highest at 0.189 mg/kg 48 hours after the last administration. Thereafter, residual radioactivity steadily decreased to < LOQ at the end of depuration period.

The highest total radioactive residues were found 8 hours after the last dose in **liver** with 0.191 mg/kg and in **kidney** with 0.743 mg/kg decreasing to 0.014 and 0.065 mg/kg, respectively at the end of the depuration period (7 days). The total radioactive residues found in **fat** and **skin** ranged between 0.02 and 0.06 mg/kg over the whole depuration period. Residues in **muscle** were also low with 0.03 mg/kg 8 hours after the last dose and < 0.01 mg/kg at the end.

B.7.2.2.2. *Poultry- study 2*

Reference:	KCA 6.2.2/02 *Nature of the Residues of ^{14}C – Fenoxaprop-ethyl in Laying Hens*
Author(s), year:	[redacted] 1994a
Report/ Doc. Number:	HWI 6187-132/500 BM / A53203
Guideline(s):	EPA, 171-4 (October 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 503	o Dosing for 5 consecutive days instead of at least 7 days
Comment (RMS):	However, the study is considered applicable to provide the required information.

Animal information:

Species/breed	Laying hens (white leghorn)
Number of tested animals	25 (out of 50)
Weight (range)	1.4 -1.5 kg
Egg Production	5-6/per hen/test period
Housing	Individually in stainless steel metabolism cages
Acclimatisation period	12days
Diet	Hen feed *ad libitum*
Water	Fresh tap water *ad libitum*
Feed consumption	
During acclimation (mean)	0.117 kg/hen/day
During test period (range)	0.114 – 0.142 kg /hen/day
Environmental conditions	
Temperature	16-21 C
Light exposure	16-hour illumination

Material and Methods:

Four groups of 5 laying hens (group 2-5) were orally dosed with ^{14}CHoe 033171 via crop intubation once daily for 5 consecutive days at a dose level of **0.74 mg/kg body weight** (chlorophenyl label) and **0.81 mg/kg body weight** (dioxyphenyl label), respectively after the morning collection of excreta and eggs. One group of 5 hens (group 1, control) remained untreated to act as a source of control tissue for recovery and stability experiments.
The administered dose corresponded to a dietary concentration of 9 mg/kg feed based on a mean feed consumption of 0.126 kg/animal/day during the test period. A summary is given in the table below.

Dosing	Nominal dose [mg /kg bw/day]		Dietary concentration [mg/kg feed]		Average feed consumption per day [kg /animal]
	Chlorophenyl label	Dioxyphenyl label	Chlorophenyl label	Dioxyphenyl label	
Once daily, for 5 days,. capsules	0.74	0.81	8.8	9.7	0.126

Two groups á 5 hens (group 2-3) were dosed with chlorophenyl-U-^{14}C- labeled Hoe 033171 (Figure 7.2.1.1-3) and other two groups á 5 hens (group 4-5) with the dioxyphenyl -1-^{14}C- labeled (Figure 7.2.1.1-2) compound.
Excreta were sampled once daily during administration. Eggs were collected twice daily and pooled (one sampled p.m. and one a.m. the following day). Eggs and excreta produced after the last dose and before sacrifice were labeled as the Day 5 (sacrifice) collection. All groups were sacrificed approx. 6 hours after the final dose. Any eggs in the oviduct as well as samples of the principal edible tissues (liver, fat, muscle) and the auxiliary

tissues (heart, kidney, skin, blood and the content of the gastrointenstinal tract) were taken for extraction analysis. The total radioactive residues in all tissues and in the separated egg yolks and whites were determined by combustion and LSC. Representative samples of the principal edible tissues and eggs from the two dosing schemes were homogenised followed by several extraction steps (e.g. acetonitrile/water), acid and base hydrolysis and analysed by TLC and HPLC chromatography.

To ensure that storage stability issues were addressed, control samples of egg yolk, muscle, fat and liver were fortified with ^{14}C-fenoxaprop-ethyl and analysed by extraction and chromatography after varying periods of time**.** Control samples were fortified at a concentration of approximately 1 mg equivalent dioxyphenyl-U-^{14}C-fenoxaprop-ethyl/kg of control sample. Duplicate aliquots of the fortified samples were combusted to verify the concentrations of radioactivity. The fortified sample was divided into subsamples. One subsample each of muscle, liver, and egg yolk was immediately stored between -60 to -80°C. The remaining subsamples for muscle, liver, egg yolk, and fat were stored between -10 and -30°C. Once the subsamples of muscle, liver, and egg yolk (stored at -60 to -80°C) were frozen, the fortified subsamples were lyophilized, then extracted with the specified volume of organic solvent and centrifuged to separate the layers. The supernatant was removed from the residue, and transferred to a flask. This procedure was generally performed three times. The supernatants were pooled and evaporated to near dryness using a rotary evaporator. The concentrated sample was transferred to a volumetric flask, brought to volume, and radioassayed in duplicate by LSC. The residues were also radioassayed. A portion of the extract was also analyzed by TLC. One subsample of fat was extracted using the general procedure outlined above after storage for one week. One subsample each of muscle, liver, egg yolk and fat was extracted using the general procedure outlined above after storage for 24 months.

Findings:

The majority of the administered dose, 97.6 % (chlorophenyl-label) and 97.8 % (dioxyphenyl-label), was excreted directly. A maximum of 0.44 % (chlorophenyl-label) of the dose was retained in all remaining tissues. In egg white less than 0.01% of the administered dose was recovered, in egg yolk 0.03% (chlorophenyl-label). In the gastrointestinal tract and contents, values of 2% (chlorophenyl-label) to 3.9 % (dioxyphenyl-label) were detected. The results are summarised in the table below.

Table 7.2.2.2-1 Percent of total administered radioactivity recovered in each matrix for laying hens administered an oral dose of ^{14}C-Fenoxaprop-ethyl for 5 Consecutive Days (Pooled Samples, Five Hens Per Group)

Matrix	**Chlorophenyl label**		**Dioxyphenyl label**		**Not labeled**
	Dose level : 0.74 mg/kg bw/day		Dose level : 0.81 mg/kg bw/day		n.a.
	Group 2	**Group 3**	**Group 4**	**Group 5**	**Group 1**
	% of the dose	% of the dose	% of the dose	% of the dose	
Liver	0.14	0.11	0.05	0.11	n.a.
Kidney	0.12	0.13	0.06	0.11	n.a.
Muscle (breast)	0.04	0.03	< 0.01	< 0.01	n.a.
Muscle (thigh)	0.03	0.02	< 0.01	0.01	n.a.
Heart	< 0.01	< 0.01	< 0.01	< 0.01	n.a.
Fat (abdominal)	0.03	0.02	0.03	0.02	n.a.
Skin (+ adj. fat)	0.03	0.03	0.02	0.02	n.a.
Blood	0.05	0.04	0.01	0.02	n.a.
Total in tissues	**0.44**	**0.38**	**0.17**	**0.29**	n.a.
Egg white	< 0.01	< 0.01	< 0.01	< 0.01	n.a.
Egg yolk	0.03	0.03	0.01	0.01	n.a.
GI tract and contents	1.90	2.02	1.83	3.87	n.a.
Excreta	**96.8**	**97.6**	**97.8**	**93.8**	n.a.
Total recovered	99.2	100.0	99.8	98.0	n.a.

n.a.= not applicable

The highest residues were found in the organs associated with excretion (kidney. liver and GI-tract) ranging from 0.53 mg as-equ/kg (dioxyphenyl-label) to 0.64 mg as-equ/kg (chlorophenyl-label) in kidney, 0.15 mg as-equ/kg (dioxyphenyl-label) to 0.18 mg as-equ/kg (chlorophenyl-label) in liver and 0.73 mg as-equ/kg (chlorophenyl-label) to 1.43 mg as-equ/kg (dioxyphenyl-label) in the GI-tract. An overview is given in the table below.

Table 7.2.2.2-2 Radioactive residues in tissues and eggs for laying hens administered an oral dose of ^{14}C-Fenoxaprop-ethyl for 5 Consecutive Days (Pooled Samples, Five Hens Per Group)

Matrix		Chlorophenyl label		Dioxyphenyl label		Not labeled
		Group 2	Group 3	Group 4	Group 5	Group 1
		mg equiv./kg	mg equiv./kg	mg equiv./kg	mg equiv./kg	Control
Liver		0.179	0.143	0.076	0.146	n.a.
Kidney		0.608	0.638	0.303	0.530	n.a.
Muscle (breast)		0.016	0.014	0.004	0.007	n.a.
Muscle (thigh)		0.019	0.016	0.006	0.010	n.a.
Heart		0.049	0.040	0.017	0.031	n.a.
Fat (abdominal)		0.073	0.067	0.057	0.054	n.a.
Skin (+ adj. fat)		0.048	0.039	0.024	0.032	n.a.
Blood		0.164	0.145	0.035	0.079	n.a.
GI tract and contents		0.727	0.694	0.737	1.430	n.a.
Egg white	Day1	0.004	0.003	0.004	0.002	n.a.
	Day 2	0.007	0.006	0.009	0.006	n.a.
	Day3	0.007	0.006	0.009	0.006	n.a.
	Day4	0.007	0.007	0.009	0.006	n.a.
	Day5	0.007	0.005	0.010	0.006	n.a.
	Day5#	0.007	0.007	0.009	0.005	n.a.
Egg yolk	Day1	n.a.	n.a.	n.a.	n.a.	n.a.
	Day 2	n.d.	n.d.	n.d.	n.d.	n.a.
	Day3	0.008	0.012	0.009	0.002	n.a.
	Day4	0.038	0.036	0.027	0.027	n.a.
	Day5	0.059	0.065	0.049	0.048	n.a.
	Day5#	0.101	0.082	0.056	0.058	n.a.

#.. sacrifice day n.a.= not applicable n.d.= not detectabale

Samples of the edible tissues (liver, muscle, fat) and eggs from the hens dosed with chlorophenyl-U-^{14}C-fenoxaprop-ethyl (**Group 3**) and hens dosed with dioxyphenyl-U-^{14}C-fenoxaprop-ethyl (**Group 4**) were taken for extraction analysis. Several samples were analyzed, despite having residues levels at or below the level of significance of 0.01 mg/kg, in order to provide as complete a picture of the metabolic profile as possible. All matrices were fully characterized and bound residues released by utilization of a wide range of techniques. These techniques included exhaustive extraction with solvents of low to high polarity, organic solvent/aqueous partitioning, acid hydrolysis and base saponification. The majority of the residues in all samples could be recovered by solvent extraction and hydrolysis leaving 0.004 mg/kg or less fibre bound. The results are summarized below.

Table 7.2.2.2-3 Distribution of Radioactivity in extracts of tissues and eggs following repeated oral administration of ^{14}C- Fenoxaprop-ethyl (Hoe 033171) to laying hens

Matrix	Fraction	Total Radioactive Residue			
		chlorophenyl-^{14}C label		dioxyphenyl-^{14}C label	
		mg/kg	%TRR	mg/kg	%TRR
Liver	ACN:H_20	0.143	100	0.076	100
	Total extracted	**0.143**	**100**	**0.076**	**100**
Muscle (thigh)	ACN:H_20	0.006	40.4	0.003	54.9
	MeOH:H_20	0.002	15.2	0.002	26.5
	EtOAc	0.003	18.6	<0.001	8.7
	MeOH	0.003	16.3	<0.001	6.1
	Total extracted	**0.014**	**90.5**	**0.005**	**96.2**
Fat (abdominal)	Hexane	< 0.001	0.9	<0.001	0.2
	Hexane:DCM (80:20)	< 0.001	1.3	<0.001	0.3
	DCM	0.009	13.0	n.a.	n.a.
	Water	0.015	22.3	n.a.	n.a.
	MeOH	0.008	11.2	n.a.	n.a.
	EtOH:H_20 (80:20)	n.a.	n.a.	0.030	51.8
	ACN:H_20 (80:20)	n.a.	n.a.	0.004	6.9

Matrix	Fraction	Total Radioactive Residue			
		chlorophenyl-^{14}C label		dioxyphenyl-^{14}C label	
		mg/kg	%TRR	mg/kg	%TRR
	DCM:MEOH (80:20)	0.006	9.8	0.007	13.0
	Hexan-Ether	0.011	15.8	n.a.	n.a.
	ACN	0.004	5.8	0.005	9.1
	Total extracted	**0.053**	**80.1**	**0.046**	**81.3**
Egg yolk	Hexane:DCM (80:20)	0.006	8.5	0.006	8.5
	EtOH	0.004	8.0	0.031	50.5
	ACN	0.002	2.6	0.002	2.6
	DCM :MeOH (80 :20)	0.025	35.8	0.025	35.8
	Other eluents	0.021	27.4	0.021	27.4
	Total extracted	**0.060**	**82.3**	**0.060**	**82.3**
Egg white	ACN	n.a.	n.a.	0.008	80.6
	Total extracted	**n.a.**	**n.a.**	**0.008**	**80.6**

Metabolites were identified in the various extracts, after extensive clean-up, by co-chromatography against authentic standards, using either thin layer or high performance liquid chromatography. Confirmation of the identity of the major metabolites was obtained using a second chromatographic technique.

Parent compound fenoxaprop-ethyl (Hoe 033171) was not observed in any tissue. With both radiolabels, the free acid Hoe 053022 was determined in liver (24.3 % and 33.9 %, respectively), in muscle (14.4 % and 22.9 %, respectively) and in egg yolk (0.6 % and 13.9 %, respectively). In fat Hoe 053022 (acid) was only detected in the dioxyphenyl labeled hens at a level of 4.9 %.The chlorobenzoxazolone Hoe 054014, derived from cleavage of the ether bridge between the two ring systems, was the major metabolite in the chlorophenyl-labeled tissue (23.3 % in muscle), fat (13.4 %), organs (42.9 % in liver) and egg yolks (12.4 %). The metabolite from the corresponding mioety of the molecule was identified, after base hydrolysis, as hydroxyphenoxypropionic acid Hoe 020686 (HOPP Acid) in egg yolk (14.8 %) following dioxphenyl-label dosing. Only the egg-white from the dioxyphenyl-dosed hens (maximum residue 0.010 mg/kg) was analyzed, but residues were too low for further characterisation. In the chlorophenyl-dosed egg yolk the metabolite Hoe 040356 was observed which resulted from the loss of the propanoic acid from the intact ring system. After cleavage of the ether-linkage in this metabolite, again the Hoe 054014 was formed. The results are summarized in the table below.

Table 7.2.2.2-4 Distribution of Radioactivity in tissues and eggs following repeated oral administration of chlorophenyl- ^{14}C- Fenoxaprop-ethyl (Hoe 033171) to laying hens

Chlorophenyl-^{14}C								
	Liver		Muscle		Fat		Egg yolk	
	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR
TRR -Total Radioactive residues	**0.143**	**100**	**0.016**	**100**	**0.067**	**100**	**0.074**	**100**
ERR - Extracted Radioactive Residues	0.143	100	0.014	90.5	0.053	80.1	0.060	82.3
Hoe 033171 (Parent)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Hoe 053022 (free acid)	0.035	24.3	0.002	14.4	n.d.	n.d.	< 0.001	0.6
Hoe 054014	0.062	42.9	0.003	23.3	0.009	13.4	0.009	12.4
Hoe 040356	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.004	6.5
Hoe 020686	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Total identified	0.097	67.2	0.005	37.7	0.009	13.4	0.014	19.5
URR – Unextracted Radioactive Residues	< 0.001	< 0.1	0.002	9.6	0.004	6.4	0.004	5.3

Table 7.2.2.2-5 Distribution of Radioactivity in tissues and eggs following repeated oral administration of 1-dioxyphenyl- ^{14}C- Fenoxaprop-ethyl (Hoe 033171) to laying hens

1-dioxyphenyl-^{14}C								
	Liver		**Muscle**		**Fat**		**Egg yolk**	
	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR
TRR -Total Radioactive residues	**0.076**	**100**	**0.006**	**100**	**0.057**	**100**	**0.060**	**100**
ERR - Extracted Radioactive Residues	0.076	100	0.005	96.2	0.046	81.3	0.047	76.7
Hoe 033171 (Parent)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Hoe 053022 (free acid)	0.026	33.9	0.001	22.9	0.003	4.9	0.009	13.9
Hoe 054014	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Hoe 040356	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Hoe 020686	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.009	14.8
Total identified	0.026	33.9	0.001	22.9	0.003	4.9	0.018	28.7
URR – Unextracted Radioactive Residues	< 0.001	< 0.1	< 0.001	3.9	0.001	2.3	0.001	2.0

Table 7.2.2.2-6 Extraction Recoveries for ^{14}C-Fenoxaprop-ethyl Fortified Control Matrices

	% recovery of fortified radioactivity							
Time interval	**Initial**			**7 days**	**24 month**			
Matrix	**Muscle**	**Liver**	**Egg yolk**	**Fat**	**Muscle**	**Liver**	**Egg yolk**	**Fat**
Extract	46.7	73.2	95.1	96.9	46.7	14.1	104.5	120.1
Residue	43.0	36.2	8.4	3.8	58.4	98.9	6.9	1.1
Total	89.7	109.7	103.5	100.7	105.1	113.0	111.4	121.2

The residue extractability in egg yolk and fat samples was quantitative and was recovered as unchanged fenoxaprop-ethyl even after periods of up to two years. Although the total recovery of residue from similarly fortified muscle and liver samples was quantitative after two years, the extractability was reduced and in the case of the liver, the extractable residue was recovered as fenoxaprop acid (HOE 053022). The integrity of the residue of the actual treated samples of liver and muscle, however, was not compromised since these samples were analyzed rapidly (less than 10 weeks after sacrifice).

Conclusion:

Four groups of 5 laying hens were orally dosed with ^{14}C-Hoe 033171 once daily for 5 consecutive days at a dose level of 0.74mg/kg body weight (chlorophenyl label) and 0.81 mg/kg body weight (dioxyphenyl label), respectively. The majority of the administered radioactivity (98%) was excreted directly and 1.8% to 3.9% was found in the gastrointestinal tract and contents. A maximum of 0.44% of the dose was retained in the remaining tissues. Eggs contained maximum 0.03% of the radioactivity, which was mainly recovered in the yolks. Total radioactive residues in the tissues were low with the highest residues found in the organs associated with excretion; the gastrointestinal tract (0.69 to 1.43 mg/kg), the kidney (0.30 to 0.64 mg/kg) and the liver (0.08 to 0.18 mg/kg). Residues in eggs were also low with equal or less than 0.1 mg/kg.
The parent compound Hoe 033171 was not found in any tissue, but fenoxaprop acid, Hoe 053022 was found in nearly all tissues. Residues in egg white were too low for analysis. The major metabolite in the chlorophenyl-dosed tissues and egg yolk was Hoe 054014 (6-chloro-2,3- dihydro-benzoxazol-2-one), derived from cleavage of the ether bridge between the two ring systems. The metabolite from the corresponding half of the molecule, Hoe 020686 (HOPP acid), was identified in egg yolk, following dioxyphenyl-label dosing. The only other metabolite observed in any sample was Hoe 040356 [4-(6-chloro-2- benzoxazolyloxy)-phenol], which was identified in chlorophenyl-dosed egg yolk and resulted from the loss of the propanoic acid moiety from the intact ring systems. Fenoxaprop-ethyl, when administered to hens, is mainly excreted (98% of the administered dose), residues in tissues and eggs are low and not anticipated to accumulate significantly in the tissues or eggs.
The principal route of metabolism is de-esterification to the free acid (Hoe 053022), followed by cleavage of the ether linkage between the rings, giving Hoe 054014 and Hoe 020686. An alternative metabolic route in egg yolks was loss of the propanoic acid moiety from Hoe 053022. A large proportion of these metabolites were present as conjugates and fiber bound residues.

B.7.2.2.3. *Lactating ruminants-Study 1*

Reference:	KCA 6.2.3/01 *Hoe 033171-^{14}C- Metabolism in the lactating goat following repeated oral administration*
Author(s), year:	[redacted] 1989 [redacted] 1990b (Amendment)
Report/ Doc. Number:	CT1D040889/ A41369 OE90/034/A42690 (Amendment)
Guideline(s):	EPA, 171-4 (October 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 503	o Dosing for 3 consecutive days instead of at least 7 days o Extreta and milk sampled once a day o In liver extract and liver hydrolysis extract some very polar peaks could not be separated with TLC and only partly separated in HPLC. No quantification/identification possible.
Comment (RMS):	However, the study is considered applicable to provide the required information.

Animal information:

Species/breed	Lactating British Saanen goat (Capra hircus)
Number of tested animals	1 female
Weight	46.5 kg (at arrival), 44.5 kg (study begin), 46 kg (24hr after the last dose)
Housing	Individually in stainless steel metabolism cages
Acclimatisation period	14 days
Diet	500g of a concentrate (2x daily), hay ad libitum
Water	Fresh tap water *ad libitum*

Material and Methods:

^{14}C-Hoe 033171 (see Figure 7.2.1.1-3) was administrated in gelatine capsules orally to a lactating goat (2 years old) once daily via capsule at a nominal dose level of 250 mg/day corresponding **5.5 mg/kg body weight/day** for three consecutive days after the morning milking. The goat were fed twice daily at each time of milking. Nearly all feed offered was consumed. The goat was hand-milked twice daily and milk samples were collected at each time. Excreta were sampled over a period of 24 hours. Within 24 hours following the final dose the goat was sacrificed and samples of liver, kidney, fat and muscle were taken. All samples were stored deep frozen prior to analysis (within 9 weeks for all tissue samples and within 14 weeks for milk). There was no evidence of sample instability on storage.

Samples of faeces, muscle, fat, kidney and liver were extracted with acetonitrile:water (4:1, v/v) and analysed for total radioactivity by liquid scintillation counting (LSC). Samples of milk, tissues, faeces, urine and fat were analysed for metabolites by TLC and HPLC either directly after filtration (e.g. urine) or after a sequence of solvent extractions (ethyl acetate, acetonitrile, hexane, MeOH). One sample of milk was treated with ß-glucuronidase/arylsulphatase and incubated at 37°C overnight (including a control sample without enzyme-treatment). The extracts were partitioned between acetonitrile and hexane and were then analysed by co-chromatography against authentic standards, using either thin layer (TLC) or high performance liquid chromatography (HPLC).

Findings:

Renal elimination accounted for 35.6% and faecal elimination for 52.1% of the total cumulative dose up to 24 hours following the final dose. Thus 24 hours following the final dose (at sacrifice) 87.7% of the total cumulative dose had been excreted. Elimination in milk accounted for 0.54% of the total dose. Total recovery of radioactivity, including tissues, was 89.2% of the total cumulative dose.

At sacrifice, concentrations of radioactivity in the organs of excretion were 7.7 mg as-equv./kg for the kidney and 1.96 mg as.-equiv/kg for liver, respectively. Levels of radioactivity in fat and muscle at that time were low at

levels of 0.31 and 0.15 mg as.-equ/kg, respectively. Concentrations of radioactivity in milk reached a maximum of 1.35 mg as.-equ/kg following the third dose and were slightly higher than those following the second dose. A total of only 0.54 % of the cumulative dose was secreted into the milk after 72 hours.
Hoe 033171 was a major component in faecal (66 % of TRR) and in milk extracts after incubation at 37°C with or without ß-glucuronidase (44 % and 34 %, respectively). It was rapidly metabolised to the free acid Hoe 053022, which was observed as the major component in urine (51 % of TRR), kidney (62% of TRR), liver (18% of TRR), muscle (26% TRR) and milk extracts (5.6 % to 8.6 % of TRR). Hydroxybenzoxazolone Hoe 064124 was detected in the milk extract after incubation at 37°C and treatment with ß-glucuronidase (19 % of TRR). The chlorobenzoxazolone metabolite Hoe 054014 was liberated after acidic hydrolysis in tissues (2.0 % to 7.7 % of TRR) and milk extracts (0.83 % to 1.7 % of TRR).
Each sample residue (after extraction) was subjected to acid hydrolysis (6M HCL). This procedure liberates all compound related fragments as 6-chloro-2,3- dihydro-benzoxazol-2-one (Hoe 054014) and any related hydroxylated derivatives. The results are summarised in the table below.

Table 7.2.2.3-1 Excretion and distribution of radioactivity following repeated oral administration of ^{14}C-chlorophenyl-labeled Hoe 033171 to a lactating goat.

Sample	Sample time	% of total cumulative dose	Hoe 033171	Hoe 053022	Hoe 054014		Hoe 064124	Total identified	Un-known
			Extract	Extract	Extract	Residue#	Extract		
Urine	0-24h	32.1							
	24-48h	32.9							
	48-72	**35.6**	n.d.	51%	n.d.	-	n.d.	51.0%	49%
Faeces	0-24h	37.6							
	24-48h	48.5							
	48-72	**52.1**	66%	16%	n.d.	-	n.d.	82.0%	6.0%
Milk	0-24h	0.31							
	0-6h	0.07							
	6-24h	0.31							
	24-48h	0.47							
	24-30h	0.27							
	30-48h	0.47							
	48-72h	**0.54**	0.83 % 0.011 ppm	5.6 % 0.076 ppm	0.83 % 0.011 ppm	46% 0.62 ppm	n.d.	53.3%	0.26% 0.004ppm
	48-54h	0.41							
	54-72h	0.54							
Milk 37°C with enzyme			34% 0.459 ppm	8.6% 0.116 ppm	1.7% 0.023 ppm	5.7% 0.077ppm	19% 0.252 ppm	69.0%	20.0% 0.27 ppm
Milk 37°C without enzyme			44% 0.594 ppm	8.1% 0.109 ppm	1.7% 0.023 ppm	8.6% 0.116 ppm	0.7% 0.009 ppm	63.1%	32.7% 0.441 ppm
Kidney [a]	24h after final dose	**0.15**	n.d.	62% 4.8 ppm	7.7% 0.59 ppm	13.0% 1.0 ppm	n.d.	82.7%	13.0% 1.0 ppm
Liver [b]	24h after final dose	**0.25**	n.d.	18% 0.35 ppm	6.4% 0.13 ppm	9.8% 0.19 ppm	n.d.	34.2%	31.2% 0.62 ppm
Fat [c]	24h after final dose	**0.12**	n.d.	15% 0.047 ppm	3.8% 0.012 ppm	8.2% 0.025 ppm	n.d.	27.0%	17.0% 0.053 ppm
Muscle [d]	24h after final dose	**0.42**	n.d.	26% 0.039 ppm	2.0% 0.003 ppm	6.5% 0.010 ppm	n.d.	34.5%	33.0% 0.050 ppm
Total recovered		**89.2**							

n.d. not detected
#... unextractable radioactivity subjected to acid hydrolysis (6M HCL).
[a] 143g (fresh weiht) [b] 942g (fresh weight) [c] 6.6 % estimated body fat [d] 45.5 % estimated body muscle

The aqueous residues (i.e. extracted milk) subjected to the acid hydrolysis liberating 5.7% and 8.6% milk radioactivity respectively. Analysis by TLC showed a single component which co-chromatographed with benzoxazolone Hoe 054014. A total of 69.0% of milk radioactivity was identifiable in the enzyme treated milk. Finally 53.3% of milk radioactivity would be determined as Hoe 054014 following acid hydrolysis. Acid hydrolysis of the kidney residue and subsequent analysis by TLC showed one component, which co-chromatographed with benzoxazolone Hoe 054014, accounted for 13% of the kidney radioactivity and another unidentified origin bound component accounted for 13% of the kidney radioactivity. Thus, a total of 82.7% of kidney radioactivity was identifiable. TLC analysis of the liver residue after acid hydrolysis showed a single

component which co-chromatographed with benzoxazolone Hoe 054014 and accounted for 9.8% of liver radioactivity and one single unidentifiable origin bound component which accounted for 10.2% of liver radioactivity. Analysis of the fat residue after acid hydrolysis showed a smaller component, accounting for 8.2% of fat radioactivity co-chromatographed with benzoxazolone Hoe 054014 and a larger component, accounting for 17% of fat radioactivity, which was origin bound and unidentifiable. Acid hydrolysis of the muscle residue and subsequent analysis by TLC showed a major component, accounting for 33% muscle radioactivity, which was origin bound and not identifiable and a minor component co-chromatographed with benzoxazolone Hoe 054014 and accounted for 6.5% muscle radioactivity. Thus, a total of 34.5% of muscle radioactivity was identifiable.

Conclusion:
Fenoxaprop- ethyl (Hoe 033171) is excreted mainly via faeces and urine (87 % of administered dose) following repeated oral administration to a lactating goat at a nominal dose level of 250 mg/day (corresponding 5.5 mg/kg/day).
Absorption of Hoe 033171 is incomplete since 35.6% of the total dose was renally excreted and the faeces which accounted for 52.1% of the total dose contained largely unchanged Hoe 033171. Parent Hoe 033171 is evidently rapidly metabolised following absorption since unchanged pesticide was not detected in urine or tissues. Parent compound was however a major component in milk although the total dose in milk was very low at 0.54%.
Following absorption, metabolism to the free acid Hoe 053022 is a principal pathway as this was a major component in all tissue extracts. Benzoxazolone Hoe 054014 was a minor component in all tissue and milk extracts. Hydroxybenzoxazolone Hoe 064124 was detected in milk extract after treatment with ß-glucuronidase. Residues in polar (muscle) and lipophilic (fat) tissues as well as in the organs of excretion (kidney, liver) are low (fat 0.12 %, muscle 0.42 %, kidney 0.15 % and liver 0.25 % of the administered dose). Thus it is unlikely that accumulation of residues, derived from Hoe 033171 and its degradation products, has occurred.

B.7.2.2.4. *Lactating ruminants-Study 2*

Reference:	KCA 6.2.3/03 *Hoe 033171-^{14}C, nature of residues in milk and tissues of cows after dosing 50 mg / cow and day at three consecutive days*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	[redacted], 1985 Fo.337/85 EPA, 171-4 (October 1982) Yes
Previous evaluation :	**In the DAR (2005) not considered necessary** Now assessed for the purpose of renewal of a.s. approval
Deviations from OECD Guideline 503	o Dosing for 3 consecutive days instead of at least 5 days
Comment (RMS):	The study has deficiencies concerning analysis and characterisation of residues in urine and faeces samples, which were not reported. However the study is considered applicable to provide the required information.

Animal information:

Species/breed	Lactating Cow (Frisian Holstein)
Number of tested animals	1 female/3 year old
Weight	460 kg
Housing	Individually in stainless steel metabolism cages
Acclimatisation period	Until feed uptake and milk yield were constant
Diet	1 kg/day, hay ad libitum
Water	municial tap water *ad libitum*

Material and Methods:
^{14}C-Hoe 033171 (see Figure 7.2.1.1-3) was administrated in capsules by means of an applicator orally to a lactating cow once daily at a nominal dose level of 50 mg/per cow and day corresponding **0.1 mg/kg body weight/day** for three consecutive days after the morning milking and before daily feeding. Urine was sampled at

0-4h, 4-8h, 8-24h, 24-48h, 48-71h after the first dose, faeces were sampled once daily. Milk was sampled twice daily. 24 hours following the final dose the cow was sacrificed and samples of liver, kidney, fat and muscle were taken. All samples were stored deep frozen prior to analysis. Samples of milk, liver, kidney, fat and urine were analysed for total radioactivity by liquid scintillation counting (LSC).
Samples of the different tissues were analysed according to analytical method AL 06/84 (Künzler, K.; Pleines, J.; 1984) where the sample material is boiled for 8 hours with hydrochloric acid in acetcnitrile under reflux. The active ingredient is split into 6-chloro-2,3-dihydro-benzoxazole-2-one in the process. It is then diluted with water to 50 % concentration and the undissolved material removed by filtration. Aliquots of the filtrate are added to an Extrelut column. Impurities are washed out of the column with hexane. The saponified active ingredient is eluted with 250 ml 20 % diethyl ether in hexane, the eluate is evaporated, acetylated with acetic anhydride, purified and determined by GC-ECD as 3- acetyl-6-chloro-2,3-dihydro-benzoxazole-2-one. Limit of determination is 0.02 mg/kg. With additions of 0.02 - 0.5 mg/kg of the active ingredient to the untreated control samples the recovery rates amounted to 75 - 90 % (85 % on average).

Findings:
In milk a maximum of 0.056 mg /kg was determined 54 hours after the first dose. At that time 75% of the total residues in milk were identified as Hoe 054014. At sacrifice (24 hours after the final dose), the residues in liver and kidney were 0.11 mg/kg and 0.24 mg/kg, respectively. At that time 32 % of the total residues in liver and 23% in kidney were assigned as Hoe 054014 (chlorobenzoxazolone), which was liberated by acidic hydrolysis. The total residue concentration in muscle was low with 0.005 mg a.i. equiv./kg, the total residue concentration in subcutaneous and kidney fat was 0.02 and 0.016 mg a.i. equiv./kg, respectively. No Hoe 054014 was detected. In the relevant tissues (fat and muscle) only low residue levels were determined, despite the administration of the exaggerated dose of 50 mg/cow.

Table 7.2.2.4-1 Radioactive concentrations and characterisation of radioactive residues in milk and tissues following repeated oral administration of ^{14}C-chlorophenyl-labelled Hoe 033171 to a lactating cow.

Sample	Sample time	Hoe 033171 mg ai-equiv/kg	Hoe 054014 Calculated as mg as-equiv/kg	% of the total residue represented as Hoe 054014
Milk	6.5 h post application	0.005		
	23 h post application	0.036		
	30 h post application	0.047		
	47 h post application	0.050		
	54 h post application	0.056	0.042	75
	71 h post application	0.053		
Kidney	24h after final dose	0.24	0.056	23
Liver	24h after final dose	0.11	0.035	32
Kidney fat	24h after final dose	0.016	< 0.005	-
Subcutaneous fat	24h after final dose	0.02	< 0.005	-
Muscle	24h after final dose	0.005	n.a.	-

n.a.= not analysed

Conclusion:
Due to the rapid conversion of the unpolar ester to the corresponding carboxylic acid Hoe 053022, it is expected that Hoe 033171 does not tend to accumulate in any tissue, neither in polar (muscle) nor in lipophilic (subcutaneous and kidney fat) nor in excretion organs (kidney, liver) after oral administration to cows at nominal dose level of 50 mg/day (**0.1 mg/kg body weight/day**) for three consecutive days. ^{14}C-Hoe 033171 is rapidly converted to its polar free acid and further metabolites before lipophilic tissues are reached. 75 % of the total residues in milk (0.056 mg/kg) and about 50 % of the residues in liver (0.24 mg/kg) and kidney (0.11 mg/kg) were assigneable to chlorobenzoxazolone metabolite Hoe 054014.

B.7.2.2.5. *Pigs*

Following oral administration, ^{14}C-fenoxaprop-P-ethyl or its racemic compound fenoxaprop-ethyl elimination was observed to be rapid and almost complete in rat, goat and hen. Only low levels of radioactive residues could be found in the tissues at the time of sacrifice, with the higher levels being located in the principal organs of metabolism and excretion, the liver and kidney. Fenoxaprop-P-ethyl residues showed no tendency for accumulation. The main residue components were identified as fenoxaprop-P-acid and the benzoxazolone metabolite AE F054014 in hen goat and rat.

Therefore it was concluded that the principal pathway of metabolisation is the same in goat, hen and rat and consequently a metabolism study in pig is not necessary

B.7.2.2.6. *Fish*

The potential of pesticide residues to accumulate in fish tissue is determined to a significant extent by the lipophilicity of the active substance (expressed as the n-octanol-water partition coefficient, POW). The accumulation of compounds of relatively low lipophilicity (log POW < 3) via the diet is known to be negligible as far as reported residues in fish are taken into account. Fish metabolism studies are therefore required only for active substances where the log P_{OW} is greater than or equal to three (SANCO/11187/2013, 31 January 2013 rev. 3)

The log P_{OW} of Fenoxaprop-P-ethyl is 4.58 however no fenoxaprop-P-ethyl residues in cereal harvest commodities have been detected. Residues in cereal grain are all below the LOQ of 0.01 mg/kg. Residues in harvest commodities do consist of the metabolites fenoxaprop-P-acid (AE F088406) and benzoxazolone (AE F054014) and their conjugates. Their log P_{OW} values are given in the table below.

Table 7.2.2.6-1 Log P_{ow} values for metabolites of fenoxaprop-P-ethyl

Metabolite	log P_{OW}	pH	Study No.:
Fenoxaprop-P-acid AE F088406	1.9	5	Fischer, A.; 2016; KCA 2.7/10
	0.3	7	
	0.0	9	
Benzoxazolone AE F054014	1.7	5	Fischer, A.; 2015; KCA 2.7/08
	1.5	7	

The log P_{OW} values of fenoxaprop-P-ethyl acid and benzoxazolone are far below 3 in acidic as well as in basic solutions.

According to Commission Regulation (EU) No 283/2013 of 01 March 2013 “Metabolism studies on fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications”

Additionally, with the cattle and the hen feeding study the residues in fat and muscle were comparable. Fenoxaprop-P-ethyl is not considered to be fat soluble and a fish metabolism study is therefore considered not necessary.

Additionally, it is considered that no green material or forages nor straw will be part of the fish diet. Residues in cereal grain are all below the LOQ of 0.01 mg/kg. Therefore the dietary burden of fenoxaprop-P-ethyl derived residues in fish feed is considered negligible.

According to the data requirements published in Commission Regulation (EU) No 283/2013 of 01 March 2013, Section 6.2.5 “Metabolism studies on fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications.”

However, no official test method or guidance document is available for conducting a study on the “metabolism, distribution and expression of residues” in fish. Also, no feeding table with plant commodities for fish feed is available. Therefore, it cannot be concluded whether livestock fish might be exposed to residues of fenoxaprop-P-ethyl in parts of plants that have been treated with this active substance.

In these cases, waiving of this particular data requirement is considered acceptable according to the “Guidance document for applicants on preparing dossiers for the approval of a chemical new active substance and the renewal of approval of the chemical active substance according to regulation (EU) No. 283/2013 and regulation (EU) No. 284/2013” (SANCO/10181/2013-rev.2 of 2-May-2013).

B.7.2.2.7. *Overall conclusion on the metabolism in livestock*

No new metabolism study in livestock was submitted for the purpose of renewal of the active substance approval. The animal metabolism was studied in the DAR (2005) was studied on laying hen (2) and lactating ruminants (2) with the ^{14}C-labeled racemic compound Hoe 033171 (Fenoxprop-ethyl). The metabolism in the rat and additionally even in plants showed no obvious difference in the metabolic behaviour for both the racemic compound Hoe 033171 and the P-enatiomer Hoe 046360; therefore no animal metabolismus studies with the P-enantiomer have been required.

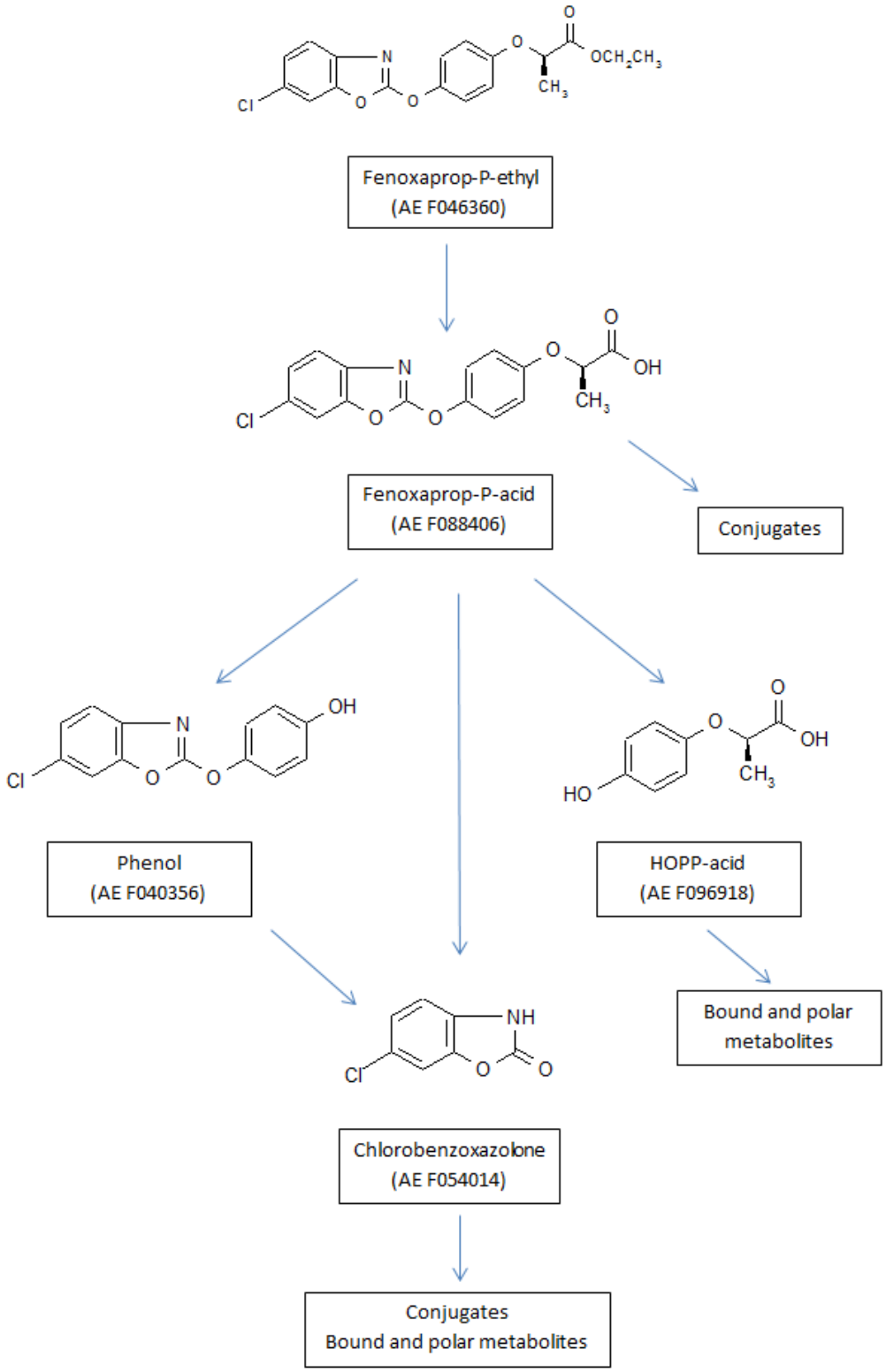
In **poultry** following repeated oral administration to laying hens at a nominal dose level of either 0.81 mg/kg/day via capsule and 0.41 mg/kg bw by crop infusion, the majority of the administered radioactivity (91-98%) was excreted, eggs contained maximum 0.3 % of the radioactivity. No parent compound Hoe 033171 was detected in any tissue. Mayor residue component in all tissues and egg yolk (residue in egg white too low for identification) was the chlorobenzoxazolone (AE F054014) followed by fenoxaprop acid AE F053022 (racemic mixture of AE F088406). Total radioactive residues in the tissues were low with the highest residues found in the organs associated with excretion; the gastrointestinal tract (0.69 to 1.43 mg/kg), the kidney (0.30 to 0.64 mg/kg) and the liver (0.08 to 0.18 mg/kg). Residues in eggs were also low with equal or less than 0.01 mg/kg.

In **ruminants** Fenoxaprop- ethyl (Hoe 033171) is excreted mainly via faeces and urine (87 % of administered dose) following repeated oral administration via capsule to a lactating goat at a nominal dose level of 5.5 mg/kg/day. The parent Hoe 033171 is evidently rapidly metabolised following absorption since unchanged pesticide was not detected in urine or tissues. Mayor residue component in all tissues and milk was the chlorobenzoxazolone (AE F054014) followed by fenoxaprop acid (AE F053022; racemic mixture of AE F088406). Residues in polar (muscle) and lipophilic (fat) tissues as well as in the organs of excretion (kidney, liver) are low (fat 0.12 %, muscle 0.42 %, kidney 0.15 % and liver 0.25 % of the administered dose). Thus it is unlikely that accumulation of residues, derived from Hoe 033171 and its degradation products, has occurred.

A **fish** metabolism study is considered not necessary. The log P_{OW} of Fenoxaprop-P-ethyl is 4.58 however Fenoxaprop-P-ethyl residues in cereal grain are all below the LOQ of 0.01 mg/kg. Additionally, it is considered that no green material or forages nor straw will be part of the fish diet. The dietary burden of fenoxaprop-P-ethyl derived residues in fish feed is therefore considered negligible. Moreover residues in cereal harvest commodities consist of the metabolites fenoxaprop-P-acid (AE F088406) and chlorobenzoxazolone (AE F054014) and their conjugates. The log P_{OW} values of fenoxaprop-P-ethyl acid and benzoxazolone are far below 3 in acidic as well as in basic solutions.

As a conclusion, the lactating ruminant and poultry metabolism studies both indicate that the metabolism of fenoxaprop-P-ethyl in livestock involves hydrolysis into fenoxaprop acid and further cleavage of the ether bond forming chlorobenzoxazolone (Hoe 054014) and HOPP acid (Hoe 020686) This is in agreement with the findings of the rat metabolism study where hydrolysis to fenoxaprop-P is also the primary step of the metabolic pathway. As the principle metabolic steps are consistent in rat, hen and goat no studies are required on the metabolism in pigs. The proposed metabolic pathway is presented in the Figure below.

Figure 7.2.2.7-1 Metabolism scheme of fenoxaprop-P-ethyl residues in poultry



B.7.2.3. Defintion of residues

B.7.2.3.1. *Plants*

One new metabolism study in spring wheat conducted with [^{14}C]-Fenoxaprop-P-ethyl has been submitted for the purpose of renewal of the active substance approval (B.7.2.1.1). The study confirms the results of the metabolism studies on wheat, barley, soybean and rice have previously evaluated for Annex I inclusion under 91/414/EEC. The studies were deemed acceptable following evaluation and peer review at EU level.

The plant metabolism studies were conducted with fenoxaprop-P-ethyl AE F046360 as well as with the racemic substance fenoxaprop-ethyl AE F033171. The substances were labelled either in the chlorophenyl ring or the dioxyphenyl ring to provide complete information on the degradation profile.

There is no obvious difference in the metabolic behaviour of the racemic compound and the P-enantiomer. In both cases the active substance in plant undergoes ester hydrolysis forming the free acid fenoxaprop-P (AE F088406, or AE F053022 for the racemic mixture), which is still herbicidally active. Further metabolism proceeds through cleavage of the ether-linkage between the benzoxazolone and the phenoxy- moieties of the substance from 2 to 7 days after application. Major constituent of the residue after this cleavage are chlorbenzoxazolone (AE F054014) and HOPP-acid (AE F096918) as free or conjugated forms. The rat metabolism proceeds through the same major steps as plant metabolism and it can be considered that the plant metabolism is covered by the toxicological studies conducted with the parent compound either fenoxaprop-P-ethyl or fenoxaprop-ethyl.

The <u>influence of the safener mefenpyr-diethyl</u> (B.7.2.1.6) on the metabolism of fenoxaprop-P-ethyl was investigated on barley shoots showing that the metabolic profile was independent of the presence or absence of the safener.
It was also shown that <u>no racemisation either of the parent compound or the free acid</u> (B.7.2.1.9) occurs during plant metabolism.
The rat metabolism proceeds through the same major steps as plant metabolism and it can be considered that the plant metabolism is covered by the toxicological studies conducted with the parent compound either fenoxaprop-P-ethyl or fenoxaprop-ethyl.

The validated analytical methods for residues derived from fenoxaprop-P-ethyl start with a hydrolysis step which converts the active ingredient, the free acid fenoxaprop-p as well as other metabolites or conjugates still containing the chlorobenzoxazolone moiety to chlorobenzoxazolone (AE F054014). This common moiety approach was chosen because most of the aged residues of fenoxaprop-P-ethyl were determined to be conjugated. After harsh hydrolysis the predominant residue in plant matrices could be identified as chlorobenzoxazolone (AE F054014).
For the purpose of renewal of the active substance approval **a new analytical method for plant matrices** *"Modification M001 to method 00874 for the determination of residues of AE F046360, AE F088406, and AE F054014 in/on matrices of plant origin by HPLC-MS/MS (Method and validation)* (please refer to B.5.2.1) has been submitted. The method determines the sum (total residue) of AE F046360, AE F088406 and AE F054014. The analytical target is AE F054014. The method 00874/M001 is considered applicable as a residue analytical method as well as for enforcement purposes.

According to OECD Guidance on the definition of residue (ENV/JM/MONO(2009)30) the residue definition for monitoring/MRL enforcement (RD-Mo) should focus on those residue components suitable as analyte of multi-residue methods, as well as suitable as general marker compound in food commodities concerned.

Considering that there is no obvious difference in the metabolic behaviour of the racemic compound fenoxaprop-ethyl and the P-enantiomer and that the parent compound and its free acid form cannot be considered as valid indicator of the residue situation at harvest. The requirement of an enantio-selective method of analysis is not reasonable since the analytical target is 6-chloro-2,3- dihydrobenzoxazol-2-one (AE F054014).

The residue definition for monitoring and risk assessment for the purpose of renewal of the active substance approval is proposed as outlined in the table below compared to the residue definition as decided during 91/414 peer review (EFSA, 2007).

Table 7.2.3.1-1 Existing and proposed residue definitions for fenoxaprop-P-ethyl in plants

	Residue definition	
	EFSA conclusion **[EFSA Scientific Report (2007) 121, 1-76]**	**Proposal for purpose of renewal**
Residue definition for monitoring	Sum of fenoxaprop-P-ethyl and all metabolites which may be converted to 6-chloro-2,3-dihydrobenzoxazol-2-one, expressed as fenoxaprop-P-ethyl or alternatively: Sum of fenoxaprop-ethyl and all metabolites which may be converted to 6-chloro-2,3- dihydrobenzoxazol-2-one, expressed as fenoxaprop-ethyl.	Sum of fenoxaprop-ethyl and all metabolites which may be converted to 6-chloro-2,3-dihydrobenzoxazol-2-one, expressed as fenoxaprop-ethyl. There is no obvious difference in the metabolic behaviour of the racemic compound fenoxaprop-ethyl and the P-enantiomer. Since the parent compound and its free acid form cannot be considered as valid indicator of the residue situation at harvest, the requirement of an enantio-selective method of analysis is not reasonable. The analytical target is the non enantioselective compound 6-chloro-2,3-dihydrobenzoxazol-2-one.
Residue definition for risk assessment	Sum of fenoxaprop-P-ethyl and all metabolites which may be converted to 6-chloro-2,3-dihydrobenzoxazol-2-one, expressed as fenoxaprop-P-ethyl	Sum of fenoxaprop-P-ethyl and all metabolites which may be converted to 6-chloro-2,3- dihydrobenzoxazol-2-one, expressed as fenoxaprop-P-ethyl.
Conversion factor (monitoring to risk assessment)	None	Not relevant The analytical method determines the sum (total residue) of fenoxaprop-P-ethyl (parent), fenoxaprop-P (acid) and 6-chloro-2,3- dihydrobenzoxazol-2-one (AE F054014). The analytical target is AE F054014.

B.7.2.3.2. *Animals*

No new metabolism study in livestock was submitted for the purpose of renewal of the active substance approval. Studies on laying hens, cow and lactating goats have previously evaluated in the submission for Annex I inclusion under 91/414/EEC and deemed acceptable following peer review at EU level.

The metabolism studies were conducted with the radiolabeled racemic compound fenoxaprop-ethyl (AE F033171) only. The comparison with the rat metabolism showed an identical pathway for both the racemic compound AE F033171 and the P-enatiomer AE F046360, thus no metabolism studies with the P-enantiomer have been required.

Fenoxaprop-ethyl (AE F033171) or its degradation products were excreted almost completely by farm animals showing no accumulating behaviour following repeated administration to ruminats or poultry. There were also no signs for a significant transfer of residues into eggs, milk or tissues.

The metabolism of fenoxaprop-P-ethyl in livestock involves hydrolysis into fenoxaprop acid and further cleavage of the ether bond forming chlorobenzoxazolone (AE F054014) and HOPP acid (AE F020686) This is in agreement with the findings of the rat metabolism study where hydrolysis to fenoxaprop-P is also the primary step of the metabolic pathway. The principle metabolic steps are consistent in rat, hen and goat.

During the EU review for Annex I inclusion under 91/414/EEC no residue definition for livestock was considered necessary.

For the purpose of renewal of the active substance approval **a new analytical method for animal matrices** *Validation of analytical BCS method 01316 for the determination of residues of fenoxaprop-P-ethyl and its metabolites fenoxaprop-P and AE F054014 (using LC-MS/MS in animal tissues: liver, kidney, muscle, milk, egg, fat)" (*please refer to B.5.2.1) has been submitted. Specimen material was extracted under acidic organic conditions. At these conditions fenoxaprop-P-ethyl (AE F046360) and fenoxaprop P acid (AE F088406) are converted into benzoxazolone AE F054014 (6-chloro-2,3- dihydrobenzoxazol-2-one). After clean up the residue

extract was then analysed for residues of AE F054014 by HPLC-MS/MS for two mass transitions.

With respect to the no-residue situation in grain and the low uptake of fenoxaprop residues by lactating cows from straw of treated cereals it is justified to determine AE F054014 as the only analytical target for monitoring purposes. Considering that the parent compound and its free acid form cannot be considered as valid indicator, the requirement of an enantio-selective method of analysis is not reasonable since the analytical target is 6-chloro-2,3- dihydrobenzoxazol-2-one. Therefore the residue definition for monitoring and risk assessment for the purpose of renewal of the active substance approval is proposed as outlined in the table below compared to the residue definition as decided during 91/414 peer review (EFSA, 2007).

Table 7.2.3.2-1 Existing and proposed residue definitions for fenoxaprop-P-ethyl in livestock

	Residue defintion	
	EFSA conclusion **[EFSA Scientific Report (2007) 121, 1-76]**	**Proposal for purpose of renewal**
Residue definition for monitoring	Not required	Sum of fenoxaprop-ethyl and all metabolites which may be converted to 6-chloro-2,3-dihydrobenzoxazol-2-one, expressed as fenoxaprop-ethyl. The parent compound and its free acid form cannot be considered as valid indicator for monitoring since the analytical target is the non enantioselective compound 6-chloro-2,3- dihydrobenzoxazol-2-one. The requirement of an enantio-selective method of analysis is not reasonable.
Residue definition for risk assessment	Not required	Sum of fenoxaprop-P-ethyl and all metabolites which may be converted to 6-chloro-2,3- dihydrobenzoxazol-2-one, expressed as fenoxaprop-P-ethyl.
Conversion factor (monitoring to risk assessment)	None	Not relevant The analytical method determines the sum (total residue) of fenoxaprop-P-ethyl (parent), fenoxaprop-P (acid) and 6-chloro-2,3- dihydrobenzoxazol-2-one (AE F054014). Analytical target is the non enantioselective compound 6-chloro-2,3- dihydrobenzoxazol-2-one.

B.7.3. MAGNITUDE OF RESIDUE TRIALS IN PLANTS

The magnitude of residues on treated cereal crops has previously been investigated in a number of supervised residue trial studies on wheat, barley and rye. These trials were included within the submission for Annex I inclusion under 91/414/EEC and were deemed acceptable following evaluation and peer review at EU level (Review Report SANCO/3778/2007). The representative uses and critical GAPs of fenoxaprop-P-ethyl for the purpose of renewal of the active substance approval and for Annex I inclusion under 91/414/EEC (marked grey) are outlined in the table below.

Table 7.2.3.2-1 Critical EU GAPs for fenoxaprop-P-ethyl

Type of GAP	Crop	Region	Application details			PHI (d)	Reference
			Method / growth stage	No of applications	Max. Rate (kg as/ha)		
Renewal	Wheat, durum wheat, rye, triticale	NEU SEU	spraying / BBCH 11-39	1	0.083	F	Dossier for renewal of the a.s.
	Barley	NEU SEU	spraying / BBCH 12-32	1	0.083	F	
DAR, 2005	Wheat (s+w), durum wheat, raye, w-rye, tricale, barley (s+w)	NEU SEU	spraying / BBCH 10-32	1	0.083	F	EFSA Scientific Report (2007) 121, 1-76

F= preharvest interval is determined by the vegetation period of the crop

Fenoxaprop-P-ethyl (Hoe 046360) was applied post-emergence to annual grass weeds from the two-leaf stage up to tillering in cereals (wheat, rye and barley). The Fenoxaprop-P-ethyl based oil in water formulation (69 g/L active substance) contain 75 g/L of the safener Mefenpyr-diethyl (Hoe 107892), which is absorbed by the foliage in a similar manner as the herbicide itself. The safener enhances the rate of Fenoxaprop-P-ethyl metabolism via the free acid Fenoxaprop-P to water soluble, non phytotoxic products without changing the metabolic pathway.

Table 7.2.3.2-2 Overview on the residue trials in cereals (DAR, 2005 and newly submitted trials)

Crop	Region	Growth stage	Number of Trials				Total	Reference
		Vegetation period	1991	1992	1995	1996		
Wheat (s+w)	NEU	BBCH 29-31	2	3		2	7	DAR, 2005
	SEU	BBCH 29-31				2	2	
	SEU	BBCH 37-41			11		11	
Rye (s+w)	NEU	BBCH 29-31	2	2			4	
Barley (s+w)	NEU	BBCH 29-31	2	1			3	
	SEU	BBCH 29-31	2				2	
							29	
		Vegetation period	2010	2011	2013	2014		
Wheat	NEU	BBCH 39			4	4	8	KCA 6.3.1/15, KCA 6.3.1/16
	SEU	BBCH 39	4	3			7	KCA 6.3.1/17, KCA 6.3.1/18
							15	

In the DAR (2005) a total of **29 residue trials** on cereals (wheat, barely, rye and durum wheat) were provided. 14 residue trials condcuted in the NEU (Germany, France) and 4 residue trials from the SEU (France, Italy) supporting the use up to growth stage BBCH 32. A total of 11 residue trials on wheat conducted in the SEU (Italy, France, Spain) supporting applications up to BBCH 39. Most of these trials have been carried out by using EW (oil in water) formulations containing the active substance (Hoe 046360) and the safener Mefenpyr-diethyl (Hoe 107892). Fenoxaprop-P-ethyl was applied once per season at an application rate of about 0.08 kg as / ha. The trial locations were spread over the main growing areas of the EU Northern and the EU Southern zone. Samples were taken for analysis from the harvest commodities grain and straw. Additionally for most trials, shoot samples were taken on the day of application (DAA 0) and on later sampling dates in order to determine a decline of residues. The trials were reported in sufficient detail and were supported by acceptable analytical information. All samples were analysed for the parent compound Fenoxaprop-P-ethyl (Hoe 046360) including the metabolites Fenoxaprop-P (Hoe 088406) and chlorobenzoxazolone (Hoe 054014) by GC in combination with an ECD and MSD, respectively.

Findings:

Fenoxaprop-P-ethyl (Hoe 046360) was applied to cereals once per season with application rates between 0.083 and 0.089 kg as/ha at BBCH 29-41. In all field trials samples were taken from shoots and the harvest commodities grain and straw. The storage time (< 24 month) and the storage conditions (at or below -18°C) are suitable to obtain reasonable results.

In the residue trials conducted in the EU North (France, Germany) values were in all cases below the LOQ, 0.02 mg/kg for cereal grain and 0.05 mg/kg for cerela straw.

In the residue trials conducted in Spain (2), France (3) and Italy (8), representing the EU-South, the residue values for grain were below the LOQ of 0.02 mg/kg, whereas the residue levels for straw ranged between 0.1 and 0.89 mg/kg.

Additionally all samples were also anaylsed for the safener Mefenpyr-diethyl (Hoe 107892) and its metabolites Hoe 094270 (in grain), Hoe 113225 (shoot and straw) and Hoe 109453 (shoot and straw). No residues above the LOQ (0.01 mg/kg for cereal grain and 0.05 mg/kg for cereal straw) were detected.

Since the cGAP for Annex I inclusion envisaged an application between BBCH 10-32, the residue trials on cereals conducted with applications up to BBCH 39 were not considered for Annex I inclusion of the active substance. A summary of the residue trials evaluated during the EU review (DAR, 2005) of the active substance is given in the tables below.

Table 7.2.3.2-3 Overview of residue trials on cereals evaluated in the EU review (DAR, 2005) conducted in the Northern EU

Trial ID/Trial No Location Country, Year	Commodity/ Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Date of treatment or no. of treatment and last date	Growth stage at last treatment or date	Portion analysed	Residues [mg/kg][#]	PHI [days]	Reference in the dossier for renewal of the a.s.
			g as/ha	water L/ha	kg as/hL						
ER91DEU530 Trial No. 0101 D-2090 Drage-Elbstorf Germany, 1992	Winter Wheat/ Orestis	1) 10/10/90 2) 24/06/91- 08/07/91 3) 15/08/91	87	300	0.029-	1 07/05/91	29-31	Shoot Grain Straw	3.82 0.13 < 0.02* < 0.02* < 0.05*	0 41 63 100 100	KCA 6.3.1_01 Junker, Raquet, Klug, 1993 (A53042)
ER91DEU530 Trial No. 0401 D-6230 F.-Höchst Germany, 1992	Winter Wheat/ Rector	1) 18/10/90 2) 10/06/91- 28/06/91 3) 14/08/91	87	300	0.029	1 07/05/91	29-31	Shoot Grain Straw	2.37 0.064 0.042 < 0.02* < 0.05*	0 31 57 99 99	
ER92DEU530 Trial No. 0401 D-65618 Niederselters Germany, 1992	Spring Wheat/ Star	1) 08/04/92 2) no data 3) 26/08/92	87	300	0.029-	1 21/05/92	29-31	Shoot Grain Straw	6.7 0.15 0.03 < 0.02* < 0.05*	0 27 39 97 97	KCA 6.3.1_02 Junker, Raquet, 1992 (A53045)
ER91DEU532 Trial No. 0101 D-2093-Ashausen Germany, 1991	Winter Rye/ Halo	1) 10/11/90 2) 18/06/91- 02/07/91 3) 15/08/91	87	300	0.029	1/ 09/04/91	29-31	Shoot Grain Straw	6.93 < 0.02* < 0.02* < 0.02* < 0.05*	0 34 75 118 118	KCA 6.3.1_03 Junker, Raquet, Klug, 1993 (A53047)
ER91DEU532 Trial No. 0401 D-6230 F.-Höchst Germany, 1991	Winter Rye/ Danko	1) 18/10/90 2) 27/05/91- 12/06/90	87	300	0.029	1/ 06/08/91	29-31	Shoot Grain Straw	8.1 0.04 0.05 < 0.02* < 0.05*	0 46 88 129 129	
ER91DEU532 Trial No. 0101 D-21435 Stelle-Ashausen Germany, 1992	Winter Rye/ Marder	1) 14/10/91 2) 27/05/92- 08/06/92 3) 07/08/92	87	300	0.029-	1/ 22/04/92	31	Shoot Grain Straw	6.6 0.14 < 0.02 < 0.02* < 0.05*	0 28 50 105 105	KCA 6.3.1_04 Junker, Raquet, 1993 (A53048)
ER91DEU532 Trial No. 0501 D-18190 Niekreuz Germany, 1992	Winter Rye/ Borellos	1) 22/10/91 2) 25/05/92- 04/06/92 3) 19/08/92	87	300	0.029-	1/ 26/04/92	29-31	Shoot Grain Straw	4.5 0.08 < 0.02* < 0.02* < 0.05*	0 26 52 99 99	

Trial ID/Trial No Location Country, Year	Commodity/ Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Date of treatment or no. of treatment and last date	Growth stage at last treatment or date	Portion analysed	Residues [mg/kg][#]	PHI [days]	Reference in the dossier for renewal of the a.s.
			g as/ha	water L/ha	kg as/hL						
ER92DEU531 Trial No 0101. D-21436 Marschacht-Oldershausen Germany, 1992	Winter Barley/ Kendo	1) 19/09/91 2) 18/05/92-27/05/92 3) 08/07/92	87	300	0.029	1/ 21/04/92	29-31	Shoot Grain Straw	5.4 0.21 0.04 < 0.02* < 0.05*	0 28 43 78 78	KCA 6.3.1_05 Junker, Raquet, 1993 (A53049)
ER91DEU531 Trial No.0101 D-2093 Stelle-Ashausen Germany, 1991	Spring Barley/ Alexis	1) 19/03/91 2) 17/06/91-29/06/91 3) 13/08/91	87	300	0.029	1/ 24/05/91	29-31	Shoot Grain Straw	3.8 0.46 0.21 < 0.02* < 0.05*	0 24 39 81 81	KCA 6.3.1_06 Junker, Raquet, Klug, 1993 (A53050)
ER91DEU531 Trial No.0301 D-8906 Gersthofen Germany, 1991	Spring Barley/ Aura	1) 11/04/91 2) 26/06/91-22/07/91 3) 13/08/91	87	300	0.029	1/ 23/05/91	29-31	Shoot Grain Straw	1.5 0.09 0.05 < 0.02* < 0.05*	0 28 46 82 82	
ER91FRA00500 Trial No.0102 95510 Amenucourt France, 1991	Winter wheat/ Artaban	1) 23/11/90 2) no data 3) 14/08/91	82.8	200	0.0414	1/ 11/04/91	29-31	Grain Straw	< 0.02* < 0.05*	125 125	KCA 6.3.1_07 (A50817)
ER91FRA00700 Trial No.0102 95510 Amenucourt France, 1991	Durum wheat/ Ambral	1) 23/11/90 2) no data 3) 14/08/91	82.8	200	0.0414	1/ 11/04/91	29-31	Grain Straw	< 0.02* < 0.05*	125 125	KCA 6.3.1_08 (A50818)
EA960114FR01 62860 Inchy-en-Artois (Pas de Calais) France, 1996	Winter wheat/	1) 07/11/95 2) no data 3) 06/08/96	82.8	300	0.0298	1/ 25/04/96	31	Shoot Grain Straw	3.1 < 0.02* < 0.05*	0 103 103	KCA 6.3.1_14 (A59191)
EA960114FR02 08190 Aire (Ardennes) France, 1996	Winter wheat/	1) 07/10/95 2) no data 3) 06/08/96	82.8	300	0.0298	1/ 26/04/96	31	Shoot Grain Straw	4.9 < 0.02* < 0.05*	0 101 101	

[#]…Residues expressed in mg Fenoxaprop-P-ethyl/kg (Hoe 04630)

Table 7.2.3.2-4 Overview of residue trials on cereals evaluated in the EU review (DAR, 2005) conducted in the Southern EU

Trial ID/Trial No Location Country, Year	Commodity/ Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Date of treatment or no. of treatment and last date	Growth stage at last treatment or date	Portion analysed	Residues [mg/kg][#]	PHI [days]	Reference in the dossier for renewal of the a.s.
			g as/ha	water L/ha	kg as/hL						
ER95ECS510 FRA000102 47200 Taillebourg France, 1995	Common winter wheat/ soissons	1) 28/10/94 2) 04/05/95 3) 06/07/95	87	200	0.0414	1/ 20/04/95	37-41	Shoot Grain Straw	2.3 < 0.02* < 0.02* 0.575	0 32 77 77	KCA 6.3.1_11 Helgers, Idstein, Junker, 1996 (A57042)
ER95ECS510 ESP000102 41310 Brenes/Sevilla Spain, 1995	Common wheat/ Cajeme	1) 19/12/94 2) 23/03/95 3) 19/06/95	82.7	300	0.0276	1/ 16/03/95	39	Shoot Grain Straw	3.1 0.590 < 0.02* 0.11	0 26 95 95	
ER95ECS510 ESP000202 41310 Brenes/Sevilla Spain, 1995	Common wheat/ Mexa	1) 19/12/94 2) 20/03/95 3) 19/06/95	82.7	300	0.0276	1/ 16/03/95	39	Shoot Grain Straw	2.3 0.57 < 0.02* 0.1	0 26 95 95	
ER95ECS510 ITA000102 71024 Candela Italy, 1995	Durum wheat/ Simeto	1) 20/11/94 2) no data 3) 22/06/95	82.7	300	0.0276	1/ 13/04/95	39	Shoot Grain Straw	1.1 0.09 < 0.02* 0.270	0 42 70 70	
ER95ECS510 ITA000202 85025 Melfi Italy, 1995	Durum wheat/ Duilio	1) 10/12/94 2) no data 3) 20/06/95	82.7	300	0.0276	1/ 13/04/95	39	Shoot Grain Straw	0.86 0.08 < 0.02* 0.22	0 42 68 68	
ER95ECS510 ITA000302 71100 Foggia Italy, 1995	Durum wheat/ Ofanto	1) 02/12/94 2) no data 3) 16/06/95	82.7	300	0.0276	1/ 11/04/95	37-39	Shoot Grain Straw	1.7 0.3533 < 0.02* 0.23	0 43 66 66	
ER95ECS510 ITA000402 71048 Stornarella Italy, 1995	Durum wheat/ Simeto	1) 10/12/94 2) no data 3) 26/06/95	82.7	300	0.0276	1/ 20/04/95	37-39	Shoot Grain Straw	1.5 0.42 < 0.02* 0.89	0 35 59 59	

Trial ID/Trial No Location Country, Year	Commodity/ Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Date of treatment or no. of treatment and last date	Growth stage at last treatment or date	Portion analysed	Residues [mg/kg][#]	PHI [days]	Reference in the dossier for renewal of the a.s.
			g as/ha	water L/ha	kg as/hL						
ER95ECS510 ITA000502 71022 Ascoli Satriano Italy, 1995	Durum wheat/ Appulo	1) 10/12/94 2) no data 3) 26/06/95	82.7	300	0.0276	1/ 20/04/95	37-39	Shoot Grain Straw	4.2 0.69 < 0.02* 0.57	0 34 67 67	
ER95ECS510 ITA000602 71024 Candela Italy, 1995	Durum wheat/ Ofanto	1) 10/12/94 2) no data 3) 26/06/95	82.7	300	0.0276	1/ 29/04/95	39	Shoot Grain Straw	5.1 0.47 < 0.02* 0.725	0 25 58 58	
ER91FRA00600 Trial No.0102 60510 Fay St. Quentin France, 1991	Winter barley/ Plaisant	1) 03/10/90 2) no data 3) 29/07/91	82.8	200	0.0414	1/ 09/04/91	29-31	Grain Straw	< 0.02* < 0.05*	111 111	KCA 6.3.1_09 (A50836)
ER91FRA00600 Trial No.0202 47200 Taillebourg France, 1991	Winter barley/ Baraka	1) 29/11/90 2) 16/05/91-29/05/91 3) 08/07/91	82.8	200	0.0414	1/ 29/03/91	29-31	Grain Straw	< 0.02* < 0.05*	101 101	KCA 6.3.1_10 (A50837)
ER95ECS510 ITA000303 71100 Foggia Italy, 1995	Durum wheat/ Ofanto	1) 02/12/94 2) no data 3) 16/06/95	83.9	300	0.028	1/ 11/04/95	37-39	Shoot Grain Straw	2.25 0.27 < 0.02* 0.2	0 43 66 66	
ER95ECS510 ITA000403 71048 Stornarella Italy, 1995	Durum wheat/ Simento	1) 10/12/94 2) no data 3) 16/06/95	83.6	300	0.0279	1/ 18/04/95	39	Shoot Grain Straw	4.0 0.42 < 0.02* 0.74	0 35 59 59	
EA960114FR03 32130 Labastide Saves France, 1996	Winter wheat/	4) 10/11/95 5) no data 6) 11/07/96	82.8	300	0.0298	1/ 25/03/96	31	Shoot Grain Straw	3.2 < 0.02* < 0.05*	0 108 108	KCA 6.3.1_14 (A59191)
EA960114FR04 82370 Corbarieu France, 1996	Winter wheat/	4) 20/11/95 5) no data 6) 10/07/96	82.8	300	0.0298	1/ 05/04/96	31	Shoot Grain Straw	3.7 < 0.02* 0.05	0 96 96	

[#]…Residues expressed in mg Fenoxaprop-P-ethyl/kg

For the **purpose of renewal** of the active substance approval **additional 15 residue trials** were provided.
8 additional trials on wheat conducted in the NEU (Netherlands, Belgium, Germany, France, UK) and 7 residue trials on wheat conducted in the SEU (Spain, Portugal, France, Italy, Greece) supporting applications up to growth stage BBCH 39 were submitted. The new trials were analysed according to the same method principle but with lower LOQs.

Analytical Method 00874/M001 (fenoxaprop-P-ethyl)

Shoot, straw and grain samples were analysed for fenoxaprop-P-ethyl (AE F046360) (including its metabolites AE F088406, AE F054014 and corresponding conjugates) following extraction via reflux for five hours with acetonitrile/concentrated hydrochloric acid (9/1, v/v). During this process fenoxaprop-P-ethyl and fenoxaprop-P (AE F088406) are converted to the benzoxazolone metabolite AE F054014. Therefore the determination of AE F054014 represents a sum parameter including the analytes fenoxaprop-P-ethyl (AE F046360), fenoxaprop-P (AE F088406), benzoxazolone metabolite (AE F054014) and corresponding conjugates. After addition of de-ionised water the refluxed sample extract is filtered and made up to volume with acetonitrile/water (1/1, v/v). An aliquot is evaporated to the aqueous remainder. Water is added and the extract is cleaned via Chromabond XTR cartridge. The eluate is evaporated to dryness and the remainder is dissolved in acetonitrile/water (1/1, v/v) using ultrasonication. The final extract is subjected to HPLC-MS/MS using mass transition 167.8 → 131.8. The analytical target is AE F054014.

The quantification was done by external standardisation with matrix-matched standards. During each set of analysis, a calibration curve was established with at least five concentration levels and used for the quantitation. For each calibration curve, the correlation coefficient R was above 0.99. The **LOQ**, defined as the lowest validated fortification level, was **0.01 mg/kg for all sample materials** (cereal grain, cereal green material and straw).

The residue analytical method 00874/M001 is suitable to determine residues of fenoxaprop-P-ethyl (AE F046360) and its metabolites in cereal grain and cereal straw and complies to the SANCO guideline 825/00 rev 8.1. For further details please refer to Volume 3, B.5.2.1

Mefenpyr-diethyl (Safener)

Mefenpyr-diethyl is a safener used in combination with herbicides and was not reviewed under Directive 91/414/EEC. In order to facilitate the re-registration / zonal assessment of products containing mefenpyr-diethyl, France and Austria in a work-sharing project prepared an assessment report for this substance in the format of a DAR. France was responsible for the sections “Phys-Chem Properties” (B.1-B.5), Environmental Fate and Ecotoxicology (B.8-B.9) and Austria for sections Toxicology and Residue Data (B.6-B.7). A bilateral peer-review in the form of comments took place between the two rapporteurs; the respective reporting tables were made available to be “peer-reviewed” (in an unscheduled procedure on voluntary basis) by all MS. The revised assessment report is available on CIRCABC.
However for purpose of renewal of the active substance approval for fenoxaprop-P-ethyl no assessment on the safener mefenpyr-diethyl was conducted.

B.7.3.1. New residue trials on Wheat (EU North) – Study 1

Reference:	KCA 6.3.1/15 **Determination of the residues of fenoxaprop-P-ethyl and mefenpyr-diethyl in/on wheat after spray application of Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144 in Germany, Belgium and the Netherlands**
Author(s), year: Report/ Doc. Number:	Schulte, G.; 2015 13-2018
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC EC Guidance working document 7029/VI/95 rev.5 (1997-07-22) OECD 509 Adopted 2009-09-07, OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial US EPA OCSPP Guideline No. 860.1500
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable

Material and Methods:

Fenoxaprop-P-ethyl was applied once to winter wheat or durum wheat at growth stage BBCH 39 (flag leaf stage) at an application rate **0.083 kg fenoxaprop-P-ethyl/ha** (1.2 L/ha). The Fenoxaprop-P-ethyl based oil in water formulation (69 g/L active substance) contained 75 g/L of the safener Mefenpyr-diethyl. No additional adjuvants, surfactants or mixing partners were used for the application.
This study comprised four supervised residue trials with wheat in Germany, Belgium and the Netherlands during the 2013 season. At each trial site there was one untreated plot in addition to the treated plot. The treated and untreated plots were cultivated in the same manner.
In one trial (13-2018-02; Belgium), the test item was underdosed due to a lower product application rate (1093 mL/ha instead of 1200 mL/ha) resulting in an actual application rate of 0.075 kg/ha for fenoxaprop-P-ethyl. The deviation is less than 25% and well within the EU´s standard acceptance criteria for use pattern equality.

Untreated control samples of green material were taken prior to application (BBCH 39) and 7 days after application (BBCH 49-54). Treated samples of green material were taken immediately after application and 3 days (BBCH 39-45), 7 days (BBCH 49-54) and 14 days after application (BBCH 58-65). Samples of untreated and treated grain and straw were taken at harvest, 61-82 days after application (BBCH 89). The field samples were stored in a freezer at -18°C or below until preparation of the examination samples. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample. Shoot, straw and grain samples were analysed for fenoxaprop-P-ethyl (AE F046360) (including its metabolites AE F088406, AE F054014 and corresponding conjugates) according to the common moiety method 00874/M001.

The storage period of deep-frozen untreated and treated samples intended for the analysis of fenoxaprop-P-ethyl and its metabolites ranged up to 617 days for untreated samples and up to 561 days for treated samples. The storage periods are covered by the storage stability studies in grain and straw, i.e. analytes are proven to be stable for a period of at least 24 months (refer to B.7.1.1).

The stability of the final extracts was demonstrated during the validation of the method 00874/M001 for at least two weeks at 4 ± 3 °C.

Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The average recoveries were within the acceptable range of 70 – 110%, the RSD values were below 20%. For the detailed results see the table below.

Table 7.2.3.2-1 Concurrent Recovery data for fenoxaprop-P-ethyl in wheat

Study Trial No. Plot No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
13-2018 13-2018-01 13-2018-01-T GLP: yes 2013	Wheat	green material	fenoxaprop-P-ethyl	2	0.01	86; 99	86	99	93	
				2	0.1	79; 96	79	96	88	
				1	1.0	82	82	82	82	
				1	6.0	92	92	92	92	
				1	15	104	104	104	104	
						overall	**79**	**104**	**91**	10.1
		Grain	fenoxaprop-P-ethyl	1	0.01	101	101	101	101	
				1	0.1	110	110	110	110	
				1	1.0	83	83	83	83	
						overall	**83**	**110**	**98**	14
		Straw	fenoxaprop-P-ethyl	1	0.01	92	92	92	92	
				1	0.1	84	84	84	84	
				1	1.0	74	74	74	74	
						overall	**74**	**92**	**83**	10.8

Fortified with fenoxaprop-P-ethyl, determined as AE F054014 and calculated as fenoxaprop-P-ethy

Findings:

No residues of fenoxaprop-P-ethyl (sum parameter for fenoxaprop-P-ethyl, fenoxaprop-P and AE F 054014, determined as AE F 054014) above the limit of quantification of the method were found in any of the untreated samples. In all treated grain samples, residues of fenoxaprop-P-ethyl were below LOQ (<0.01 mg/kg). In treated green matter, initial residues of fenoxaprop-P-ethyl ranged between 2.0-13 mg/kg, declining to 0.37-3.0 mg/kg, 0.35-1.6 mg/kg and 0.22-0.32 mg/kg after 3, 7 and 14 days, respectively. Residues of fenoxaprop-P-ethyl in treated straw at harvest amounted to 0.14- 0.45 mg/kg. The results are summarised in the table below.

Table 7.2.3.2-2 Residue summary for fenoxaprop-P-ethyl on wheat samples in the EU North- Study 1

Trial No. / Location / Country Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s/ha	Water (l/ha)	g a.s/hl				Fenoxaprop-P-ethyl		
	(a)	(b)				(c)				(d)	(e)
13-2018-01 51399 Burscheid Germany, 2013	Wheat Winnetou; Winter wheat	1) 29.10.2012 2) 17.06.2013 - 24.06.2013 3) 10.08.2013 - 31.08.2013	82.8	300	27.6	03.06.2013/0	39	green material grain straw	11 3.0 1.6 0.32 <0.01 0.14	0 3 7 14 82 82	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 359 days/377 days green material: 514 days/511 days grain: 457 days/475 days
13-2018-02 6210 Villers-Perwin Belgium, 2013	Wheat Matrix; Winter variety with good yield	1) 20.10.2012 2) 18.06.2013 - 03.07.2013 3) 05.08.2013 - 12.08.2013	75	273	28	06.06.2013/0	39	green material grain straw	13 1.8 0.41 0.23 <0.01 0.25	0 3 7 14 61 61	
13-2018-03 1771 SJ Wieringerwerf Netherlands, 2013	Wheat Touareg; Winterwheat with a high yield	1) 30.11.2012 2) 23.06.2013 - 07.07.2013 3) 18.08.2013 - 25.08.2013	82.8	300	27.6	07.06.2013/0	39	green material grain straw	2.6 1.1 0.45 0.29 <0.01 0.45	0 3 7 14 76 76	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 361 days/369 days green material: 515 days/511 days grain: 459 days/561 days
13-2018-04 13-2018-04-T Netherlands 2132 MG Hoofddorp Europe, North F 2013	Wheat Tabasco; Very late, food wheat (biscuit	1) 17.11.2012 2) 24.06.2013 - 03.07.2013 3) 10.08.2013 - 20.08.2013	82.8	300	27.6	11.06.2013/0	39	green material grain straw	2.0 0.37 0.35 0.22 <0.01 0.34	0 3 7 14 64 64	

Analyte: fenoxaprop-P-ethyl, fenoxaprop-P, AE F054014
Final determination as: AE F054014
Residues calculated as: fenoxaprop-P-ethyl

B.7.3.2. New residue trials on Wheat (EU North) - Study 2

Reference:	KCA 6.3.1/16 **Determination of the residues of mefenpyr-diethyl and fenoxaprop-P-ethyl in/on wheat after spray application of Fenoxaprop-p-ethyl & Mefenpyr-diethyl EW 144 in Germany, the United Kingdom and northern France**
Author(s), year:	Braune, M.; van Berkum, S.; 2016
Report/ Doc. Number:	14-2006
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop field Trials
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable

Material and Methods:

Fenoxaprop-P-ethyl was applied once to wheat at growth stage BBCH 39 (flag leaf stage) at an application rate **0.083 kg fenoxaprop-P-ethyl/ha** (1.2 L/ha). The Fenoxaprop-P-ethyl based oil in water formulation (69 g/L active substance) contained 75 g/L of the safener Mefenpyr-diethyl.
This study comprised four supervised residue trials with wheat in Germany, France and Great Britain during the 2014 season. At each trial site there was one untreated plot in addition to the treated plot. The treated and untreated plots were cultivated in the same manner. No additional adjuvants, surfactants or mixing partners were used for the application.

Untreated control samples of green material were taken prior to application (BBCH 39), treated samples of green material were taken immediately after application. Samples of untreated and treated grain and straw were taken at harvest, 62-84 days after application (BBCH 89). The field samples were stored in a freezer at -18°C or below until preparation of the examination samples. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample. Shoot, straw and grain samples were analysed for fenoxaprop-P-ethyl (AE F046360) (including its metabolites AE F088406, AE F054014 and corresponding conjugates) according to the common moiety method 00874/M001.

The storage period of deep-frozen untreated and treated samples intended for the analysis of fenoxaprop-P-ethyl and its metabolites ranged up to 471 days for untreated samples and up to 546 days for treated samples. The storage periods are covered by the storage stability studies in grain and straw, i.e. analytes are proven to be stable for a period of at least 24 months (refer to B.7.1.1).

The stability of the final extracts was demonstrated during the validation of the method 00874/M001 for at least two weeks at 4 ± 3 °C.

Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The average recoveries were within the acceptable range of 70 – 110%, the RSD values were below 20%. For the detailed results see the table below.

Table 7.2.3.2-1 Concurrent Recovery data for fenoxaprop-P-ethyl in wheat

Study Trial No. Plot No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
14-2006 14-2006-01 14-2006-01-T GLP: yes 2014	Wheat	green material	fenoxaprop-P-ethyl	2	0.01	96,87	87	96	92	
				1	0.1	96	96	96	-	
				1	10	99	99	99	-	
						overall	**87**	**99**	**95**	5.5
		Grain	fenoxaprop-P-ethyl	2	0.01	80,98	80	98	89	
						overall	**80**	**98**	**89**	-
		Straw	fenoxaprop-P-ethyl	2	0.01	93,95	93	95	94	
				1	0.1	108	108	108	-	
				1	0.6	90	90	90	-	
						overall	**90**	**108**	**97**	8.2

Fortified with fenoxaprop-P-ethyl, determined as AE F054014 and calculated as fenoxaprop-P-ethy

Findings:
No residues of fenoxaprop-P-ethyl (sum parameter for fenoxaprop-P-ethyl, fenoxaprop-P and AE F 054014, determined as AE F 054014) above the limit of quantification of the method were found in any of the untreated samples. In all treated grain samples, residues of fenoxaprop-P-ethyl were below LOQ (<0.01 mg/kg). In treated green matter, initial residues of fenoxaprop-P-ethyl ranged between 1.6-2.3 mg/kg. Residues of fenoxaprop-P-ethyl in treated straw at harvest amounted to 0.07- 0.34 mg/kg. The results are summarised in the table below.

Table 7.2.3.2-2 Residue summary for fenoxaprop-P-ethyl on wheat samples in the EU North- Study 2

Trial No. / Location / Country Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s/ha	Water (l/ha)	g a.s/hl				Fenoxaprop-P-ethyl		
	(a)	(b)				(c)				(d)	(e)
14-2006-01 51399 Burscheid Germany, 2014	Wheat Tobak; Winter wheat	1) 30.09.2013 2) 26.05.2014 - 02.06.2014 3) 15.07.2014 - 15.08.2014	82.8	300	27.6	05.05.2014/0	39	Green material grain straw	1.8 < 0.01 0.7	0 84 84	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 459 days/463 days green material: 534days/523 days grain: 452 days/456 days
14-2006-01 59457 Werl Germany, 2014	Wheat Winnetou; wheat, winter	1) 30.10.2013 2) 01.06.2014 - 15.06.2014 3) 15.07.2014 - 20.08.2014	82.8	300	27.6	16.05.2014/0	39	Green material grain straw	1.6 < 0.01 0.20	0 69 69	
14-2006-03 SG8 8SS Great Chishill, Royston UK, 2014	Wheat Solstice	1) 11.10.2013 2) 01.06.2014 - 16.06.2014 3) 25.07.2014 - 14.08.2014	82.8	200	41.4	19.05.2014/0	41	Green material grain straw	1.9 < 0.01 0.34	0 72 72	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 457 days/471 days green material: 520days/546 days grain: 450 days/464 days
14-2006-04 37310 Chambourg sur Indre France, 2014	Wheat Rustic; Winter wheat	1) 20.10.2013 2) 15.05.2014 - 25.05.2014 3) 01.07.2014 - 20.07.2014	82.8	300	27.6	23.04.2014/0	39	Green material grain straw	2.3 < 0.01 0.27	0 84 84	

Analyte: fenoxaprop-P-ethyl, fenoxaprop-P, AE F054014
Final determination as: AE F054014
Residues calculated as: fenoxaprop-P-ethyl

B.7.3.3. New residue trials on Wheat (EU South) – Study 1

Reference:	KCA 6.3.1/17 **Determination of the residues of fenoxaprop-p-ethyl and mefenpyr-diethyl in/on wheat and wheat, durum after spray application of Fenoxaprop-p-ethyl & Mefenpyr-diethyl EW 144 in the field in Spain, Portugal, southern France and Italy**
Author(s), year:	Schulte, G.; Reineke, A.; 2011
Report/ Doc. Number:	10-229
Guideline(s):	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC guidance working document 7029/VI/95 rev. 5 (1997-07-22)
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable

Material and Methods:

Fenoxaprop-P-ethyl was applied once to wheat or durum wheat at growth stage BBCH 39 (flag leaf stage) at an application rate **0.083 kg fenoxaprop-P-ethyl/ha** (1.2 L/ha). The Fenoxaprop-P-ethyl based oil in water formulation (69 g/L active substance) contained 75 g/L of the safener Mefenpyr-diethyl. No additional adjuvants, surfactants or mixing partners were used for the application.
This study comprised four supervised residue trials with wheat in Spain, Potugal, France and Italy during the 2010 season. At each trial site there was one untreated plot in addition to the treated plot. The treated and untreated plots were cultivated in the same manner.

Untreated control samples of green material were taken prior to application (BBCH 39), treated samples of green material were taken immediately after application. Samples of untreated and treated grain and straw were taken at harvest, 59-77 days after application (BBCH 89). The field samples were stored in a freezer at -18°C or below until preparation of the examination samples. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample. Shoot, straw and grain samples were analysed for fenoxaprop-P-ethyl (AE F046360) (including its metabolites AE F088406, AE F054014 and corresponding conjugates) according to the common moiety method 00874/M001.

The storage period of deep-frozen untreated and treated samples intended for the analysis of fenoxaprop-P-ethyl and its metabolites ranged up to 399 days for untreated samples and up to 397 days for treated samples. The storage periods are covered by the storage stability studies in grain and straw, i.e. analytes are proven to be stable for a period of at least 24 months (refer to B.7.2.1.1B.7.1.1).

The stability of the final extracts was demonstrated during the validation of the method 00874/M001 for at least two weeks at 4 ± 3 °C.

Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The average recoveries were within the acceptable range of 70 – 110%, the RSD values were below 20%. For the detailed results see the table below.

Table 7.2.3.2-1 Concurrent Recovery data for fenoxaprop-P-ethyl in wheat

Study Trial No. Plot No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortifi-cation level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
10-2209 10-2209-01 10-2209-01-T GLP: yes 2011	Wheat	green material	fenoxaprop-P-ethyl	4	0.01	79, 102, 75, 95	75	102	87	14.2
				2	0.5	112, 105	105	112	109	-
				2	5.0	111, 109	109	111	110	-
						overall	**75**	**112**	**98**	14.8
		Grain	fenoxaprop-P-ethyl	4	0.01	70, 78, 73, 74	70	78	74	4.5
				2	0.5	77, 79	77	79	78	-
						overall	**70**	**79**	**75**	4.6
		Straw	fenoxaprop-P-ethyl	4	0.01	74, 77, 70, 82	70	78	76	6.7
				2	0.5	73, 72	72	73	73	-
						overall	**70**	**82**	**75**	5.7

Fortified with fenoxaprop-P-ethyl, determined as AE F054014 and calculated as fenoxaprop-P-ethy

Findings:

No residues of fenoxaprop-P-ethyl (sum parameter for fenoxaprop-P-ethyl, fenoxaprop-P and AE F 054014, determined as AE F 054014) above the limit of quantification of the method were found in any of the untreated samples. In all treated grain samples, residues of fenoxaprop-P-ethyl were below LOQ (<0.01 mg/kg). In treated green matter, initial residues of fenoxaprop-P-ethyl ranged between 2.9-4.4 mg/kg. Residues of fenoxaprop-P-ethyl in treated straw at harvest amounted to 0.23- 0.30 mg/kg. The results are summarised in the table below.

Table 7.2.3.2-2 Residue summary for fenoxaprop-P-ethyl on wheat samples in the EU South- Study 1

Trial No. / Location / Country Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s/ha	Water (l/ha)	g a.s/hl				Fenoxaprop-P-ethyl		
	(a)	(b)				(c)				(d)	(e)
10-2209-01 08520 Marata Spain, 2010	Wheat Montcada	1) 16.11.2009 2) 25.04.2010 - 09.05.2010 3) 20.06.2010 - 30.07.2010	0.083	400	0.021	09.04.2010/0	BBCH 39 Flag leaf stage	Green material grain straw	3.0 < 0.01 0.27	0 77 77	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 320 days/314 days green material: 397days/383 days grain: 320 days/314 days
10-2209-02 2580-260 Santana da Carnota, Portugal, 2010	Wheat Pison	1) 20.01.2010 2) 18.05.2010 - 25.05.2010 3) 01.07.2010 - 10.07.2010	0.083	400	0.021	23.04.2010/0	BBCH 39 Flag leaf stage	Green material grain straw	4.4 < 0.01 0.30	0 69 69	
10-2209-03 86380 Vendeuvre Du Poirtou France, 2010	Wheat Ceganne	1) 25.10.2009 2) 24.05.2010 - 31.05.2010 3) 06.07.2010 - 20.07.2010	0.083	300	0.028	05.05.2010/0	BBCH 39 Flag leaf stage	Green material grain straw	3.4 < 0.01 0.23	0 64 64	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg Storage max. : straw: 307 days/310 days green material: 371days/369 days grain: 307 days/310 days
10-2209-04 40128 Bologna Italy, 2010	Wheat, durum Jan Carlo	1) 18.11.2009 2) 05.05.2010 - 20.05.2010 3) 01.07.2010 - 10.07.2010	0.083	350	0.024	07.05.2010/0	BBCH 39 Flag leaf stage	Green material grain straw	2.9 < 0.01 0.29	0 59 59	

Analyte: fenoxaprop-P-ethyl, fenoxaprop-P, AE F054014
Final determination as: AE F054014
Residues calculated as: fenoxaprop-P-ethyl

B.7.3.4. New residue trials on Wheat (EU South) – Study 2

Reference:	KCA 6.3.1/18 **Determination of the residues of fenoxaprop-p-ethyl and mefenpyr-diethyl in/on wheat and durum wheat after spray application of fenoxaprop-p-ethyl & mefenpyr-diethyl EW 144 in the field in Spain, Portugal and Greece**
Author(s), year:	Schulte, G.; 2012
Report/ Doc. Number:	11-2041
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC EC Guidance working document 7029/VI/95 rev.5 (1997-07-22) OECD 509 Adopted 2009-09-07, OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial US EPA OCSPP Guideline No. 860.1500
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable

Material and Methods:

Fenoxaprop-P-ethyl was applied once to winter wheat or durum wheat at growth stage BBCH 39 (flag leaf stage) at an application rate **0.083 kg fenoxaprop-P-ethyl/ha** (1.2 L/ha). The Fenoxaprop-P-ethyl based oil in water formulation (69 g/L active substance) contained 75 g/L of the safener Mefenpyr-diethyl. No additional adjuvants, surfactants or mixing partners were used for the application.
This study comprised three supervised residue trials with wheat in Spain, Portugal and Greece during the 2011 growing season. At each trial site there was one untreated plot in addition to the treated plot. The treated and untreated plots were cultivated in the same manner.
In one trial (11-2041-04, Greece), the test item was underdosed due to a lower application rate (0.062 instead of 0.083 kg as/ha). The deviation is nearly 25%, but nevertheless considered acceptable.

Untreated control samples of green material were taken prior to application (BBCH 39), treated samples of green material were taken immediately after application. Samples of untreated and treated grain and straw were taken at harvest, 59-74 days after application (BBCH 89). The field samples were stored in a freezer at -18°C or below until preparation of the examination samples. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample. Shoot, straw and grain samples were analysed for fenoxaprop-P-ethyl (AE F046360) (including its metabolites AE F088406, AE F054014 and corresponding conjugates) according to the common moiety method 00874/M001.

The storage period of deep-frozen untreated and treated samples intended for the analysis of fenoxaprop-P-ethyl and its metabolites ranged up to 505 days for untreated samples and up to 408 days for treated samples. The storage periods are covered by the storage stability studies in grain and straw, i.e. analytes are proven to be stable for a period of at least 24 months (refer to B.7.1.1).

The stability of the final extracts was demonstrated during the validation of the method 00874/M001 for at least two weeks at 4 ± 3 °C.

Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The average recoveries were within the acceptable range of 70 – 110%, the RSD values were below 20%. For the detailed results see the table below.

Table 7.2.3.2-1 Concurrent Recovery data for fenoxaprop-P-ethyl in wheat

Study Trial No. Plot No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
11-2041 11-2041-01 11-2041-01-T GLP: yes 2011	Wheat	green material	fenoxaprop-P-ethyl	3	0.01	88, 79, 87	79	88	85	5.8
				3	0.10	103, 84, 73	73	103	87	17.5
				1	2.0	71	71	71	71	
						overall	**71**	**103**	**84**	12.9
		Grain	fenoxaprop-P-ethyl	3	0.01	73, 68, 71	71	80	76	6.2
				3	0.10	73, 68, 69	68	73	70	3.8
						overall	**68**	**80**	**73**	6.7
		Straw	fenoxaprop-P-ethyl	3	0.01	80, 95, 80	80	95	85	10.2
				3	0.10	74, 90, 82	74	90	82	9.8
				1	2.0	97	97	97		
						overall				

Fortified with fenoxaprop-P-ethyl, determined as AE F054014 and calculated as fenoxaprop-P-ethy

Findings:

No residues of fenoxaprop-P-ethyl (sum parameter for fenoxaprop-P-ethyl, fenoxaprop-P and AE F 054014, determined as AE F 054014) above the limit of quantification of the method were found in any of the untreated samples. In all treated grain samples, residues of fenoxaprop-P-ethyl were below LOQ (<0.01 mg/kg). In treated green matter, initial residues of fenoxaprop-P-ethyl ranged between 1.1-2.3 mg/kg. Residues of fenoxaprop-P-ethyl in treated straw at harvest amounted to 0.18- 0.42 mg/kg. The results are summarised in the table below.

Table 7.2.3.2-2 Residue summary for fenoxaprop-P-ethyl on wheat samples in the EU South- Study 2

Trial No. / Location / Country Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s/ha	Water (l/ha)	g a.s/hl				Fenoxaprop-P-ethyl		
	(a)	(b)				(c)				(d)	(e)
11-2041-01 E-41610 Paradas Spain, 2011	Wheat ST-4; winter wheat	1) 25.11.2010 2) 05.04.2011 - 15.04.2011 3) 01.06.2011 - 30.06.2011	82.8	300	27.6	21.03.2011/0	39	Green material grain straw	2.3 <u>< 0.01</u> 0.42	0 74 74	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg <u>Storage max. :</u> straw: 355 days/352 days green material: 408days/399 days grain: 353 days/350 days
11-2041-03 P-2005-017 Santarém Portugal, 2011	Wheat Jordão ; Long cicle	1) 27.11.2010 2) 10.04.2011 - 18.04.2011 3) 05.06.2011 - 15.07.2011	82.8	300	27.6	30.03.2011/0	39	Green material grain straw	1.3 <u>< 0.01</u> 0.28	0 68 68	
11-2041-04 GR-60100 Aronas - Pieria Greece, 2011	Wheat Antonio	1) 20.11.2010 2) 12.05.2011 - 19.05.2011 3) 27.06.2011 - 27.06.2011	62.1	300	20.7	26.04.2011/0	39	Green material grain straw	1.1 <u>< 0.01</u> 0.18	0 59 59	Fenoxaprop-P-ethyl & Mefenpyr-diethyl EW 144, SPI:Spraying Merthod 00874/M001 LOQ: 0.01 mg/kg <u>Storage max. :</u> straw: 334 days green material: 372days grain: 332 days

Analyte: fenoxaprop-P-ethyl, fenoxaprop-P, AE F054014
Final determination as: AE F054014
Residues calculated as: fenoxaprop-P-ethyl

B.7.3.5. Overall conclusion on the magnitude of residue trials in plants

A sufficient number of residue trials on cereals (wheat, durum wheat, barley and rye) for both the northern and the southern Europe are available. A total of 26 residue trials (8x NEU, 18x SEU) with application rates between 62-83 g as/ha (within ± 25%) are available supporting BBCH 37-41. To support applications up to BBCH 32 a total of 18 residue trials (14x NEU, 4x SEU) with an application rates of 83 – 87 g as/ha were provided.
The new trials were analysed according to the same method principle but with lower LOQs. No residues in **cereal grain** samples could be determined neither in the residue trials for the EU review (<0.02 mg/kg, LOQ) nor in the newly submitted trials (<0.01 mg/kg, LOQ). Residues in **cereal straw** applied up to growth stage BBCH 32 were below the LOQ of 0.05 mg/kg. Straw residues with trials applied up to BBCH 39 showed residues between 0.1 and 0.89 mg/kg.
According to Guidance Document « *Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs* » (Sanco 7525/VI/95, Rev. 10.2, September 2016) extrapolation from wheat to barley, rye and triticale is considered acceptable since application was before forming of the edible part (before BBCH 51). An overview on the available residue trials is given in the tables below. The original data submitted for Annex I inclusion under 91/414/EEC are marked grey.

Table 7.2.3.2-1 Overview on residue trials covering the supported GAP (1x 83 g as/ha) for BBCH 37-41

Crop	Zone	No of trials	Rate	Growth stage	Residue levels	HR	STMR	Reference
			g as/ha	BBCH	mg/kg	mg/kg	mg/kg	
Wheat grain	NEU	8	75-83	39-41	8x < 0.01*	< 0.01*	< 0.01*	KCA 6.3.1/15, KCA 6.3.1/16
Wheat straw					0.14, 0.2, 0.25, 0.27, 2x 0.34, 0.45, 0.7	0.70	0.31	
	Total	**8**						
Wheat grain	SEU	11	83-87	37-41	11x < 0.02*	< 0.02*	< 0.02*	DAR, 2005
Wheat straw					0.10, 0.11, 0.20, 0.22, 0.23, 0.27, 0.57, 0.58, 0.73, 0.74, 0.89	0.89	0.27	
Wheat grain	SEU	7	83, 62 (1x)	39	7x < 0.01*	< 0.01*	< 0.01*	KCA 6.3.1/17, KCA 6.3.1/18
Wheat straw					0.18, 0.23, 0.27, 0.28, 0.29, 0.30, 0.42	0.42	0.28	
	Total	**18**						

*.. LOQ

Table 7.2.3.2-2 Overview on residue trials covering the supported GAP (1x 83 g as/ha) for BBCH 32

Crop	Zone	No of trials	Rate	Growth stage	Residue levels	HR	STMR	Reference
			g as/ha	BBCH	mg/kg	mg/kg	mg/kg	
Wheat grain	NEU	7	83-87	29-31	7x <0.02*	< 0.02*	< 0.02*	DAR, 2005
Wheat straw					7x <0.05*	< 0.05*	< 0.05*	
Barley grain	NEU	3	87	29-31	3x <0.02*	< 0.02*	< 0.02*	
Barley straw					3x <0.05*	< 0.05*	< 0.05*	
Rye grain	NEU	4	87	29-31	4x <0.02*	< 0.02*	< 0.02*	
Rye straw					4x <0.05*	< 0.05*	< 0.05*	
	Total	**14**						
Wheat grain	SEU	2	83	29-31	2x <0.02*	< 0.02*	< 0.02*	DAR, 2005
Wheat straw					2x <0.05*	< 0.05*	< 0.05*	
Wheat grain	SEU	2	83	29-31	2x <0.02*	< 0.02*	< 0.02*	
Wheat straw					2x <0.05*	< 0.05*	< 0.05*	
	Total	**4**						

*.. LOQ

B.7.4. FEEDING STUDIES

With regard to the representative uses of fenoxaprop-P-ethyl for the purpose of renewal of the active substance, the livestock feedstuffs that may have incurred residues derived from fenoxaprop-P-ethyl are cereal grain and straw.
Livestock dietary burden is calculated using the EFSA dietary burden calculator 2017. The potential levels of fenoxaprop-P-ethyl residues in the total diet of livestock were estimated based on median and highest residue levels observed in these commodities during supervised field trials conducted according to the respective critical GAPs and presented in B.7.3. The input values are summarized in the table below.

Table 7.2.3.2-1 Input values for the dietary burden calculation

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Barley straw	0.05	STMR	0.05	HR
Rye straw[#]	0.28	STMR	0.89	HR
Wheat, triticale straw	0.28	STMR	0.89	HR
Barley grain	0.02	STMR	0.02	HR
Rye grain[#]	0.01	STMR	0.01	HR
Wheat, triticale grain	0.01	STMR	0.01	HR

[#]...extrapolated from wheat

Table 7.2.3.2-2 Results of the dietary burden calculation

Animals	Median dietary burden	Maxiumum dietary burden	Above trigger value	Maximum dietary burden	Highest contributing commodities
	mg/kg bw	mg/kg bw	0.004 mg/kg bw	mg/kg DM	
Beef cattle	0.002	0.005	Yes	0.22	Wheat straw
Dairy cattle	0.003	0.008	Yes	0.22	Wheat straw
Ram/Ewe	0.005	0.014	Yes	0.40	Wheat straw
Lamb	0.006	0.018	Yes	0.43	Wheat straw
Pig (breeding)	0.001	0.001	No	0.02	Barley grain
Pig (finishing)	0.001	0.001	No	0.02	Barley grain
Poultry broiler	0.001	0.001	No	0.02	Wheat gluten meal
Poultry layer	0.004	0.008	Yes	0.12	Wheat straw
Turkey	0.001	0.001	No	0.02	Wheat gluten meal

According to the presented dietary burden calculation the maximum expected dietary burden of fenoxaprop-p-ethyl derived residues was above the EU trigger level of 0.004 mg/kg bw/day in 5 species.
Therefore there is a requirement to consider livestock feeding studies and the potential transfer of residues into food of animal origin for the supported uses of fenoxaprop-P-ethyl.

One new feeeding study in laying hens conducted with [^{14}C]-Fenoxaprop-P-ethyl has been submitted for the purpose of renewal of the active substance approval.

A feeding study on lactating cows has previously been included in the submission for Annex I inclusion under 91/414/EEC. The study was deemed acceptable following evaluation and peer review at EU level. A summary of

the new data and the original submitted data which were considered for the purpose of renewal is presented in the following table.

Table 7.2.3.2-3 Available feeding studies

Animal	No of animals	Analyte	Application rate	Sampling	Reference in the dossier for renewal of the a.s. (Reference in the RAR)	
New submitted study for the purpose of renewal of the active substance approval.						
Laying hens	52	AE F046360 (Fenoxaprop-P-ethyl)	0.11 mg/kg bw (1X) 0.32 mg/kg bw (3X) 1.1 mg/kg bw (10X)	Eggs, tissues (liver, abdominal fat, skin & subcutaneous fat, muscle)	[redacted] 2016	KCA 6.4.1/01 (B.7.4.1)
Originally submitted and evaluated studies (DAR, 2005) to be considered for purpose of renewal						
Lactating cow	3	Hoe 033171 (Fenoxaprop-ethyl) Hoe 054014 (benzoxazolone)	0.2 mg/kg DM (1X) 0.6 mg/kg DM (3X) 2.0 mg/kg DM (10X)	Milk, kidney, liver, muscle, fat	[redacted] 1987a	KCA 6.4.2/01 (B.7.4.2)

B.7.4.1. Poultry

Reference:	KCA 6.4.1/01 ***Fenoxaprop-P-ethyl: Residues of fenoxaprop-P-ethyl and its metabolites in eggs and tissues of laying hens***
Author(s), year:	[redacted] 2016
Report/ Doc. Number:	ENK0021/M-556580-01-1
Guideline(s):	OECD 505 OCSPP 860.1480
GLP:	Yes
Previous evaluation :	New study submitted for the purpose of renewal of a.s. approval
Comment (RMS):	The study is considered acceptable.

The purpose of this study was to quantify the residues of fenoxaprop-P-ethyl (AE F046360), fenoxaprop-P (AE F088406) and its benzoxazolone metabolite (AE F054014) including conjugates in eggs and tissues of laying hens following administration of fenoxaprop-P-ethyl. The study consisted of one control and four treated groups, the test material was administered orally in gelatin capsules for a minimum period of 28 days, to simulate oral ingestion of incurred residues in crops used as feedstuffs.

Animal information:

Species/breed	Bovans Brown (laying strain) domestic fowl (Gallus gallus domesticus)
Number of tested animals	52 females
Age	At least 24 weeks at arrival
Weight (range)	1.45 – 2.28 kg (at start of the treatment)
Egg Production (mean)	0.71 - 1/per bird/day (5-7 eggs/bird/week)
Housing	Group 1 -4 housed in pens of galvanized steel and concrete construction in a purpose built facility which provided a suitable range of environmental conditions for the species. Each pen contained a concentrate feed hopper and a source of fresh drinking water. Wood shavings (analyzed for microbiological and chemical contaminants) were provided as litter; wet litter was removed/replenished as necessary.
Acclimatisation period	approximately 14 days
Diet	Basal diet used with special quality control layer diet in meal

	Form *ad libitum*
Water	Fresh water *ad libitum*
Feed consumption (range)	0.12-0.195 kg/hen/day
Environmental conditions	
Temperature	20 ±4°C
Humidity	40-70 %
Light exposure	16-hour illumination/ 8 hour dark photoperiod

Material and Methods:

Four groups of 12 laying hens (group 2-4) received gelatine capsules containing fenoxaprop-P-ethyl at dose levels of 0.2 mg/bird (1X, group 2), 0.6 mg/bird (3X, group 3) and 2.0 mg/bird (10X, group 4) once daily for at least 28 consecutive days until study terminantion or depuration. One group of 4 hens remained as control (group 1) and received pure carboxymethylcellulose (CMC) throughout the treatment period. An overview on the study design is given in the table below.

Table 7.2.3.2-1 Study design

Group		**Treatment**	**Dose**			**Number of replicate sub-groups**	**Number of birds**	
No	**Dose-level**		mg/bird	mg/kg bw[1]	mg/kg DM		**per group**	**per subgroup**
1	-	Control	-	-	-	1	4	-
2	1X	Fenoxaprop-P-ethyl	0.2	0.11	1.4	3	12	4
3	3X	Fenoxaprop-P-ethyl	0.6	0.32	4.2	3	12	4
4	10X	Fenoxaprop-P-ethyl	2	1.1	15	3	12	4
4a	10X D	Fenoxaprop-P-ethyl	2	1.1	13	3	12	4

4a = Depuration group [1]… based on a mean body weight of ca. 1.82 kg

The birds were observed at least twice daily for any clinical abnormalities or signs of reaction to treatment. Body weights were determined at intervals and food consumption was monitored weekly. Egg production was recorded daily on a pen basis. Egg samples were taken from all replicates daily throughout the test period and were submitted for assay or stored frozen. All eggs produced from Day -1 to termination were collected and wiped with a clean damp towel. Egg samples were taken for analysis on Days -1, 1, 3, 5, 7, 10, 14, 21, 28, 30*, 31*, 35* and 37* (* = depuration phase). The egg contents (whites + yolks combined, shells discarded) of eggs during the study were pooled within each sub-group, giving one composite sample per time point in Group 1, three unique composite samples each per time point in Groups 2, 3 and 4 and two unique composite samples in Group 4a (depuration). The fresh egg samples submitted for analysis were assayed during the study to allow the occurrence and accumulation of residues to be monitored and to provide confirmation that residue concentration reached steady state during the treatment period (no evidence of continuing accumulation, i.e. evidence of attainment of plateau concentrations). All eggs produced on other days (i.e. those not selected for analysis) were stored frozen (nominally at -20°C) as whole eggs in suitably labeled plastic containers; however, they were not subsequently analyzed.

At termination of the experimental period (birds were dosed up to and including the day of termination), all hens were sacrificed within 6 hours after final dose administration (Groups 1-4, zero withdrawal) and 3, 7 and 10 days after final dose administration (depuration, Group 4a, 1 sub-group at each time point) by cervical dislocation/exsanguination followed by a macroscopic post mortem examination. Selected tissues (skin, underlaying subcutaneous fat, skeletal muscle, abdominal fat as available and liver as whole organ) were retained for determination of residue concentrations. Individual organ/tissue weights were not reported. For each tissue, the samples from all 4 birds in each sub-group were coarsely chopped, pooled and mixed, giving three unique composite samples per tissue type per treatment group. These samples were divided into two aliquots.

Analytical procedure

The analytical methods used in this study were designed to determine Fenoxaprop-P-ethyl and any metabolites hydrolysable to benzoxazolone in samples of egg, muscle, liver and fat. The methods were validated for active ingredients Fenoxaprop-P-ethyl, Fenoxaprop P and benzoxazolone at 0.01 mg/kg and 0.1 mg/kg ai in the investigated hen tissues and eggs in the separate validation study ENK0020 (Burton 2016; B.5.1.2.3). The LOD of the analytical system for benzoxazolone was shown to be 0.01 ng/mL (approximately 0.001 mg/kg Fenoxaprop-P-ethyl equivalents in chicken egg, muscle and liver and 0.002 mg/kg Fenoxaprop-P-ethyl equivalents in fat).

Egg samples (shell removed) were received either frozen or refrigerated. Frozen samples were defrosted as required and homogenised in the receipt pot by whisking vigorously with a fork until homogenous in appearance. These were weighed for analysis and excess egg sample stored at approximately -20°C.
Muscle, liver, subcutaneous fat and abdominal fat samples stored at approximately -20°C were homogenised in frozen condition with dry ice in a blender and left in a freezer for at least 16 hours for the dry ice to sublime prior to weighing for analysis.
The analytical method comprised of extraction and hydrolysis of the respective sub-sample (5g) with acetonitrile:hydrochloric acid (90:10 v:v). During this process Fenoxaprop-P-ethyl, Fenoxaprop-P and conjugates are extracted and hydrolysed to produce an extract of the common moiety benzoxazolone. For egg samples the homogenate is heated at 73°C for 6 hours, with swirling every 30 minutes and a 30 minute shake to extract and hydrolyse residues to benzoxazolone. For tissue samples the homogenate is heated under reflux conditions for 5 hours using a mantle and condenser to extract and hydrolyse residues to benzoxazolone. Blood samples are heated in a sealed glass tube on a heating block for 5 hours. The reactant mixture is subjected to SPE clean-up using an HLB cartridge. Extracts of skin/fat were subjected to additional SPE clean-up using a PSA cartridge. Quantitation was performed using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS) monitoring two ion transitions (m/z 168>132 and m/z 170>132) to satisfy the confirmatory analysis requirement.
Found residue concentrations were presented in terms of Fenoxaprop-P-ethyl equivalents. Procedural recovery samples were prepared and analysed concurrent with study samples fortifying sub-samples of control matrix with a known volume of Fenoxaprop-P-ethyl, Fenoxaprop-P or benzoxazolone standard solution and subjecting them to the analytical procedure.

Table 7.2.3.2-2 Procedural recoveries in the hen feeding study

Analyte	Matrix	Fortification level (mg/kg)	n	Recovery single values (%)	Mean recovery (%)
Fenoxaprop-P-ethyl	Egg	0.01	7	102, 96, 99, 98, 99, 94, 107	99
		0.1	5	93, 98, 102, 102, 100	99
	Muscle	0.01	1	98	-
	Liver	0.01	1	93	-
		2	2	98, 104	101
	Fat	0.01	1	91	-
		0.1	1	96	-
		0.25	2	97, 99	98
Fenoxaprop-P	Egg	0.01	7	90, 93, 88, 93, 93, 87, 94	91
		0.1	5	95, 101, 98, 104, 90	98
	Muscle	0.1	1	109	-
	Liver	0.1	1	97	-
		2	2	91, 98	95
	Fat	0.1	2	97, 100	99
		0.25	2	99, 105	102
Benzoxazolone	Egg	0.01	6	98, 101, 92, 96, 97, 96	97
		0.1	6	104, 94, 97, 99, 97, 94	98
	Muscle	0.1	1	104	-
	Liver	0.1	1	96	-
		2	2	95, 99	97
	Fat	0.01	1	100	-
		0.1	1	102	-
		0.25	2	99, 105	102

Findings:

No fenoxaprop-P-ethyl derived residues were detected in any samples from untreated birds during the study. Food consumption remained generally constant during the study period.

Eggs:

There was no evidence that treatment with fenoxaprop-P-ethyl influenced the egg production. Mean egg production remained generally constant during the study period at approximately 5 to 7 eggs per bird per week (0.71 – 1 eggs per bird per day).

During days 1 to 3 no residues of fenoxaprop-P-ethyl AE F046360 (<0.0025 mg/kg) could be detected in eggs of animals dosed at 0.2 mg/bird (1X). Starting with day 4 residues below the limit of quantitation (0.01 mg/kg) could be observed and stayed at that level for the remaining sampling points throughout the study. In the treated group dosed at 0.6 mg/bird (3X) fenoxaprop-P-ethyl equivalent residues were seen from day 5 or 7 these levels were at or below the limit of quantitation (0.01 mg/kg). Quantifiable residues occurred in all animals in the treated group dosed at 2 mg/bird (10X) from day 3 of the study. Levels generally increased over the treatment period and reached a plateau concentration during the second week of dose administration. The results are summarized below.

Table 7.2.3.2-3 Summary of Fenoxaprop-P-ethyl equivalents in eggs (mg/kg)

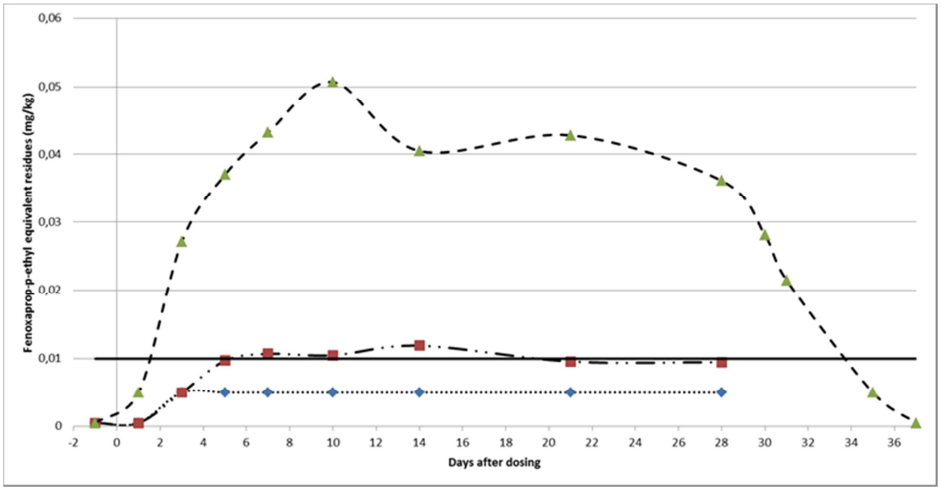


Table 7.2.3.2-4 Summary of mean values for Fenoxaprop-P-ethyl equivalents in eggs (mg/kg)

Group	Dose		Repli-cate	No of birds	Day								
No	mg/ bird	mg/ kg bw[1]			-1	1	3	5	7	10	14	21	28
1	-		1	4	ND	ND	ND	ND	ND	ND	ND	ND	ND
2 (1X)	0.2	0.11	1	4	ND	ND	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
			2	4	ND	ND	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
			3	4	ND	ND	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
			mean	**12**	**ND**	**ND**	**< LOQ**	**< LOQ**	**< LOQ**	**< LOQ**	**< LOQ**	**< LOQ**	**< LOQ**
3 (3X)	0.6	0.32	1	4	ND	ND	< LOQ	< LOQ	< LOQ	< LOQ	0.0123	< LOQ	< LOQ
			2	4	ND	ND	< LOQ	0.011	0.012	0.012	0.0125	0.011	0.012
			3	4	ND	ND	< LOQ	0.011	0.012	0.011	0.011	< LOQ	< LOQ
			mean	**12**	**ND**	**ND**	**< LOQ**	**< LOQ**	**0.011**	**0.011**	**0.012**	**< LOQ**	**< LOQ**
4 (10X)	2	1.1	1	4	ND	NS	0.030	0.038	0.043	0.060	0.048	0.041	0.024
			2	4	ND	0.015	0.032	0.040	0.048	0.063	0.044	0.053	0.046
			3	4	ND	ND	0.024	0.038	0.039	0.042	0.037	0.042	0.040
			mean	**12**	**ND**	**0.013**	**0.029**	**0.039**	**0.043**	**0.055**	**0.043**	**0.045**	**0.037**
4a (10X)	2	1.1	1	4	ND	ND	0.029	0.037	0.045	0.050	0.042	0.042	0.038
			2	4	ND	ND	0.020	0.033	0.042	0.039	0.032	0.038	0.034
			mean	**8**	**ND**	**ND**	**0.025**	**0.035**	**0.044**	**0.045**	**0.037**	**0.040**	**0.036**

4a = Depuration group ND= < 0.001 mg/kg NS= no sample LOQ= < 0.01 mg/kg

[1]… based on nominal dose rate (mean body weight of ca. 1.82 kg)

Depuration								
Group	**Dose**		**Repli-cate**	**No of birds**	**Day**			
No	**mg/ bird**	**mg/ kg bw[1]**			**30**	**31**	**35**	**37**
4a (10X)	2	1.11	1	4	0.030	0.021		
			2	4	0.027	0.022	< LOQ	ND
			mean	**8**	**0.028**	**0.022**	**<LOQ**	**ND**

[1]… based on nominal dose rate (mean body weight of ca. 1.82 kg)
ND= < 0.001 mg/kg LOQ= < 0.01 mg/kg

Tissues:

In tissues, the highest fenoxaprop-P-ethyl residues occurred in the liver (0.15 – 1.30 mg/kg); lower residues were found in abdominal (0.01 – 0.24 mg/kg) and subcutaneous fat (< 0.01 – 0.16 mg/kg) and the lowest residue concentrations occurred in muscle (< 0.01 – 0.11 mg/kg).

Following withdrawal of dosing residues of fenoxaprop-P-ethyl rapidly declined to levels below the LOQ within 7 days in eggs, liver and muscle. Remaining residues at Day 10 of the depuration phase were detected in subcutaneous fat (0.022 mg/kg) and abdominal fat (0.10 mg/kg), respectively. An overview table is given in the table below.

Table 7.2.3.2-5 Summary of highest values for Fenoxaprop-P-ethyl equivalents in tissues (mg/kg)[#]

Group	**Dose**		**Repli cate**	**No of birds**	**Depuration Period (Days)**	**Tissues**			
No	**mg/ bird**	**mg/ kg bw[1]**				**Liver**	**Muscle**	**Abdominal fat**	**Subcutaneous fat**
1	-	-	1	4	0	ND	ND	ND	ND
2 (1X)	0.2	0.11	1	4		0.058	< LOQ	0.011	0.011
			2	4		0.146	< LOQ	0.012	< LOQ
			3	4		0.046	< LOQ	0.011	< LOQ
			max	**12**	**0**	**0.146**	**< LOQ**	**0.012**	**< LOQ**
3 (3X)	0.6	0.32	1	4		0.335	0.025	0.026	0.040
			2	4		0.157	< LOQ	0.036	< LOQ
			3	4		0.463	0.014	0.041	0.016
			max	**12**	**0**	**0.463**	**0.025**	**0.041**	**0.040**
4 (10X)	2	1.1	1	4		1.17	0.112	0.109	0.163
			2	4		0.41	0.038	0.236	0.053
			3	4		1.30	0.097	0.160	0.144
			max	**12**	**0**	**1.30**	**0.112**	**0.236**	**0.163**
4a (10 X D)	2	1.1	1	4	3	0.035	0.011	0.14	0.037
			1	4	7	0.011	<LOQ	0.20	0.024
			1	4	10	<LOQ	<LOQ	0.10	0.022

4a= Depuration [1]… based on a mean body weight of 1.82 kg
ND= < 0.001 mg/kg LOQ= < 0.01 mg/kg

#....The samples taken were pooled from each subgroup with a sub-sample (5 g) taken from this pooled sample for analysis by LC-MS/MS.

For liver the residue levels for replicate 2 showed different residue levels compared to the corresponding samples from replicates 1 and 3. The analysis of each matrix type was conducted in individual analytical batches with no significant variation that could lead to concerns over the repeatability. Recovery for all matrices was between 91% and 102%, recovery values for liver were 93, 97 and 96%. The applicant stated that the differences especilly for replicate 2 may partly be due the biological variation and due to the fact that the birds were devided into groups for necrospsy and tissue sampling being terminated on different calendar days.

Table 7.2.3.2-6 MRL and HR calculations for poultry food commodities (animal model 2017)

MRL & HR Calculations				
Matrices	**Muscle**	**Fat**	**Liver**	**Eggs**
Tf Level 1 (closest level)	0.010	0.001	0.011	0.010
Tf Level 2	0.001	0.001	0.012	0.000
Tf Level 3	0.001	0.002	0.010	0.000
Interpolation	Burden<L1	Burden<L1	Burden<L1	Burden<L1
Linear regression	<30% L1	<30% L1	<30% L1	<30% L1
HR (Tf_{CL}, It, Ln)	0.010	0.001	0.011	0.010
HR	0.010	0.001	0.011	0.010
MRL proposal	**0.01***	**0.01***	**0.015**	**0.01***
STMR	< 0.01	< 0.01	< 0.01	< 0.01

For the supported uses of fenoxaprop-P-ethyl on cereals the estimated highest residues in poultry at 1N rate are below the LOQ of 0.01 mg/kg in eggs or any edible tissues, except for liver where the residue level (0.011 mg/kg) is slightly above the LOQ. Poultry metabolism studies showed that the majority of the administered radioactivity (91-98%) was excreted, no significant residues are expected in poultry tissues or eggs after application according to the recommended GAP.

B.7.4.2. Ruminants

Reference:	KCA 6.4.2/01 *Hoe 033171- Ruminant feeding study*
Author(s), year:	[redacted] ; 1987a
Report/ Doc. Number:	LEA/R87/018 / A36705
Guideline(s):	EPA, 171-4 (October 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval. Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 505	No dosing via capsule (the dose was homogenously mixed with maize meal. This pre-mixture was then incorporated into supplementary feed and fed before the normal feed)
Comment (RMS):	The study is considered applicable to provide the required information.

As shown in plant metabolism studies and in a broad scale of field crop residue studies the active ingredient Hoe 033171 is degraded rapidly. The proposed pathway in plants shows a rapid hydrolization and formation of a group of metabolites containing the 6-chloro-2.3-dihydrobenz-oxazol-2-one-(Hoe 054014)-moiety as a common part of their molecule. Due to further cleavage a complete mineralization is achieved, respectively. After use of Hoe 033171 in accordance to the proposed label in most of the crops no detectable residues are found at harvest time. Only on forage crops where mainly immature crop parts are used for animal feed and where relatively short time lapses between application and cutting low residues may be present at feeding time.
The objective of this study was to determine the residues in the tissues and milk upon feeding lactating cows with feed containing the test chemicals. The selective herbicide Hoe 033171 and its metabolite chlorobenzoxazolone (Hoe 054014) were fed in equal amounts to lactating cows at 3 dose levels for a period of 4 weeks.

Animal information:

Species/breed	Lactating cows, Holstein Friesians
Number of tested animals	14
Age (range)	3 -11 years
Weight (range)	500-770 kg
Milk production (range)	8 – 35 L
Housing	Normal husbandry conditions in a stanchion stable with slats and semiliquid manure handling. The troughs were equipped with a special separation device at each place in order to enable a complete separation of the cows to their neighbours during feeding and to ensure that each cow takes up his individual ration. Mastitis was regulary tested. Udder were sanitized with agent daily before each milking.
Acclimatisation period	14 - 21days
Diet	20 kg maize silage, 2 kg hay, 2 kg sugar beet chip, 2 kg supplementary feed per animal and day. All feed items (except concentrated feed stuff) were provided to the animals in constant daily amounts during the study period. All items except maize silage were taken up quantitatively. Daily consumption of maize silage was determined by weighing back the amount left over in the trough.
Water	Municipal tap cattle bowl
Feed consumption	26 kg/animal/day (fresh weight) and 11.1 kg /animal/day dry weight

Material and Methods:

Hoe 033171 and its metabolite Hoe 054014 (= 6-chloro-2.3-dihydro-benzoxazol-2-one) were mixed with the daily diet and fed to lactating cow.

Figure 7.2.3.2-1 Feed composition table

Constituents	**Fresh weight (kg/animal/day)**	**Dry weight (kg/animal/day)**	**Comments**
Maize silage	20.0	5.8	
Hay	2.0	1.7	
Sugar beet chip	2.0	1.8	
Supplementary feed	2.0	1.8	Oat meal, mineral feed, propylenglycol, maize meal
Total amount	26.0	11.1	

All items except maize silage were taken up quantitatively. Daily consumption of maize silage was determined by weighing back the amount left over in the trough.

Maize meal was taken as premix material with 10g (1x dose), 30g (3x dose) and 100g (10x dose) per animal and day containing the daily dose of active ingredient and metabolite. For administration premix was mixed with the supplementary feed and maize silage (10x dose group) and fed each morning before milking and before the bulk of feed was fed.

One group of 3 cows (1X) received 3 mg and two groups of 4 cows each received 9 mg (3X) and 30 mg (10X) per substance per animal for 28 consecutive days. One group of 3 cows remained as control group. The dose rates are calculated for 600 kg bodyweight per animal, corrections were made for cows with lower or higher bodyweight. An overview on the study design is given in the table below.

Table 7.2.3.2-1 Study design

Group No	**Dose level**	**No of animals**	**Dose**					
			mg a.i	mg M1	mg a.i.	mg M1	mg a.i.	mg M1
			per animal		**per kg body weight**		**per kg feed (DM)**	
1	-	3	-	-	-	-	-	-
2	1X	3	3	3	0.005	0.005	0.2	0.2
3	3X	4	9	9	0.015	0.015	0.6	0.6
4	10X	4	30	30	0.05	0.05	2.0	2.0

a.i.= Hoe 033171 M1= Hoe 054014 [1]… based on a body weight of 600 kg

Individual milk samples were collected prior to dosing 20 days (10 x-rate and control group) and 13 days (1 x- and 3 x-rate group) before first dosing. Further milk samples were taken 9 days (10 x-rate and control group only) and 1 day (all groups) before dosing, on the start of dosing and 1, 2, 3, 4, 7, 14, 21 and 28 days after start of dosing. A milk sample consisted of two subsamples taken in the evening on the day before and in the morning of the sampling day. Morning and evening milk samples from each cow were analysed separately. Within the groups of treated animals the stainless steel milk container was washed and rinsed with acetone to remove potential residues from previous milkings.
All cows (except one from the 10 x-dose group) were slaughtered on the day of last dosing (day 28). Three samples each of muscles (ca. 600 g eacg of longissimus dorsi, semimembranaceaus and triceps) and fat (ca. 500 g each perirenal, omental and mediastinal), one sample of ca. 200-300 g of both kidneys and ca. 500 g of the liver as well as a blood sample (3x 50 ml) were taken from each cow. The depuration of residues in milk, blood, tissues and organs was investigated on one cow from the 10 x-dose group due to trace residues detected occasionally in the milk of the 3x- and 10x-rate dose group animals during the dosing period. This cow (No. 160) was sacrificed 15 days after the last dosing (day 43).

Analytical procedure
The samples were analysed according to method AL 06/84 (Kuenzler, K.; Pleines, J.; 1984) by refluxing with hydrochloric acid in acetonitrile for 8 hours resulting in the cleavage of the relevant residual compounds (the active ingredient its free acid and other metabolites containing the 6-chlorobenzoxazol moiety) to the common mojety Hoe 054014. After filtration and cleanup with extrelut, impurities are washed out of the column with hexane. Then the hydrolysis product was eluted with 20 % diethylether in hexane, the eluate was evaporated, acetylated with acetic anhydride. The resulting derivate Hoe 083312 (3-acetyl-6-chloro-2.3-dihydrobenzoxazole-2-one) was quantified by means of GC combined with ECD-dedection (LOQ=0.01 mg/kg). The results were confirmed by simultaneous analysis of spiked control samples with recovery values of about 79 % (muscle), 72 % (blood), 85 % (milk and fat), 90 % (liver) and 104 % for kidney. Residues are expressed as fenoxaprop-ethyl equivalents.

Findings:
At the **1x dose group** (3 mg Hoe 033171 + 3 mg 054014/cow/day) no detectable residues were determined in milk, blood, kidney, fat, muscles and liver.

At the **3x dose group** (9 mg Hoe 033171 + 9 mg 054014/cow/day) a maximum residue level of 0.01 mg/L in milk, 0.01 mg/kg in kidney and 0.05 mg/kg in liver was detected. At the **10x dose group** (30 mg Hoe 033171 + 30 mg 054014/cow/day) maximum residue levels of 0.03 mg/L was detetctd in milk, 0.09 mg/kg in kidney and 0.2 mg/kg in liver.
Samples of muscles showed detectable residues at 0.02 mg/kg once in each group. In all dose rate groups no residues above the LOQ (0.01 mg/kg) were determined in fat. Residues in blood were only detected in the 10x dose group with a maximum of 0.02 mg/kg. During the depuration phaseof one 10 x-dose cow only on Day 1 after last dosing a detectable residue was found in the milk. Blood, tissues and organs did not show any residue at slaughtering 15 days after last dosing.

An overview is given in the tables below. Milk values are given as the highest value obtained of the morning and the evening sample.

Table 7.2.3.2-2 Residue levels in milk after feeding cows with a mixture of Hoe 033171/Hoe 054014 (1:1) at 3 different dose levels; values calculated as mg Hoe 033171/L milk

Group	Dose		No of cows	Day								
No	mg ai.+M1/ animal	mg a.i.+M1/ kg bw[1]		0	1	2	3	4	7	14	21	28
1	-	-	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	<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
			mean	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**
2 (1X)	3+3	0.005+ 0.005	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	<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
			mean	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**
3 (3X)	9+9	0.015+ 0.015	4	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.02	<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	<0.01	<0.01	<0.01	<0.01	0.01	<0.01
			mean	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**0.01**	**<0.01**

a.i. (active ingredient) = Hoe 033171 M1 = metabolite Hoe 054014 [1]…..based on a body weight of 600 kg

Group	Dose		No of cows	Day								
No	mg ai.+M1/ animal	mg a.i.+M1/ kg bw[1]		0	1	2	3	4	7	14	21	28
4 (10X)	30+30	0.05+ 0.05	4	<0.01	<0.01	0.02	0.02	0.02	0.01	0.02	<0.01	<0.01
				<0.01	0.01	0.02	0.03	0.01	0.02	<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	0.02	<0.01	0.01	0.01	<0.01	<0.01
			mean	**<0.01**	**0.01**	**0.02**	**0.02**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**

a.i. (active ingredient) = Hoe 033171 M1 = metabolite Hoe 054014
[1]…..based on a body weight of 600 kg

Depuration									
Group No	**Dose**		**No of cows**	**Day**					
	mg ai.+M1/ animal	mg a.i.+M1/ kg bw[1]		29	31	33	35	38	43
4 (10X)	30+30	0.05+0.05	1	0.02	<0.01	<0.01	<0.01	<0.01	<0.01

a.i. (active ingredient) = Hoe 033171 M1 = metabolite Hoe 054014
[1]…..based on a body weight of 600 kg

Table 7.2.3.2-3 Residue levels in tissues and organs /sampled on day 28 after feeding cows with a mixture of Hoe 033171/Hoe 054014 (1:1) at 3 different dose levels; values calculated as mg Hoe 033171/kg fresh material

Group	Dose		No of cows	Tissues and blood				
No	mg a.i. + M1/ animal	mg a.i.+M1/ kg bw[1]		**muscle**	**fat**	**blood**	**kidney**	**liver**
1 (control)	-	-	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	<0.01	<0.01	<0.01
			max	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**
2 (1X)	3+3	0.005+ 0.005	3	<0.01	<0.01	<0.01	<0.01	<0.01
				<0.01	<0.01	<0.01	<0.01	0.02
				0.02	<0.01	<0.01	<0.01	<0.01
			max	**0.02**	**<0.01**	**<0.01**	**<0.01**	**0.02**
3 (3X)	9+9	0.015+ 0.015	4	<0.01	<0.01	<0.01	<0.01	0.05
				<0.01	<0.01	<0.01	<0.01	0.02
				0.02	<0.01	<0.01	<0.01	0.01
				<0.01	<0.01	<0.01	0.01	0.02
			max	**0.02**	**<0.01**	**<0.01**	**0.01**	**0.05**
4 (10X)	30+30	0.05+ 0.05	4	<0.01	<0.01	0.02	0.04	0.10
				<0.01[#]	<0.01[#]	<0.01[#]	<0.01[#]	< 0.01[#]
				0.01	<0.01	0.02	0.06	0.10
				<0.01	<0.01	0.02	0.09	0.20
			max	**0.01**	**<0.01**	**0.02**	**0.09**	**0.20**

a.i. (active ingredient) = Hoe 033171 M1 = metabolite Hoe 054014
[1]…..based on a body weight of 600 kg
LOQ= < 0.01 mg/kg
[#] values from cow 160, sacrificed after depuration (on day 43)

Conclusion:

The purpose of the submitted feeding study in lactating cows was first to clarify if residues were actually transferred or not and secondly to serve as a basis for setting tolerance levels for food of animal origin.

The selective herbicide Hoe 033171 and the metabolite chlorobenzoxazolone (Hoe 054014) were fed in equal amounts to 3 groups of 3-4 lactating cows at 3 different dose levels (1x, 3x, 10x) for a period of 28 consecutive days.
The dose chosen for feeding to the 1 x-dose group covers a theoretical residue content at the expected tolerance level of 0.2 mg/kg for the parent compound as well as for the metabolite Hoe 054014 in 100 % of the daily feed. Due to the rapid degradation of Hoe 033171 on plant material the probability that this level of contamination is reached under practical conditions is very low.

A contamination of 0.2 mg Hoe 033171 and 0.2 mg Hoe 054014 per kg of the daily feed for dairy cows equivalent to a dose of 3 mg Hoe 033171 and 3 mg Hoe 054014 per cow and day at the *1x dose level* will not cause detectable residues above a limit of 0.01 mg/kg in the milk (mean value), fat and kidney. Residues in muscle and liver were slightly above the LOQ (in one of three animals).

In the *3x dose group* (9 mg Hoe 033171 + 9 mg 054014/cow/day) a mean residue level of 0.01 mg/L in milk and a maxium residue level of 0.05 mg/kg in liver was detected. Residues in fat, blood and kidney were below or at the LOQ of 0.01 mg/kg.

In the *10x dose group* (30 mg Hoe 033171 + 30 mg 054014/cow/day) a mean residue level of 0.02 mg/L was detected in milk and a maxium residue level of 0.09 mg/kg in kidney and of 0.2 mg/kg in liver. Residues in muscle and fat were below or at the LOQ (in one of three animals).

After use of Hoe 033171 in accordance to the proposed label in most of the crops no detectable residues are found at harvest time. Only on immature crop parts used for animal feed and where relatively short time lapses between application and cutting low residues may be present at feeding time.
As shown in plant metabolism studies the active ingredient Hoe 033171 is degraded rapidly and the the proposed pathway in plants shows a rapid hydrolization and formation of a group of metabolites containing the 6-chloro-2.3-dihydrobenz-oxazol-2-one-(Hoe 054014)-moiety as a common part of their molecule.
Thus for MRL calculation a worst case scenario was assumed and the feeding levels (in mg/kg bw) were calculated as sum of active ingredient (Hoe 033171) and Metabolte M1 (Hoe 054014) as parent equivalents using a molecular weight factor of 2.1 (MW for Hoe 033171 of 361.8 g/mol ÷ MW for Hoe 054014 of 169.6 g/mol).

Table 7.2.3.2-4 MRL and HR calculation for cow (animal model 2017)

MRL & HR Calculations					
Matrices	**Muscle**	**Fat**	**Liver**	**Kidney**	**Milk**
Tf Level 1 (closest level)	0.008	0.01	0.008	0.01	0.01
Tf Level 2	0.003	0.01	0.008	0.002	0.01
Tf Level 3	0.001	0.01	0.01	0.005	0.001
HR	0.008	0.01	0.008	0.01	0.01
MRL proposal	**< 0.01**	**0.01**	**< 0.01**	**0.01**	**0.01**
STMR	0.002	0.01	0.02	0.01	0.01
Comment	Estimated intakes below 30% lowest feeding level. No values derived by linear regression				

Considering the renal and faecal excretion in lactating goats, pointed out in the ruminant metabolism study (B.7.2.2.3), it can be concluded that residues of Fenoxaprop-ethyl and its metabolites are rapidly excreted in cows and do not show any tendancy to accumulate. Thus for the supported uses of fenoxaprop-P-ethyl on cereals it is not expected that residues, which are significantly higher than the LOQ of 0.01 mg/kg will occur in edible tissues or milk.

B.7.4.3. Pigs

No new information is submitted. No feeding studies were conducted on pig. The dietary burden calculations do not trigger the need of a pig feeding study.

B.7.4.4. Fish

No feeding studies were conducted on fish and required necessary.

Neither cereal green material or forages nor cereal straw will be part of the fish diet. Residues in cereal grain are all below the LOQ of 0.01 mg/kg. Therefore the dietary burden of fenoxaprop-P-ethyl derived residues in fish feed is considered negligible. Please refer also to B.7.2.2.6.

B.7.5. EFFECTS OF PROCESSING

B.7.5.1. Nature of the residue

Studies on the nature of residues in processing are required where residues in commodities of plant or animal origin subject to processing may occur at a level of ≥ 0.01 mg/kg. Since the supported uses of fenoxaprop-P-ethyl on cereals do not result in significant residues in the raw agricultural commodities (RAC) at harvest (all residues in grains are < 0.01 mg/kg) studies to specifically investigate the processing nature of residue for fenoxaprop-P-ethyl are considered not required.

B.7.5.2. Distribution of the residue in peel and pulp

Fenoxaprop-P-ethyl is not used in crops with inedible peel. Therefore, studies to investigate the distribution of residues in peel and pulp are not relevant and not required.

B.7.5.3. Magnitude of residues in processed commodities

Since the supported uses of fenoxaprop-P-ethyl on cereals do not result in significant residues in the RAC at harvest (all residues in grains are < 0.01 mg/kg) no studies to determine the magnitude of residues in processed commodities are required and no data have been submitted.

B.7.6. RESIDUES IN SUCCEEDING OR ROTATIONAL CROPS

B.7.6.1. Metabolism in rotational crops

Metabolism studies in rotational crops are required if the parent compound or soil metabolites are persistent in soil or significant concentrations of metabolites in soil occur.
No new metabolism study in succeeding crops was submitted or required for the purpose of renewal of the active substance approval.

Two studies in succeeding crops have previously been included in the submission for Annex I inclusion under 91/414/EEC**.** The studies were deemed acceptable following evaluation and peer review at EU level. A summary of the original submitted data which were considered for the purpose of renewal is presented in the table below.

Rotational crops	Active substance	Label	Application rate	PBI	Reference in the dossier for renewal of the a.s. (Reference in the RAR)	
Originally submitted and evaluated studies (DAR, 2005) to be considered for purpose of renewal						
Leafy vegetables (Spinach, lettuce) root vegetables (radish, carrots), cereals (wheat, buckwheat)	Hoe 046360	Chlorophenyl-^{14}C	1x 0.113 kg as/ha, bare soil	30days, 1year	Bürkle, W.L.; Wink O., Köcher, H.; 1987	KCA 6.6.1/01 (B.7.6.1.1)
Leafy vegetables (Spinach) root vegetables (red beets), cereals (wheat)	Hoe 033171	Chlorophenyl-^{14}C	0.11 kg as/ha, rice plants (5-6 leaf stage)	111days	Schwalbe-Fehl M. ; Steinau M. ; Mueller H.J.; 1985a	KCA 6.6.1/02 (B.7.6.1.2)
		Dioxyphenyl-1-^{14}C	0.07 kg as/ha, rice plants (5-6 leaf stage)			

B.7.6.1.1. *Confined rotational crop study – Study 1*

Reference:	KCA 6.6.1/01 *Hoe 046360-^{14}C, Confined Accumulation Study on Rotational Crops Sown 30 Days and One Year after Application of 0.11 kg a.i./ha*
Author(s), year: Report/ Doc. Number: Guideline(s): GLP:	Bürkle, W.L.; Wink O., Köcher, H.; 1987 CMO41/86 / A37484 US-EPA Guidelines, subdivision N. § 165-1 (October 1982) Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 502	No PBI 120 days (covered by second study B.7.6.1.2)
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

In the confined crop rotation study conducted under outdoor conditions (but protected from rain by a transparent roof) **bare soil** was treated with U-chlorophenyl-^{14}C- labeled Hoe 046360 (see Figure 7.2.1.1-1) at an **application rate of 0.113 kg ai/ha** by homogeneous spraying with the aid of a commercially available Grapho II B sprayer.

The test container was a box of stainless steel of 1.07 m length x 0.75 m width x 0.57 m height and equipped with a subirrigation device. The bottom of the test container was covered with a layer of gravel and sand (thickness: approx. 10 cm). Fresh soil (59% sand, 31% silt, 10% clay) was filled in and the container was allowed to age for several weeks. Soil surface was 0.73 m^2, soil depth was approximately 0.45 m. The test container were located in a vegetation hall under outdoor conditions (open walls), but protected from rain by a transparent roof.

After 30 days (for assessing circumstances of crop failure), a first group of leafy vegetable (spinach and lettuce), root crop (little radish and carrots) and small grain crops (wheat and buckwheat) was sown and sampled at appropriate harvest times (Spinach 40 days, lettuce and little radishes 55days and carrots 101 days after sowing). Wheat was sampled at maturnity 101 days after sowing (grain, straw, husks and roots). In addition, the stubbles (0-10 cm height) of the plants sown one year after application were analysed as well. Buckwheat was sampled at maturity of most of the seeds 118 days after sowing. Separate radioactivity determinations were conducted on grain, green leaves, stems, the remaining blossoms and the roots.

Subsequently, after harvest of the first group, certain weeds (wild mustard, chickweed) were sown and grown in the greenhouse. The weeds were kept in a short range and the cut material was left on the surface of the test container.

One year after application of the test substance the weeds were mixed into the upper 10 cm soil layer and then a second group of rotational crop (spinach, little radish and wheat) was sown and sampled after maturity of the plants (spinach 46 days, little radish 75 days and wheat 131 days after sowing). The analysis of each crop was carried out by combustion of samples (leaves for spinach and lettuce, the bulbs of little radish, carrot roots and grain of wheat and seeds of buckwheat) and determination of radioactivity by LSC (the LOQ values refere to fresh plant material, except grain and seeds).

Dosing/Sampling regime:

Days after treatment	Action	Soil samples taken
0	Application of 0.113 kg as/ha U-^{14}C-chlorophenyl-labeled Hoe 046360 to bare soil	yes
30	Sowing of the rotational crops (1st group): leafy vegetable (spinach and lettuce), root crop (little radish and carrots), small grain crops (wheat and buckwheat)	no
55	-	yes
70	Harvest of spinach	yes
75	Harvest of little radish	yes

Days after treatment	Action	Soil samples taken
85	Harvest of lettuce	no
131	Harvest of carrots, wheat and buckwheat	yes
148	Harvest of buckwheat	no
157	Re-cultivation of the soil surface, sowing of wild mustard and chickweed	no
365	Re-cultivation of the soil surface, sowing of the rotational crops (2nd group): Spinach, little radishes, wheat	yes
411	Harvest of spinach, little radish	yes
440	Harvest of slowly grown radishes	no
496	Harvest of wheat	yes

Measurement of radioactivity:

Aliquot portions of the solid samples were combusted in a Sample- Oxidizer (model 306, Co. Packard Instr.). The formed $^{14}CO_2$ was absorbed in 8 mL of Carbo-Sorb (alkylamine, Co. Packard Instr.) and mixed with 12 mL of scintillation cocktail type 808 E consisting of 2.5-diphenyl-oxazole, p-bis-(o-methylstyryl)-benzene, emulsifier, pseudocumene and acetic acid. Combustion efficiencies were determined with aid of a standard with known radioactivity content. The resulting values were used to compensate numerically uncomplete efficiencies of sample combustion. Aliquot portions of liquid samples were added to 10 mL of scintillation cocktail type 808 E. All the measurements were carried out at least twice by means of the liquid scintillation counter.

Findings:

The uptake of each type of crop was insignificant, whether sown 30 days or one year after soil treatment. For the crops, sown 30 days after application, residues of 0.001 mg as-equ/kg up to 0.004 mg ai-equv./kg fresh weight were determined in lettuce leaves, little radish bulbs and carrot roots, residues of 0.02 and 0.12 mg ai-equv./kg fresh weight were detected in buckwheat roots and wheat roots, respectively. For the crops, sown 1 year after application, residues were below the LOQ in spinach leaves, little radish bulbs and wheat grain. Residues in the remaining plant parts of wheat were between 0.02 mg ai-equv./kg fresh weight in wehat straw and 0.07 mg ai-equv./kg fresh weight in wheat roots. For detailed results please refer to the summary table below.

Table 7.6.1.1-1 Radioactive Residues in rotaional crops after application of 0.113 kg ^{14}C-Hoe 046360/ha to bare soil

Rotational Crop	Plant part analysed	Sampling date DAA (DAS)	Radioactivity concentration [mg as-equ/kg fresh weight]	LOQ [mg as-equv./kg]
sown 30 days after application				
Spinach	leaves	70 (40)	< LOQ	0.001
	stems		< LOQ	0.0004
	roots		0.012	0.0005
Lettuce	leaves	85 (55)	0.003	0.001
	roots		0.010	0.0004
Little radish	leaves	75 (45)	0.001	0.0003
	bulbs		0.001	0.0002
Carrot	leaves	131 (101)	0.004	0.003
	roots		0.003	0.0002
Wheat	grain	131 (101)	< LOQ	0.005
	husks		< LOQ	0.010
	straw		< LOQ	0.006
	roots		0.122	0.005
Buckwheat	seeds	131, 148	< LOQ	0.004
	leaves	148	< LOQ	0.004
	stems	148	< LOQ	0.003
	roots	148	0.024	0.002
	blossoms	131, 148	< LOQ	0.006
sown one year after application				
Spinach	leaves	411 (46)	< LOQ	0.001
Little radish	leaves	440 (75)	0.002	0.001
	bulbs		< LOQ	0.002
Wheat	grain	496 (131)	< LOQ	0.003

	husks		0.014	0.009
	straw		0.022	0.014
	stubbles (0-10cm)		0.027	0.009
	roots		0.071	0.007

DAA= **d**ays **a**fter **a**pplication DAS= **d**ays **a**fter **s**owing

Soil samples taken up to a depth of 20 cm (divided into 5 cm increments) were analysed at the time of treatment and repeatedly 55, 70, 75, 131, 365, 411 and 496 days after application. Plastic tubes (approx. 3 cm inner diameter, 40 cm length) were bored in the soil in order to take core samples. The sample tubes were pulled out and sawn into 5 cm sections. The resulting soil layers were analysed separately for the content of radioactivity. In this way, the radioactivity distribution throughout the soil depth could be determined.

The total radioactivity in the top 5 cm layer decreased from initial 0.12 mg as - equ/kg dried soil (0 DAA) to a mean level of 0.06 mg ai-equ/kg on day 496 after application showing a rapid diminution during the first 55 days followed by a slow decrease later on. The results are summarised in the table below.

Table 7.6.1.1-2 Radioactive Residues in soil after application of ^{14}C-Hoe 046360 at a rate 0.113 kg as/ha.

Soil depth	Sampling date [DAA]	Radioactive residues [mg as-equ/kg dry soil]
0-5 cm	0	0.121
	55	0.059
	70	0.104
	75	0.083
	131	0.055
	365	0.047
	411	0.036
	496	0.056
5-10 cm	0	< LOQ
	55	< LOQ
	70	< LOQ
	75	< LOQ
	131	0.004
	365	< LOQ
	411	< LOQ
	496	0.006
10-15 cm	0	< LOQ
	55	< LOQ
	70	< LOQ
	75	< LOQ
	131	< LOQ
	365	< LOQ
	411	< LOQ
	496	< LOQ

DAA= **d**ays **a**fter **a**pplication LOQ = 0.002 mg as-equ/kg

In order to characterize these residues, soil sampled immediately after treatment was extracted once with a mixture of of acetonitrile and water (4:1, v/v) and analyzed by high performance liquid chromatography (HPLC). Aliquots of the soil sampled at later dates were extracted by use of a percolation method in order to cover additionally aged residues. 50 - 100 g of moist soil were packed into a glass tube (length: 40 cm, inner diameter: 18 mm). A mixture of acetonitrile and water (4:1, v/v) penetrated the soil column within approx. 8 hours in upward direction. The extracts were concentrated and analyzed by HPLC.

Radioactivity extracted at day 0 could be attributed to a 48 % portion of the hydrolyzed parent compound (Hoe 053022, 2-(4-(6-chloro-2- benzoxazolyloxy)-phenoxy)-propionic acid, 0.04 mg/kg soil) and a 52 % portion of 6-chloro-2,3-dihydro-benzoxazol-2-one (Hoe 054014, 0.02 mg/kg soil) by comparison of the retention times with those of authentic reference compounds. The unchanged parent compound was not detectable, at all.
Apart from the extraction immediately after application, only 15 - 21 % of the total radioactivity contained in the soil at the corresponding sampling date could be extracted. Due to the low radioactivity level of these extracts HPLC analysis failed.
In spite of the low but measurable radioactivity levels in the soil throughout the entire test period the uptake by rotational crops was negligible indicating an incorporation of the radioactivity into the soil matter.

A transition factor (plant residues/soil residues) calculated for all crops tested within this study showed ratios < 0.1 (related to the radioactivity in soil at the time of harvest) in the edible plant parts indicating that an uptake of radioactive residues via the soil occurs only to a low extent. For wheat straw the transition factor was higher, probably because of weight reduction due to the loss of water increases the radioactivity concentration in the plant parts. However, Fenoxaprop-P-ethyl was not accumulated by plants after uptake from soil and was not translocated into deeper soil layers.

Table 7.6.1.1-3 Uptake of ^{14}C-Hoe 046360 residues from soil (Transition factors)

Rotational Crop	Plant part analysed	Sampling date Plant/Soil (DAA)	Residues in plant [mg as-equ/kg]	Residues in soil (0-5 cm) [mg as-equ/kg]	Transition factor (plant/soil)
sown 30 days after application					
Lettuce	leaves	85/75	0.003	0.083	0.04
Carrot	leaves	131/131	0.004	0.055	0.07
	roots		0.003	0.055	0.05
Wheat	grain	131/131	0.005	0.055	0.09
sown one year after application					
Spinach	leaves	411/411	0.001	0.036	0.03
Little radish	leaves	440/411	0.002	0.036	0.06
	bulbs		0.002	0.036	0.06
Wheat	grain	496/496	0.003	0.056	0.05
	straw		0.022	0.056	0.39

DAA= **d**ays **a**fter **a**pplication

Conclusion:

Total radioactive residues in plants sown 30 days and one year after application of ^{14}C-Hoe 046360 to bare soil under outdoor conditions at an application rate of 0.113 kg as/ha were low or even below the limits of detection for all crops at all time points investigated. The measurements in soil samples showed that the parent compound Hoe 046360 was rapidly degraded in soil since on day 0 (start of the experiment) only the hydrolysed free acid Hoe 088406 and the metabolite chlorobenzoxazolone Hoe 054014 were detectable and did not leach to soil layers deeper than 10 cm. The calcualted transition factors (plant residues/soil residues) were low indicating that uptake of radioactivity into the soil matter or edible plant parts is considered negligible.

B.7.6.1.2. *Confined rotational crop study – Study 2*

Reference:	KCA 6.6.1/02 *Hoe 033171-^{14}C, Confined Accumulation Study on Rotational Crops Planted 111 Daysafter Treatment of the First Crop*
Author(s), year:	Schwalbe-Fehl M.. Steinau M.. Mueller H.J.; 1985a
Report/ Doc. Number:	(B)174/85 / A31992
Guideline(s):	US-EPA Guidelines. subdivision N. § 165-1 (October 1982)
GLP:	Yes
Previous evaluation :	**Yes (DAR, 2005)** Re-assessed for the purpose of renewal of a.s. approval Additional details of the results were included in the DRAR, in view of presenting an adequate level of detail.
Deviations from OECD Guideline 502	-
Comment (RMS):	The study is considered applicable to provide the required information.

Material and Methods:

Test container (1 for each preparation and 1 for control) of stainless steel with 0.7 m^2 and a soil depth of approximately 0.4 m were filled with normal field soil. Rice plants were directly sown into the soil. The rice plants were treated at the five to six leaf stage with **0.110 kg as/ha** U-^{14}C-chlorophenyl-labeled Hoe 033171 and with **0.070 kg as/ha** of 1-^{14}C-dioxyphenyl-labeled Hoe 033171.

The mature rice plants were harvested 106 days after treatment (DAT) by cutting off shortly above the soil surface. Without any further cultivation of the treated soil (the stubbles of the rice plants were still present), spinach, red beets and wheat were sown as rotational crops 5 days later (e.g. 111 DAT). Each of the three crops was sown in a row into each container, grown outdoor and harvested at maturity. Mature spinach beets (stems, leaves) were sampled 139 days after planting (250 days after treatment of the first crop) whereas mature red

beets (leaves, stems, roots) and wheat (straw, grain, husks) were sampled 157 days after planting (268 days after treatment of the first crop). Soil samples were taken on Day 0 (day of the treatment) and 36 days, 106 days (harvest of 1st crop), 250 days and 268 days after treatment by means of plastic tubes (approx. 3 cm inner diameter, 30 cm length). The tubes were sawn into different sections and the resulting soil layers were analysed separately for radioactivity concentration.

Dosing/Sampling regime:

Days after treatment		Soil samples taken
0	Application of 0.110 kg as/ha U-^{14}C-chlorophenyl-labeled Hoe 033171 and 0.070 kg as/ha of 1-^{14}C-dioxyphenyl-labeled Hoe 033171 to rice plants	yes
106	Harvest of mature rice plants	yes
111	Planting of the rotational crops (spinach beets, wheat, red beets)	No
250	Sampling of mature spinach beets	yes
268	Sampling of mature red beets and wheat	yes

Measurement of radioactivity:

Aliquot portions of the solid soil or plant samples were combusted in a Tricarb-Sample Oxidizer (model 306, Co. Packard Instr. GmbH). The formed ^{14}CO was absorbed in 8 ml of Carbo-Sorb (alkylamine, Co. Packard Instr.) and mixed with 12 mL of scintillation cocktail type 808 E consisting of 2.5-diphenyloxazole, p-bis-(o-methylstyryl)-benzene, emulsifier, pseudocumene and acetic acid. All radioactivity measurements were carried out by means of the liquid scintillation counters.

Findings:

The radioactivity concentrations in the various plant parts of the rotational crops were either below the limit of quantification or in the same range as the control samples. They were clearly below 0.01 mg as-equ/kg dry plant material in all cases and for both ^{14}C-label positions. The results are summarised in the table below.

Table 7.6.1.2-1 Radioactive Residues in rotaional crops after application of 0.110 and 0.070 kg ^{14}C-Hoe 033171 /ha respectively to rice plants

Rotational Crop	Plant part analysed	Sampling date DAA (DAS)	Radioactivity concentration [mg as-equ/kg dry material]	
			Hoe 033171-chlorophenyl-U-^{14}C	Hoe 033171-dioxyphenyl-1-^{14}C
sown 120 days after application				
Spinach beets	leaves	250	0.001	0.002
	stems		< LOQ (0.001)	0.002
Wheat	grain	268	< LOQ (0.002)	< LOQ (0.001)
	husks		< LOQ (0.001)	< LOQ (0.003)
	straw		0.002	< LOQ (0.001)
Red beets	roots	268	0.002	< LOQ (0.006)
	leaves		0.006	0.006
	stems		0.002	0.004

DAA= **d**ays **a**fter **a**pplication

Radioactivity in soil was only found in the upper (0 – 5 cm) layer with 0.012 to 0.015 mg as-equ/kg soil on day 0 and 0.013 mg as-equ/kg or below the LOQ of 0.005 mg as-equ/kg (for chlorophenyl- and dioxyphenyl-label. respectively) on day 268. In soil layers deeper than 5 cm, the residue concentrations were below the LOQ (0.002 mg as-equ/kg) at all sampling dates. The results are summarised in the table below.

Table 7.6.1.2-2 Radioactive Residues in soil after application of 0.110 kg and 0.070 kg ^{14}C-Hoe 033171 /ha respectively

Soil depth	Sampling date DAA	Radioactivity concentration [mg as-equ/kg dry soil]	
		Hoe 033171-chlorophenyl-U-^{14}C	Hoe 033171-dioxyphenyl-1-^{14}C
sown 120 days after application			
0-5 cm	0	0.015	0.012
	36	0.016	0.018
	106	0.002	0.008
	250	0.003	0.026
	268	0.013	< LOQ
5-10 cm	0	< LOQ	< LOQ
	36	0.002	< LOQ
	106	0.002	< LOQ
	250	0.003	< LOQ
	268	< LOQ	< LOQ
10-15 cm	0	< LOQ	< LOQ
	36	< LOQ	< LOQ
	106	< LOQ	< LOQ
	250	< LOQ	< LOQ
	268	< LOQ	< LOQ

DAA= **d**ays **a**fter **a**pplication LOQ= 0.002 mg as-equ/kg

Conclusion

The study was run at the same time with the two different chlorophenyl-U-^{14}C and dioxphenyl-1-^{14}C radioalabeled Hoe 033171, in order to gain information on both parts of the molecule. There were no significant differences between the heterocyclic part and the phenoxy moiety found indicating the good degradability of Hoe 033171 in plant material and soil. Residue concentrations in plants sown 120 days after application were mostly below the LOQ for all crops tested and at all time points investigated. Residue concentrations in soil samples at harvest time were also below the LOQ. Consequently, there is no accumulation of Hoe 033171 or its degradates in rotational crops which are planted after a treated first crop according to the anticipated agricultural practice.

B.7.6.1.3. *Overall conclusion on the metabolism in rotational crops*

The possible intake of soil residues via succeeding crops was investigated by two studies using radiolabeled Fenoxaprop-P-ethyl (chlorophenyl-U-^{14}C) and Fenoxaprop-ethyl (dioxyphenyl-1-^{14}C and chlorophenyl-U-^{14}C). Total radioactive residues in plants, sown 30 days, 120 days and one year after application were very low or even below the limits of quantification (LOQ) for all crops tested (leafy vegetables, root vegetables and cereals) at all time points investigated. Residues at low concentrations were found only in soil layers up to 5 cm, but there was no evidence either of residue uptake or accumulation by plants or soil indicating a rapid metabolisation of Fenoxaprop-P-ethyl (Hoe 046360) and its racemic compound Fenoxaprop-ethyl (Hoe 033171), respectively. Application of Fenoxaprop-P-ethyl according to the intended use will not lead to detectable residues in succeeding crops.

B.7.6.2. Magnitude of residues in rotational crops

As the metabolism studies in rotational crops have demonstrated that the fenoxaprop-P-ethyl shows no tendency for accumulation and that the use according to the intended use will not lead to detectable residues in succeeding crops, field rotational crop studies are not required.

B.7.7. OTHER STUDIES

B.7.7.1. Effect on the residue level in pollen and bee products

Studies on the effect on the residue level in pollen and bee products are considered not necessary.

Cereals are crops that are visited by honey bees for potential pollen and/or nectar collection. Residues may be taken up by honey bees during collection of nectar and/or pollen when plant protection products are used while the treated crops or adjacent non-target plants are flowering. However fenoxaprop-p-ethyl is applied on cereals early in the growing season latest at BBCH 39 (end of stem elongation) before flowering. Thus no residues are expected in pollen and bee products.

A general consideration is that for the evaluation of residues in pollen and bee products for human consumption, the relevant question regarding bee attractiveness is not whether or not the crop is occasionally visited by bees, but if the crop is foraged by honey bees to an extent of economic relevance. Only if a significant portion of pollen and nectar is collected from a cereal field not only by single bees, but from the whole colony, a relevant residue level in stored pollen and bee products could occur.
The EFSA Guidance Document on risk assessment of plant protection products on bees [EFSA Journal 2013; 11(7):3295, version of 04 July 2014] clearly indicates that this is not the case for cereal crops.

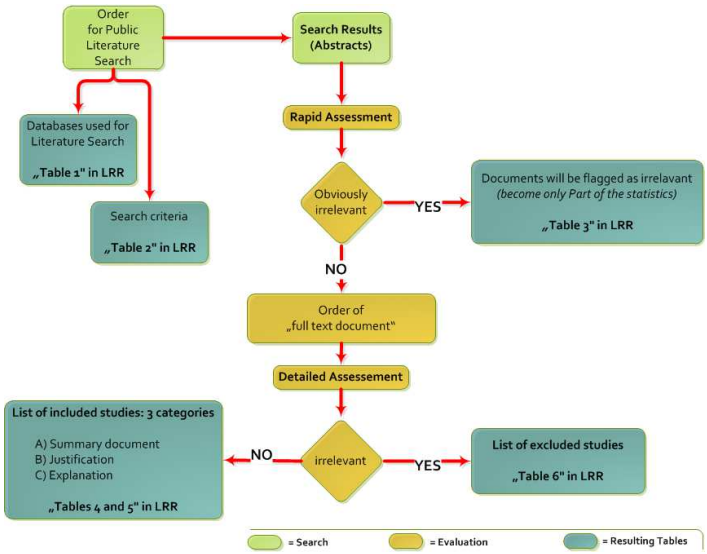
B.7.7.2. Literature research

For fenoxaprop-P-ethyl and its relevant metabolites, a total of 1250 references were identified and evaluated for potential relevance. Besides references that were clearly out of the scope of the LRR (e.g. publications dealing with chemical synthesis, or efficacy reports), the area of environmental fate and ecotoxicology were most represented in the search results. According to EFSA guidance 1135 publications have been excluded from further consideration after the rapid assessment. For 115 publications full-text documents have been obtained and assessed in detail. Ninety-one publications have been considered irrelevant after detailed assessment. In total 24 publications were evaluated as relevant for detailed assessment and has been classified for relevance according to EFSA guidance [EFSA Journal 2011; 9(2):2092].

B.7.7.2.1. Introduction

A literature review was carried out for fenoxaprop-P-ethyl and its metabolites according to the requirements of the Regulation (EU) No 844/2012" (the AIR3 renewal regulation), which itself refers to Article 8(5) of Regulation (EC) No 1107/2009. The review itself is in accordance with the EFSA Guidance document *"Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009"*.
All steps in the literature review report (LRR) are based on the EFSA Guidance Document mentioned above. The key question is whether any scientific peer-reviewed open literature published within the last ten years before the date of submission of the dossier would be relevant for the risk assessment of fenoxaprop-P-ethyl and its relevant metabolites in the context of side-effects on health, the environment and non-target species. Wherever such relevance could not be excluded, the scientific findings need to be discussed in detail in the submission for Annex I Renewal and, if necessary, the risk assessments would be updated accordingly.

B.7.7.2.2. Search strategy



The main parameters that allow the characterization of the literature search are listed below with scientific peer-reviewed open literature published between 2005-01-01 and 2016-01-11 for all compounds.
Abstracts of all references have been downloaded and evaluated. Patents were not considered in the literature search, as they are not covered by the definition "scientific peer-reviewed open literature".

A broad collection of relevant databases for the literature search was used. STN, a scientific information platform hosted by CAS, itself a division of the American Chemical Society, was selected as the preferred provider[1]. It offers a reliable scientific search service that includes all databases considered relevant to cover the requirements established in the AIR3 renewal regulation and the EFSA Guidance document [EFSA Journal 2011;9(2):2092]. Moreover, hosted databases have a defined query language for different sources which facilitates duplicate removal.

Table 3: List of data bases for the literature search

Database Name	Date of last Database Update
Agricola	2016-01-05
Biosis	2016-01-06
CABA	2016-01-07
Chemical Abstracts	2016-01-10
Derwent Drug File (DRUGU)	2016-01-08
EMBASE	2016-01-08
Esbiobase	2016-01-07
IPA	2016-01-05
Medline	2016-01-10
Pascal	2014-12-22
PQSciTech	2015-12-22
Registry	2016-01-08
Scisearch	2016-01-04
Toxcenter	2016-01-04
FSTA	2015-12-18

The information used for screening the selected databases to identify all relevant publications consists of IUPAC name, CAS name/number, common names, codes and abbreviations, molecular structure, molecular formula, molar mass and other names/codes, as far as available for Fenoxaprop-P-ethyl, fenoxaprop-ethyl and chemical names/synonyms thereof, as well as product names including the substances and chemical names/synonyms of metabolites M01, M02, M03, M04, M05, M06, M07, M08, M09, M10, M11, M12, M13, M14, M15 M16.

Table 2: List of input parameters for the database search on fenoxaprop-P-ethyl and relevant metabolites

Fenoxaprop-P-ethyl	
IUPAC name:	2-(4-(6-chloro-2-benzoxazolyl)oxy)-phenoxy)propanoic acid ethyl ester
CAS number:	66441-23-4, 71283-80-2, 113776-20-8
STN Query	(66441-23-4 OR 82110-72-3 OR 87714-45-2 OR 116573-18-3 OR 71283-80-2 OR 1223013-63-5 OR 113776-20-8 OR FENOXAPROP-ETHYL OR FENOXAPROP P-ETHYL OR HOE 046360 OR HOE 33171 OR (ACCLAIM OR FURORE OR WHIP OR PUMA OR ISOMERO OR OPTION SUPER OR (RAPSODE OR FENOVA OR FOXTROT OR COUGAR OR STARPROP OR OSKAR OR FOXTAIL OR TETRAMOR OR ARSOL OR RUMBA OR NORTON OR CHEETAH OR DOPLER OR DEPON OR FURORE OR GREENEX OR PUMA OR RALON OR RICESTAR OR WHIP OR TRIUMPH OR GREENEX OR DUKE OR ACCLAIM OR DJINN OR OPTION OR HUSSAR OR GAMO OR PROPER OR LISTEN OR BLEDOR OR RUGIR OR BAGHERA OR PRIMERA OR TIGRESS OR CORNICHE OR ATLAS OR FPE)(W)(R OR TM OR RTM) OR "ETHYL-2-(4-(6-CHLORO-2-BENZOXA 1LYL-OXY)-PHENOXY-PROPANOATE " OR "ETHYL (2R)-2-[4-(6-CHLORO-2-BENZOXAZOLYLOXY)PHENOXY]PROPIONATE" OR "ETHYL 2-[4-(6-CHLOROBENZOXAZOLYL-2-OXY)PHENOXY]PROPIONATE" OR "ETHYL 2-[4-(6-CHLORO-2-BENZOXAZOLYLOXY)PHENOXY]PROPIONATE") AND PY>2004 NOT P/DT

[1] http://www.cas.org/products/ stnfamily/index.html

ii) Metabolites (see also Document N – List of metabolites for more details)	
No.:	IUPAC name [CAS number] STN Query
M01	4-((6-chloro-1,3-benzoxazol-2-yl)oxy)phenol CAS: 70217-01-5 Query: (70217-01-5 OR "4-[(6-CHLORO-2-BENZOXAZOLYL)OXY]PHENOL" OR "6-CHLORO-2-(4-HYDROXYPHENOXY)-BENZOXAZOLE" OR HOE 040356) AND PY>2004 NOT P/DT
M02	6-chloro-1,3-benzoxazol-2(3H)-one CAS: 19932-84-4 Query: (19932-84-4 OR HOE 054014 OR "6-CHLORO-2(3H)-BENZOXAZOLONE" OR 6-CHLORO-2,3-DIHYDROBENZOXAZOL-2-ONE OR 6-CHLORO-2-BENZOXAZOLINONE OR 6-CHLOROBENZOXAZOLINONE OR 6-CHLORO-2-BENZOXAZOLONE OR 6-CHLOROBENZOXAZOLONE OR NSC 26191 OR NSC 664284) AND PY>2004 NOT P/DT
M03	2-(4-(6-chlorobenzoxazolyl-2-yloxy)phenoxy)propanoic acid CAS: 113158-40-0, 95617-09-7, 113776-21-9 Query: (113158-40-0 OR 95617-09-7 OR 73519-55-8 OR 108093-88-5 OR 131776-21-9 OR FENOXAPROP ACID OR HOE 53022 OR HOE 088406 OR "2-[4-[(6-CHLORO-2-BENZOXAZOLYL)OXY]PHENOXY]PROPANOIC ACID" OR FENOXAPROP (NOTW)(P OR ETHYL)) AND PY>2004 NOT P/DT
M04	2-(4-hydroxyphenoxy)propanoic acid CAS: 94050-90-5, 67648-61-7, 105118-15-8 Query: (94050-90-5 OR 67648-61-7 OR 95977-31-4 OR 105118-15-8 OR "2-(4-HYDROXYPHENOXY)PROPANOIC ACID" OR "2-(4-HYDROXYPHENOXY)PROPIONIC ACID" OR "2-(P-HYDROXYPHENOXY)PROPIONIC ACID" OR NSC 522955) AND PY>2004 NOT P/DT
M05	2-(4-hydroxyphenoxy)propanoic acid ethyl ester CAS: 96478-44-3, 71301-98-9, 65343-67-1 Query: (96478-44-3 OR 71301-98-9 OR 65343-67-1 OR 59012-02-1 OR "2-(4-HYDROXYPHENOXY)PROPIONIC ACID ETHYL ESTER" OR "2-(P-HYDROXYPHENOXY)PROPIONIC ACID ETHYL ESTER" OR "ETHYL 2-(4-HYDROXYPHENOXY)PROPANOATE" OR "ETHYL 2-(4-HYDROXYPHENOXY)PROPIONATE" OR "ETHYL (R)-2-(4-HYDROXYPHENOXY)PROPIONATE") AND PY>2004 NOT P/DT
M06	2-(4-((6-hydroxy-1,3-benzoxazol-2-yl)oxy)phenoxy)propanoic acid CAS: - Query: ("2-{4-[(6-HYDROXY-1-BENZOXAZOL-2-YL)OXY]PHENOXY}PROPANOIC ACID") AND PY>2004 NOT P/DT
M07	6-hydroxy-1,3-benzoxazol-2(3H)-one CAS: 78213-03-3 Query: (78213-03-3 OR NSC 603719 OR 6-HYDROXY-2,3-DIHYDROBENZOXAZOL-2-ONE OR "6-HYDROXYBENZOXAZOL-2(3H)-ONE") AND PY>2004 NOT P/DT
M08	6-chloro-5-hydroxy-1,3-benzoxazol-2(3H)-one CAS: 88412-29-7 Query: (88412-29-7 OR 6-CHLORO-1,3-BENZOXAZOLE-2,5-DIOL OR “6-CHLORO-5-HYDROXY-1,3-BENZOXAZOL-2(3H)-ONE”) AND PY>2004 NOT P/DT
M09	6-chloro-4-hydroxy-1,3-benzoxazol-2(3H)-one CAS: 88412-28-6 Query: (88412-28-6 OR 6-CHLORO-1,3-BENZOXAZOLE-2,4-DIOL OR "6-CHLORO-4-HYDROXY-1,3-BENZOXAZOL-2(3H)-ONE") AND PY>2004 NOT P/DT

M10	6-chloro-3-hexopyranosyl-1,3-benzoxazol-2(3H)-one CAS: - Query: ("6-CHLORO-3-HEXOPYRANOSYL-1,3-BENZOXAZOL-2(3H)-ONE") AND PY>2004 NOT P/DT
M11	6-chloro-2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl hydrogen sulfate CAS: - Query: ("6-CHLORO-2-OXO-2,3-DIHYDRO-1,3-BENZOXAZOL-4-YL HYDROGEN SULFATE" OR "6-CHLORO-2-HYDROXY-1,3-BENZOXAZOL-4-YL HYDROGEN SULFATE") AND PY>2004 NOT P/DT
M12	6-chloro-5-hydroxy-1,3-benzoxazole-2(3H)-thione CAS: - Query: (6-CHLORO-2-SULFANYL-1,3-BENZOXAZOL-5-OL OR "6-CHLORO-5-HYDROXY-1,3-BENZOXAZOLE-2(3H)-THIONE") AND PY>2004 NOT P/DT
M13	S-(6-chloro-1,3-benzoxazol-2-yl)cysteine CAS: 150807-93-5 Query: (150807-93-5 OR "S-(6-CHLORO-1,3-BENZOXAZOL-2-YL)CYSTEINE") AND PY>2004 NOT P/DT
M14	N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine CAS: - Query: ("N-ACETYL-S-(6-CHLORO-1,3-BENZOXAZOL-2-YL)CYSTEINE") AND PY>2004 NOT P/DT
M15	1-O-(N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteinyl)hexopyranuronic acid CAS: - Query: ("1-O-[N-ACETYL-S-(6-CHLORO-1,3-BENZOXAZOL-2-YL)CYSTEINYL]HEXOPYRANURONIC ACID") AND PY>2004 NOT P/DT
M16	gamma-glutamyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine CAS: 1228473-74-2 Query: (1228473-74-2 OR "GAMMA-GLUTAMYL-S-(6-CHLORO-1,3-BENZOXAZOL-2-YL)CYSTEINE") d his

B.7.7.2.3. Search results

For fenoxaprop-P-ethyl and its relevant metabolites, a total of 1250 references were identified (642 publications for fenoxaprop-P-ethyl, 608 for the metabolites) and evaluated for potential relevance.

No.	Name	Number of hits
A.I.*	Fenoxaprop-P-ethyl	642
M01	4-((6-chloro-1,3-benzoxazol-2-yl)oxy)phenol	4
M02	6-chloro-1,3-benzoxazol-2(3H)-one	23
M03	2-(4-(6-chlorobenzoxazolyl-2-yloxy)phenoxy)propanoic acid	485
M04	2-(4-hydroxyphenoxy)propanoic acid	60
M05	2-(4-hydroxyphenoxy)propanoic acid ethyl ester	16
M06	2-(4-((6-hydroxy-1,3-benzoxazol-2-yl)oxy)phenoxy)propanoic acid	0
M07	6-hydroxy-1,3-benzoxazol-2(3H)-one	18
M08	6-chloro-5-hydroxy-1,3-benzoxazol-2(3H)-one	0
M09	6-chloro-4-hydroxy-1,3-benzoxazol-2(3H)-one	0
M10	6-chloro-3-hexopyranosyl-1,3-benzoxazol-2(3H)-one	0
M11	6-chloro-2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl hydrogen sulfate	0
M12	6-chloro-5-hydroxy-1,3-benzoxazole-2(3H)-thione	0
M13	S-(6-chloro-1,3-benzoxazol-2-yl)cysteine	1
M14	N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine	0
M15	1-O-(N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteinyl)hexopyranuronic acid	0
M16	gamma-glutamyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine	1

*) A.I = active ingredient

The criteria for the assessments are laid down below.

For the *rapid assessment* the following topics were used to classify publications as being obviously irrelevant:

- Efficacy
- Analytical method development
- New ways of synthesis
- Studies on a molecular level, which cannot be related to environmental RA
- Non-EU monitoring studies
- Publications in non-EU language without English abstract
- Abstract refers to a conference contribution and does not contain data, full text not available
- Not relevant due to missing information: Studies with target organisms

For the *detailed assessment* publications which have passed the rapid assessment were evaluated on their full text versions and considered not relevant, because

- Target substance not a test item
- Conversion into units useful for RA not possible
- Study design / test system not sufficiently described
- Study design / test system not adequate
- Study design / test system not relevant to EU data requirements
- Test system not relevant to representative uses/GAPs
- Test method does not cover the right targets
- Test material deviates from composition of BCS active ingredient / product
- Findings not related to a certain test system
- no endpoint can be derived
- observations are not attributable (i.e. ecotox) to a specific substance
- effects are caused by a non-relevant route of exposure
- observations cannot be transferred into an endpoint

Table 4: Results of the study selection process, for each data requirement or group of data requirements searched

Data requirement(s) captured in the search (as indicated in Table 2)	A.I.[1)]	M01	M02	M03	M04	M05	M07	M13	M16
Total number of *summary records* retrieved after *all* searches of peer-reviewed literature[2]	642	4	23	485	60	16	18	1	1
Number of *summary records* excluded from the search results after rapid assessment for relevance	565	4	21	454	57	15	17	1	1
Total number of *full-text documents* assessed in detail[2]	77	--	2	31	3	1	1	--	--
Number of *publications* excluded from further consideration after detailed assessment for relevance	57	--	2	27	3	1	1	--	--
Number of *publications* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	20	--	--	4	--	--	--	--	--

1) A.I = active ingredient

2) both from bibliographic databases and other sources of peer-reviewed literature

The results of the detailed assessment are shown in Table 4 to Table 6.
Table 4 and *Table 5* contain those publications meeting the criteria, respectively ordered by data requirement or author while *Table* 7 contains the publications not meeting the relevance criteria for the detailed assessment.

Table 88: Report of all relevant studies and studies of unclear relevance after detailed assessment of full-text documents for relevance: ordered by data requirement

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 5.1. Studies on absorption, distribution, metabolism and excretion in mammals	Zhang, Yanfeng; Li, Xuefeng; Shen, Zhigang; Xu, Xinyuan; Zhang, Ping; Wang, Peng; Zhou, Zhiqiang.	2011	Stereoselective metabolism of fenoxaprop-ethyl and its chiral metabolite fenoxaprop in rabbits.	Chirality, Volume 23, Issue 10, Page 897-903, Publication Year 2011	Case b) The findings of this article do not change existing risk asessments. Majority of aged residues do no longer contain chiral center. Feeding studies are available.
KCA 5.9.2. Data collected on humans	Zawahir, Shukry; Roberts, Darren M.; Palangasinghe, Chathura; Mohamed, Fahim; Eddleston, Michael; Dawson, Andrew H.; Buckley, Nick A.; Ren, Lingling; Medley, Gregory A.; Gawarammana, Indika.	2009	Acute intentional self-poisoning with a herbicide product containing fenoxaprop-P-ethyl, ethoxysulfuron, and isoxadifen ethyl: A prospective observational study.	Clin. Toxicol., Volume 47, Issue 8, Page 792-797, Publication Year 2009	Case b) In this publication poisoning cases discussed in which fenoxaprop-P-ethyl was involved. No mortality and only mild symptoms after poisoning could be observed. This article can be regarded as supplmentary information.
KCA 6.5.3. Magnitude of residues in processed commodities	Inoue, Tomonori; Nagatomi, Yasushi; Suga, Keiko; Uyama, Atsuo; Mochizuki, Naoki.	2011	Fate of Pesticides during Beer Brewing.	J. Agric. Food Chem., Volume 59, Issue 8, Page 3857-3868, Publication Year 2011	Case b) Active ingredient artificially spiked to the grain. No active ingredient present in aged residues.The information provided can only be regarded as supportive information.

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 7.1.1. Route of degradation in soil	Zhang, Yanfeng; Liu, Donghui; Diao, Jinling; He, Zeying; Zhou, Zhiqiang; Wang, Peng; Li, Xuefeng	2010	Enantioselective Environmental Behavior of the Chiral Herbicide Fenoxaprop - ethyl and Its Chiral Metabolite Fenoxaprop in Soil	Journal of agricultural and food chemistry (2010) , Volume 58, Number 24, p. 12878-12884., Electronic ISSN: 0021-8561 Source Note: 2010 Dec. 22, v. 58, no. 24	Case a) In this publication the degradation behaviour of various forms of the active substance fenoxaprop-ethyl and its metabolite fenoxaprop-acid was investigated in three Chinese soils incubated at 25°C and about 60% of the MWHC in the dark for 25 days in maximum. Enantioselective HPLC analysis (chiral column) was performed following incubation of racemic mixtures as well as the separate enantiomers each of fenoxaprop-ethyl and fenoxaprop-acid.
KCA 7.2.1. Route and rate of degradation in aquatic systems (chemical and photochemical degradation)	Pythoglou, Paschalina; Vryzas, Zisis; Alexoudis, Christos; Senseman, Scott A.; Vassiliou, George.	2012	Influence of biotic and abiotic factors on dissipation of fenoxaprop-P-ethyl in water.	Fresenius Environ. Bull., Volume 21, Issue 10a, Page 3012-3017, Publication Year 2012	Case c) The article contains adequate information about the dissipation, distribution, degradation or metabolism of the substance of concern in air, soil, water or sediment over time. Although the dissipation study followed OECD guidelines the described methodology is out of scope for use in environmental risk assessment.
KCA 7.2.1.1. Hydrolytic degradation	Lin, Jing; Chen, Jingwen; Cai, Xiyun; Wang, Ying.	2009	Influential factors and the degradation pathway in hydrolysis of fenoxaprop-p-ethyl in buffer solutions.	Anquan Yu Huanjing Xuebao, Volume 9, Issue 1, Page 13-16, Publication Year 2009	Case c) The article contains adequate information about the degradation of the substance of concern in water but is out of scope for use in environmental risk assessment.
KCA 7.2.1.1. Hydrolytic degradation; KCA 8.2.4.1. Acute toxicity to Daphnia	Lin, Jing; Chen, Jingwen; Cai, Xiyun; Qiao, Xianliang; Huang, Liping; Wang, Degao; Wang, Zhuang.	2007	Evolution of toxicity upon hydrolysis of fenoxaprop-p-ethyl.	J. Agric. Food Chem., Volume 55, Issue 18, Page 7626-7629, Publication Year 2007	Case c) The article contains adequate information about the dissipation of the substance of water over time; EC_{50} values after 48h exposure to *Daphnia magna* are presented. However the publication is out of scope for use in environmental risk assessment.

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 7.2.1.2. Direct photochemical degradation; KCA 8.2.4.1. Acute toxicity to Daphnia	Lin, Jing; Chen, Jingwen; Wang, Ying; Cai, Xiyun; Wei, Xiaoxuan; Qiao, Xianliang.	2008	More Toxic and Photoresistant Products from Photodegradation of Fenoxaprop-p-ethyl.	J. Agric. Food Chem., Volume 56, Issue 17, Page 8226-8230, Publication Year 2008	Case c) The article contains adequate information about the dissipation, distribution, degradation or metabolism of the substance of concern in air, soil, water or sediment; 48h EC_{50} values are presented for additional metabolites. Publication is out of scope for use in environmental risk assessment.
KCA 7.5. Monitoring data	Barco-Bonilla, Nieves; Romero-Gonzalez, Roberto; Plaza-Bolanos, Patricia; Frenich, Antonia Garrido; Martinez Vidal, Jose L.; Salas, Juan J.; Martin, Isabel.	2013	Study of the distribution of 204 organic contaminants between the aqueous phase and the suspended particulate matter in treated wastewater for proper environmental control.	Desalin. Water Treat., Volume 51, Issue 10-12, Page 2497-2515, Publication Year 2013	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described method is out of scope for use in environmental risk assessment.
KCA 7.5. Monitoring data	Barco-Bonilla, Nieves; Romero-Gonzalez, Roberto; Plaza-Bolanos, Patricia; Martinez Vidal, Jose L.; Garrido Frenich, Antonia.	2013	Systematic study of the contamination of wastewater treatment plant effluents by organic priority compounds in Almeria province (SE Spain).	Sci. Total Environ., Volume 447, Page 381-389, Publication Year 2013	Case c) This article is out of scope for use in environmental risk assessment in particular representativity of sample collection.

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 7.5. Monitoring data	Hurtado-Sanchez, M. C.; Romero-Gonzalez, R.; Rodriguez-Caceres, M. I.; Duran-Meras, I.; Frenich, A. Garrido	2013	Rapid and sensitive on-line solid phase extraction-ultra high performance liquid chromatography-electro-spray-tandem mass spectrometry analysis of pesticides in surface waters	Journal of Chromatography A (2013), 1305, 193-202	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described analytical method is out of scope for use in environmental risk assessment.
KCA 7.5. Monitoring data	Jansson, Christer; Kreuger, Jenny.	2010	Multiresidue analysis of 95 pesticides at low nanogram/liter levels in surface waters using online preconcentration and high performance liquid chromatography/tandem mass spectrometry.	J. AOAC Int., Volume 93, Issue 6, Page 1732-1747, Publication Year 2010	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The descriped method is out of scope for use in environmental risk assessment.
KCA 7.5. Monitoring data	Lindqvist, Bengt-Olov; Hansson, Jan-Bertil; Joensson, Christina; Persson, Kenneth M.	2007	Presence of pesticide residues in groundwaters: monitoring in Simrishamn in 2002-2007.	Vatten, Volume 63, Issue 2, Page 159-163, Publication Year 2007	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. Out of scope for use in environmental risk assessment..
KCA 7.5. Monitoring data	Montoro, Elena Pastor; Gonzalez, Roberto Romero; Frenich, Antonia Garrido; Torres, M. Elena Hernandez; Vidal, Jose Luis Martinez.	2007	Fast determination of herbicides in waters by ultra-performance liquid chromatography/tandem mass spectrometry.	Rapid Commun. Mass Spectrom., Volume 21, Issue 22, Page 3585-3592, Publication Year 2007	Case c) The article is out of scope for use in environmental risk assessment in particular representativity of sample collection. No endpoint can be derived.
KCA 7.5. Monitoring data	Raeppel, Caroline; Fabritius, Marie; Nief, Marie; Appenzeller, Brice M. R.; Millet, Maurice	2014	Coupling ASE, silylation and SPME-GC/MS for the analysis of current-used pesticides in atmosphere	Talanta (2014), 121, 24-29	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described method is out of scope for use in environmental risk assessment

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 7.5. Monitoring data	Reemtsma Thorsten; Alder Lutz; Banasiak Ursula	2013	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites.	Water research, (2013 Jun 27) . Electronic Publication Date: 27 Jun 2013	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater and surface waters from the European zone. The described method is out of scope for use in environmental risk assessment
KCA 7.5. Monitoring data	Sauret, Nathalie; Wortham, Henri; Putaud, Jean-Philippe; Mirabel, Philippe.	2008	Study of the effects of environmental parameters on the gas/particle partitioning of current-use pesticides in urban air.	Atmos. Environ., Volume 42, Issue 3, Page 544-553, Publication Year 2008	Case c) The article reports on the presence of the substance of concern in samples collected from air in urban areas (Strasbourg, France). A new partition equation was defined for the pesticides under study using environmental parameters such as temperature, relative humidity, and organic carbon content of atmospheric aerosols. This assessment is out of scope for use in environmental risk assessment
KCA 7.5. Monitoring data	Sauret-Szczepanski, Nathalie; Mirabel, Philippe; Wortham, Henri.	2005	Development of an SPME-GC-MS/MS method for the determination of pesticides in rainwater: Laboratory and field experiments.	Environ. Pollut. (Amsterdam, Neth.), Volume 139, Issue 1, Page 133-142, Publication Year 2005	Case c) In this article the concentrations of fenoxaprop in rain samples from Strassbourg (France) are presented. However the method is outdated and thus out of scope for use in the environmetal risk assessment
KCA 7.5. Monitoring data	Tankiewicz, Maciej; Morrison, Calum; Biziuk, Marek	2013	Multi-residue method for the determination of 16 recently used pesticides from various chemical groups in aqueous samples by using DI-SPME coupled with GC-MS	Talanta (2013), 107, 1-10	Case c) The article reports on an analytical method applied to analytes of natural water samples from river, sea, canal and rain. The method is out of scope for use in environmental risk assessment

KCA- SANCO Data Point	Author(s)	Year	Title	Source	Classification of study
KCA 8.2.1. Acute toxicity to fish	Chen, Jiachang; Yang, Lin; Hu, Gengdong; Qu, Jianhong; Wu, Wei; Fan, Limin.	2006	Genetic toxicity of the herbicide puma super to grass carp.	Nongye Huanjing Kexue Xuebao, Volume 25, Issue 2, Page 295-300, Publication Year 2006	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Injection of grass carps with the substance of concern (Puma super) is out of scope for use in environmental risk assessment.
KCA 8.2.4.1. Acute toxicity to Daphnia	Wang, Ying; Chen, Jing-Wen; Lin, Jing; Cai, Xi-Yun.	2009	Evolutive process and mechanism of photoinduced toxicity of fenoxaprop-p-ethyl and 1-amino-2,4-dibromoanthraquinone.	Huanjing Kexue Yanjiu, Volume 22, Issue 7, Page 843-846, Publication Year 2009	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. It is out of scope for use in environmental risk assessment
KCA 8.2.6. Effects on algal growth	Ma, Jianyi; Wang, Shufeng; Wang, Pinwei; Ma, Liangjin; Chen, Xiling; Xu, Ruifu.	2006	Toxicity assessment of 40 herbicides to the green alga Raphidocelis subcapitata.	Ecotoxicol. Environ. Saf., Volume 63, Issue 3, Page 456-462, Publication Year 2006	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Out of scope for risk assessment
KCA 8.2.8. Further testing on aquatic organisms	Cevik, Fatma; Tutar, Mehmet.	2008	Effect of Fenoxaprop-p-ethyl on Natural Plankton of the Seyhan Dam: A Microcosm Study.	Bull. Environ. Contam. Toxicol., Volume 80, Issue 3, Page 247-250, Publication Year 2008	Case c) The article's relevance for the hazard assessment or risk characterization remained unclear after full-text analysis. It is out of scope for use in environmental risk assessment, not fulfilling AGD requirements.
KCA 8.2.8. Further testing on aquatic organisms	Huang, Fan; Guo, Zhengyuan; Xu, Zhen; Yang, Renbin.	2007	Toxicity of cyhalofop-butyl and fenoxaprop-ethyl to tadpole.	Nongye Huanjing Kexue Xuebao, Volume 26, Issue 3, Page 1063-1066, Publication Year 2007	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Using Bufo gargarizans tadpoles as target areas is out of scope for use in environmental risk assessment.

Table 89: Report of all relevant studies and studies of unclear relevance after detailed assessment of full-text documents for relevance: ordered by author(s)

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Barco-Bonilla, Nieves; Romero-Gonzalez, Roberto; Plaza-Bolanos, Patricia; Frenich, Antonia Garrido; Martinez Vidal, Jose L.; Salas, Juan J.; Martin, Isabel.	KCA 7.5. Monitoring data	2013	Study of the distribution of 204 organic contaminants between the aqueous phase and the suspended particulate matter in treated wastewater for proper environmental control.	Desalin. Water Treat., Volume 51, Issue 10-12, Page 2497-2515, Publication Year 2013	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described method is out of scope for use in environmental risk assessment.
Barco-Bonilla, Nieves; Romero-Gonzalez, Roberto; Plaza-Bolanos, Patricia; Martinez Vidal, Jose L.; Garrido Frenich, Antonia.	KCA 7.5. Monitoring data	2013	Systematic study of the contamination of wastewater treatment plant effluents by organic priority compounds in Almeria province (SE Spain).	Sci. Total Environ., Volume 447, Page 381-389, Publication Year 2013	Case c) This article is out of scope for use in environmental risk assessment in particular representativity of sample collection.
Cevik, Fatma; Tutar, Mehmet.	KCA 8.2.8. Further testing on aquatic organisms	2008	Effect of Fenoxaprop-p-ethyl on Natural Plankton of the Seyhan Dam: A Microcosm Study.	Bull. Environ. Contam. Toxicol., Volume 80, Issue 3, Page 247-250, Publication Year 2008	Case c) The article's relevance for the hazard assessment or risk characterization remained unclear after full-text analysis. It is out of scope for use in environmental risk assessment, not fulfilling AGD requirements.

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Chen, Jiachang; Yang, Lin; Hu, Gengdong; Qu, Jianhong; Wu, Wei; Fan, Limin.	KCA 8.2.1. Acute toxicity to fish	2006	Genetic toxicity of the herbicide puma super to grass carp.	Nongye Huanjing Kexue Xuebao, Volume 25, Issue 2, Page 295-300, Publication Year 2006	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Injection of grass carps with the substance of concern (Puma super) is out of scope for use in environmental risk assessment.
Huang, Fan; Guo, Zhengyuan; Xu, Zhen; Yang, Renbin.	KCA 8.2.8. Further testing on aquatic organisms	2007	Toxicity of cyhalofop-butyl and fenoxaprop-ethyl to tadpole.	Nongye Huanjing Kexue Xuebao, Volume 26, Issue 3, Page 1063-1066, Publication Year 2007	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Using Bufo gargarizans tadpoles as target areas is out of scope for use in environmental risk assessment.
Hurtado-Sanchez, M. C.; Romero-Gonzalez, R.; Rodriguez-Caceres, M. I.; Duran-Meras, I.; Frenich, A. Garrido	KCA 7.5. Monitoring data	2013	Rapid and sensitive on-line solid phase extraction-ultra high performance liquid chromatography-electro-spray-tandem mass spectrometry analysis of pesticides in surface waters	Journal of Chromatography A (2013), 1305, 193-202	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described analytical method is out of scope for use in environmental risk assessment.
Inoue, Tomonori; Nagatomi, Yasushi; Suga, Keiko; Uyama, Atsuo; Mochizuki, Naoki.	KCA 6.5.3. Magnitude of residues in processed commodities	2011	Fate of Pesticides during Beer Brewing.	J. Agric. Food Chem., Volume 59, Issue 8, Page 3857-3868, Publication Year 2011	Case b) Active ingredient artificially spiked to the grain. No active ingredient present in aged residues.The information provided can only be regarded as supportive information.
Jansson, Christer; Kreuger, Jenny.	KCA 7.5. Monitoring data	2010	Multiresidue analysis of 95 pesticides at low nanogram/liter levels in surface waters using online preconcentration and high performance liquid chromatography/tandem mass spectrometry.	J. AOAC Int., Volume 93, Issue 6, Page 1732-1747, Publication Year 2010	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The descriped method is out of scope for use in environmental risk assessment.

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Lin, Jing; Chen, Jingwen; Cai, Xiyun; Qiao, Xianliang; Huang, Liping; Wang, Degao; Wang, Zhuang.	KCA 7.2.1.1. Hydrolytic degradation; KCA 8.2.4.1. Acute toxicity to Daphnia	2007	Evolution of toxicity upon hydrolysis of fenoxaprop-p-ethyl.	J. Agric. Food Chem., Volume 55, Issue 18, Page 7626-7629, Publication Year 2007	Case c) The article contains adequate information about the dissipation of the substance of water over time; EC_{50} values after 48h exposure to *Daphnia magna* are presented. However the publication is out of scope for use in environmental risk assessment.
Lin, Jing; Chen, Jingwen; Cai, Xiyun; Wang, Ying.	KCA 7.2.1.1. Hydrolytic degradation	2009	Influential factors and the degradation pathway in hydrolysis of fenoxaprop-p-ethyl in buffer solutions.	Anquan Yu Huanjing Xuebao, Volume 9, Issue 1, Page 13-16, Publication Year 2009	Case c) The article contains adequate information about the degradation of the substance of concern in water but is out of scope for use in environmental risk assessment.
Lin, Jing; Chen, Jingwen; Wang, Ying; Cai, Xiyun; Wei, Xiaoxuan; Qiao, Xianliang.	KCA 7.2.1.2. Direct photochemical degradation; KCA 8.2.4.1. Acute toxicity to Daphnia	2008	More Toxic and Photoresistant Products from Photodegradation of Fenoxaprop-p-ethyl.	J. Agric. Food Chem., Volume 56, Issue 17, Page 8226-8230, Publication Year 2008	Case c) The article contains adequate information about the dissipation, distribution, degradation or metabolism of the substance of concern in air, soil, water or sediment; 48h EC_{50} values are presented for additional metabolites. Publication is out of scope for use in environmental risk assessment.
Lindqvist, Bengt-Olov; Hansson, Jan-Bertil; Joensson, Christina; Persson, Kenneth M.	KCA 7.5. Monitoring data	2007	Presence of pesticide residues in groundwaters: monitoring in Simrishamn in 2002-2007.	Vatten, Volume 63, Issue 2, Page 159-163, Publication Year 2007	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. Out of scope for use in environmental risk assessment..
Ma, Jianyi; Wang, Shufeng; Wang, Pinwei; Ma, Liangjin; Chen, Xiling; Xu, Ruifu.	KCA 8.2.6. Effects on algal growth	2006	Toxicity assessment of 40 herbicides to the green alga Raphidocelis subcapitata.	Ecotoxicol. Environ. Saf., Volume 63, Issue 3, Page 456-462, Publication Year 2006	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. Out of scope for risk assessment

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Montoro, Elena Pastor; Gonzalez, Roberto Romero; Frenich, Antonia Garrido; Torres, M. Elena Hernandez; Vidal, Jose Luis Martinez.	KCA 7.5. Monitoring data	2007	Fast determination of herbicides in waters by ultra-performance liquid chromatography/tandem mass spectrometry.	Rapid Commun. Mass Spectrom., Volume 21, Issue 22, Page 3585-3592, Publication Year 2007	Case c) The article is out of scope for use in environmental risk assessment in particular representativity of sample collection. No endpoint can be derived.
Pythoglou, Paschalina; Vryzas, Zisis; Alexoudis, Christos; Senseman, Scott A.; Vassiliou, George.	KCA 7.2.1. Route and rate of degradation in aquatic systems (chemical and photochemical degradation)	2012	Influence of biotic and abiotic factors on dissipation of fenoxaprop-P-ethyl in water.	Fresenius Environ. Bull., Volume 21, Issue 10a, Page 3012-3017, Publication Year 2012	Case c) The article contains adequate information about the dissipation, distribution, degradation or metabolism of the substance of concern in air, soil, water or sediment over time. Although the dissipation study followed OECD guidelines the described methodology is out of scope for use in environmental risk assessment.
Raeppel, Caroline; Fabritius, Marie; Nief, Marie; Appenzeller, Brice M. R.; Millet, Maurice	KCA 7.5. Monitoring data	2014	Coupling ASE, silylation and SPME-GC/MS for the analysis of current-used pesticides in atmosphere	Talanta (2014), 121, 24-29	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater, soil, surface waters, sediments or air from the European zone. The described method is out of scope for use in environmental risk assessment
Reemtsma Thorsten; Alder Lutz; Banasiak Ursula	KCA 7.5. Monitoring data	2013	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites.	Water research, (2013 Jun 27) . Electronic Publication Date: 27 Jun 2013	Case c) The article reports on the presence of the substance of concern in samples collected from groundwater and surface waters from the European zone. The described method is out of scope for use in environmental risk assessment

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Sauret, Nathalie; Wortham, Henri; Putaud, Jean-Philippe; Mirabel, Philippe.	KCA 7.5. Monitoring data	2008	Study of the effects of environmental parameters on the gas/particle partitioning of current-use pesticides in urban air.	Atmos. Environ., Volume 42, Issue 3, Page 544-553, Publication Year 2008	Case c) The article reports on the presence of the substance of concern in samples collected from air in urban areas (Strasbourg, France). A new partition equation was defined for the pesticides under study using environmental parameters such as temperature, relative humidity, and organic carbon content of atmospheric aerosols. This assessment is out of scope for use in environmental risk assessment
Sauret-Szczepanski, Nathalie; Mirabel, Philippe; Wortham, Henri.	KCA 7.5. Monitoring data	2005	Development of an SPME-GC-MS/MS method for the determination of pesticides in rainwater: Laboratory and field experiments.	Environ. Pollut. (Amsterdam, Neth.), Volume 139, Issue 1, Page 133-142, Publication Year 2005	Case c) In this article the concentrations of fenoxaprop in rain samples from Strassbourg (France) are presented. However the method is outdated and thus out of scope for use in the environmetal risk assessment
Tankiewicz, Maciej; Morrison, Calum; Biziuk, Marek	KCA 7.5. Monitoring data	2013	Multi-residue method for the determination of 16 recently used pesticides from various chemical groups in aqueous samples by using DI-SPME coupled with GC-MS	Talanta (2013), 107, 1-10	Case c) The article reports on an analytical method applied to analytes of natural water samples from river, sea, canal and rain. The method is out of scope for use in environmental risk assessment
Wang, Ying; Chen, Jing-Wen; Lin, Jing; Cai, Xi-Yun.	KCA 8.2.4.1. Acute toxicity to Daphnia	2009	Evolutive process and mechanism of photoinduced toxicity of fenoxaprop-p-ethyl and 1-amino-2,4-dibromoanthraquinone.	Huanjing Kexue Yanjiu, Volume 22, Issue 7, Page 843-846, Publication Year 2009	Case c) The article contains adequate information about the toxicity of the substance of concern to non-target organisms living in the environment. It is out of scope for use in environmental risk assessment

Author(s)	KCA- SANCO Data Point	Year	Title	Source	Classification of study
Zawahir, Shukry; Roberts, Darren M.; Palangasinghe, Chathura; Mohamed, Fahim; Eddleston, Michael; Dawson, Andrew H.; Buckley, Nick A.; Ren, Lingling; Medley, Gregory A.; Gawarammana, Indika.	KCA 5.9.2. Data collected on humans	2009	Acute intentional self-poisoning with a herbicide product containing fenoxaprop-P-ethyl, ethoxysulfuron, and isoxadifen ethyl: A prospective observational study.	Clin. Toxicol., Volume 47, Issue 8, Page 792-797, Publication Year 2009	Case b) In this publication poisoning cases discussed in which fenoxaprop-P-ethyl was involved. No mortality and only mild symptoms after poisoning could be observed. This article can be regarded as supplmentary information.
Zhang, Yanfeng; Li, Xuefeng; Shen, Zhigang; Xu, Xinyuan; Zhang, Ping; Wang, Peng; Zhou, Zhiqiang.	KCA 5.1. Studies on absorption, distribution, metabolism and excretion in mammals	2011	Stereoselective metabolism of fenoxaprop-ethyl and its chiral metabolite fenoxaprop in rabbits.	Chirality, Volume 23, Issue 10, Page 897-903, Publication Year 2011	Case b) The findings of this article do not change existing risk asessments. Majority of aged residues do no longer contain chiral center. Feeding studies are available.
Zhang, Yanfeng; Liu, Donghui; Diao, Jinling; He, Zeying; Zhou, Zhiqiang; Wang, Peng; Li, Xuefeng	KCA 7.1.1. Route of degradation in soil	2010	Enantioselective Environmental Behavior of the Chiral Herbicide Fenoxaprop - ethyl and Its Chiral Metabolite Fenoxaprop in Soil	Journal of agricultural and food chemistry (2010) , Volume 58, Number 24, p. 12878-12884., Electronic ISSN: 0021-8561 Source Note: 2010 Dec. 22, v. 58, no. 24	Case a) In this publication the degradation behaviour of various forms of the active substance fenoxaprop-ethyl and its metabolite fenoxaprop-acid was investigated in three Chinese soils incubated at 25°C and about 60% of the MWHC in the dark for 25 days in maximum. Enantioselective HPLC analysis (chiral column) was performed following incubation of racemic mixtures as well as the separate enantiomers each of fenoxaprop-ethyl and fenoxaprop-acid.

Table 7: Report of none-relevant studies excluded after detailed assessment of full-text documents and the removal of duplicate entries (removed due to the separated queries for the compounds, duplicates: 9): ordered by author(s)

Author	Year	Title	Source	Reason for not including in dossier
Afify, Abd El-Moneim M. R.; Attallah, Emad R.; El-Gammal, Hassan A.	2012	A modified multi-residue method for analysis of 150 pesticide residues in green beans using liquid chromatography-tandem mass spectrometry.	AFS, Adv. Food Sci., Volume 34, Issue 1, Page 24-35, Publication Year 2012	Poor data documentation
Akiyama, Yumi; Matsuoka, Tomofumi; Mitsuhashi, Takao.	2009	Multi-residue screening method of acidic pesticides in agricultural products by liquid chromatography/time of flight mass spectrometry.	J. Pestic. Sci. (Tokyo, Jpn.), Volume 34, Issue 4, Page 265-272, Publication Year 2009	Findings cannot be not related to a certain test system
Anil Gupta; Ashok Aggarwal; Chhavi Mangla; Aditya Kumar; Anju Tanwar; Gupta, A.; Aggarwal, A.; Mangla, C.; Kumar, A.; Tanwar, A.	2011	Effect of herbicides fenoxaprop - P - ethyl and 2,4-D ethyl-ester on soil mycoflora including VAM fungi in wheat crop.	Indian Journal of Weed Science (2011) , Volume 43, Number 1/2, pp. 32-40, 23 refs. ISSN: 0253-8040 Published by: Indian Society of Weed Science, Hisar	A detailed analysis indicats that the publication is not reliable. Authors have published for another active substance nearly identical text and results as shown in the complex tables 3 of the publication (see Gupta et al. (2011), EcoScan; 1: 195-199 – not part of this LRR)
Anon.	2009	Study of analytical method for pesticide residues in vegetables and fruits by GC/MS/MS.	Hiroshima-shi Eisei Kenkyusho Nenpo, Volume 28, Page 54-61, Publication Year 2009	No endpoint can be derived
Banerjee, Kaushik; Utture, Sagar; Dasgupta, Soma; Kandaswamy, Chandrasekar; Pradhan, Saswati; Kulkarni, Sunil; Adsule, Pandurang	2012	Multiresidue determination of 375 organic contaminants including pesticides, polychlorinated biphenyls and polyaromatic hydrocarbons in fruits and vegetables by gas chromatography-triple quadrupole mass spectrometry with introduction of semi-quantification approach	Journal of Chromatography, A (2012), 1270, 283-295	No endpoint can be derived
Bates, Amber N.; Henry, Gerald M.; Mckenney, Cynthia B.	2013	Tolerance of Hookers evening primrose (Oenothera elata) transplants to postemergence herbicides	Weed Technology (2013), 27(2), 401-404	The data presented in this article is not suitable to allow contribution to risk assessment.
Bozdogan, Ali Musa; Yarpuz-Bozdogan, Nigar; Tobi, Ibrahim; Sayinci, Bahadir	2015	Estimation of occupational risk in herbicide application	Fresenius Environmental Bulletin (2015), 24(7), 2275-2279	Not relevant as the calculations were not performed with the model used currently in EU. There is no indication of the values used for the calculations.

Author	Year	Title	Source	Reason for not including in dossier
Cai Yue; Zhang Shengli; Li Zengzhi; Cai, Y.; Zhang, S. L.; Li, Z. Z.	2011	Compatibility of Beauveria bassiana to some chemical insecticides and herbicides.	Chinese Journal of Biological Control (2011) , Volume 27, Number 3, pp. 316-323, 18 refs. ISSN: 2095-039X Published by: Chinese Journal of Biological Control, Chinese Academy of Agricultural Sciences, Beijing	The investigation does not report results in values reflecting agreed determinants for the hazard or exposure characterization or risk assessment under Reg. EC No 1107/2009 and information is insufficient to transfer values into such determinants
Chen, Jianmei; Shen, Weiming; Gu, Hao	2008	Determination of dissociation constants of R-(+)- 2 -(4 - hydroxyphenoxy) propanoic acid	Nongyao (2008), 47(11), 800-801, 815	The investigation does not report results in values reflecting agreed determinants for the hazard or exposure characterization or risk assessment under Reg. EC No 1107/2009 and information is insufficient to transfer values into such determinants
Chen, Lin-Mei; Sun, Qing; Chen, Ling; Jiang, Jing-Yan	2014	Effects of herbicides on N2O emissions and soil biochemical parameters in winter-wheat field	Nongye Huanjing Kexue Xuebao (2014), 33(7), 1450-1459	The investigation is made in field experiments in China, which cannot be considered as representative for EU.
Creton, Stuart; Weltje, Lennart; Hobson, Hannah; Wheeler, James R.	2013	Reducing the number of fish in bioconcentration studies for plant protection products by reducing the number of test concentrations.	Chemosphere, Volume 90, Issue 3, Page 1300-1304, Publication Year 2013	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature
Das, A. C.; Das, S. J.; Dey, S.	2012	Effect of herbicides on microbial biomass in relation to availability of plant nutrients in soil.	Journal of Crop and Weed (2012) , Volume 8, Number 1, pp. 129-132, 17 refs. ISSN: 0974-6315 Published by: Crop and Weed Science Society, West Bengal	The publication states that the compound has been mixed into the soil but does not indicate at which rate. The results can therefore not be converted to values suitable for risk assessment.
Das, Amal Chandra; Dey, Sakti	2014	Effect of Combined Application of Systemic Herbicides on Microbial Activities in North Bengal Alluvial Soil	Bulletin of Environmental Contamination and Toxicology (2014), 92(2), 183-189	The observations made relate to a mixture of active substances which is not considered representative for AIR3; results only for fenoxaprop cannot be extracted from available data
Das, Amal Chandra; Dey, Sakti	2013	Effect of Systemic Herbicides on Microbial Biomass in Relation to Availability of Some Plant Nutrients in an Alluvial Soil of West Bengal	Bulletin of Environmental Contamination and Toxicology (2013), 90(6), 666-672	The publication states that the compound has been mixed into the soil but does not indicate at which rate. The results can therefore not be converted to values suitable for risk assessment.
Dear, B. S.; Sandral, G. A.; Wilson, B. C. D.	2006	Tolerance of perennial pasture grass seedlings to pre- and post-emergent grass herbicides.	Aust. J. Exp. Agric., Volume 46, Issue 5, Page 637-644, Publication Year 2006	The data presented in this article is not suitable to allow contribution to risk assessment.

Author	Year	Title	Source	Reason for not including in dossier
Dixit, Anil [Reprint Author]; Sondhia, Shobha; Varshney, Jay G.	2011	Bio-efficacy of pinoxaden in wheat (Triticum aestivum) and its residual effect in succeeding rice (Oryza sativa) crop.	Indian Journal of Agricultural Sciences, (JUL 2011) Vol. 81, No. 7, pp. 659-661.	The article does not contain information related to the substance of concern. Furthermore it is a matter of observations for environmental responses in a region outside Europe
Dong, Weiliang; Hou, Ying; Xi, Xuedong; Wang, Fei; Li, Zhoukun; Ye, Xianfeng; Huang, Yan; Cui, Zhongli	2015	Biodegradation of fenoxaprop - ethyl by an enriched consortium and its proposed metabolic pathway	International Biodeterioration and Biodegradation (2015), 97, 159-167	Duplicate entry, This publication has been found and evaluated for the A.I, M03, M06 and M07. The test soil (chinese soil) and the test design (soil enriched with microbes) cannot be considered to be representative for an EU risk assessment
Fantke, Peter; Gillespie, Brenda W.; Juraske, Ronnie; Jolliet, Olivier.	2014	Estimating Half-Lives for Pesticide Dissipation from Plants.	Environ. Sci. Technol., Volume 48, Issue 15, Page 8588-8602, Publication Year 2014	Study design / test system used in this article is not relevant to EU data requirements
Fantke, Peter; Juraske, Ronnie; Anton, Assumpcio; Friedrich, Rainer; Jolliet, Olivier.	2011	Dynamic Multicrop Model to Characterize Impacts of Pesticides in Food.	Environ. Sci. Technol., Volume 45, Issue 20, Page 8842-8849, Publication Year 2011	Study design / test system used in this article is not relevant to EU data requirements
Farhat-Un-Nisa Shehzad; Jasmin Shah; Jan, M. R.	2012	Spectrophotometric method for the determination of fenoxaprop - p - ethyl herbicide in wheat and barley grains using charge transfer complex.	Sarhad Journal of Agriculture (2012) , Volume 28, Number 1, pp. 63-68, 20 refs. ISSN: 1016-4383 Published by: Agricultural University Peshawar, Peshawar URL (Availability): http://www.aup.edu.pk/sj_pdf/SPECTROPHOTOMETRIC percent20ME THOD percent20FOR percent20THE percent20DETERMINATION percent20OF percent20FENOXAPROP-P-ETHYL percent20HERBICIDE percent20IN percent20 percent20-149-2011.pdf	The findings of this article cannot be related to a certain test system
Finizio, A.; Villa, S.; Vighi, M.	2007	Prediction of pesticide mixtures in surface waters emitted from some relevant crops in Italy	Environmental Fate and Ecological Effects of Pesticides, Symposium Pesticide Chemistry, 13th, Piacenza, Italy, Sept. 3-6, 2007 (2007), 526-535. Editor(s): Del Re, Attilio Amerigo Maria. Publisher: Goliardica Pavese s.r.l., Pavia, Italy.	The investigation does not report results in values reflecting agreed determinants for the hazard characterization or risk assessment under Reg. EC No 1107/2009 and information is insufficient to transfer values into such determinants

Author	Year	Title	Source	Reason for not including in dossier
Gomez-Perez, Maria Luz; Plaza-Bolanos, Patricia; Romero-Gonzalez, Roberto; Martinez-Vidal, Jose Luis; Garrido-Frenich, Antonia.	2012	Comprehensive qualitative and quantitative determination of pesticides and veterinary drugs in honey using liquid chromatography-Orbitrap high resolution mass spectrometry.	J. Chromatogr., A, Volume 1248, Page 130-138, Publication Year 2012; J. Chromatogr. A, Volume 1248, Page 130-138, Publication Year 2012	No endpoint can be derived; As sample of honey does not derive from bee hive, the results are not considered to allow contribution for the bee exposure risk assessment.
Greulich, Kerstin; Alder, Lutz.	2008	Fast multiresidue screening of 300 pesticides in water for human consumption by LC-MS/MS.	Anal. Bioanal. Chem., Volume 391, Issue 1, Page 183-197, Publication Year 2008	No endpoint can be derived
Guo, Zheng-Yuan; Huang, Fan; Xu, Zhen.	2008	Residue dynamics of 10 percent fenoxaprop-P-ethyl cyhalofop-butyl EC in rice.	Shengtai Yu Nongcun Huanjing Xuebao, Volume 24, Issue 1, Page 51-54, Publication Year 2008	The article reports on potential hazard observations in the field that cannot be correlated with an agricultural treatment representative for usage of the substance of concern. No essential use.
Henning-De Jong, Irmgard; Van Zelm, Rosalie; Huijbregts, Mark A. J.; De Zwart, Dick; Van Der Linden, Ton M. A.; Wintersen, Arjen; Posthuma, Leo; Van De Meent, Dik.	2008	Ranking of agricultural pesticides in the Rhine-Meuse-Scheldt basin based on toxic pressure in marine ecosystems.	Environ. Toxicol. Chem., Volume 27, Issue 3, Page 737-745, Publication Year 2008	The observations made are based upon an application or exposure that does not allow transferring the results into a value that can be used for the purpose of the hazard assessment or risk characterization
Hong, S.-M.; Kwon, H.-Y.; Kim, T.-K.; Kim, D.-H.	2013	Analysis of pesticide residues in brown rice using modified quechers multiresidue method	Organohalogen Compounds (2013), 75, 50-53	Findings not related to a certain test system
Hua R M; Song L Y Hua R M (Reprint); Song L Y	2006	Separation of fenoxaprop - p - ethyl biodegradation products by HPTLC (vol 18, pg 85, 2005)	JPC-JOURNAL OF PLANAR CHROMATOGRAPHY-MODERN TLC, (JAN-FEB 2006) Vol. 19, No. 107, pp. 86-86. ISSN: 0933-4173.	The publication is regarded as an exploratory study as it provides information on effects on cellular or molecular level, investigates on biochemical or clinical responses or reports on metabolism or degradation from isolated micro-organisms.
Huang, Zhiqiang; Zhang, Ying; Wang, Libing; Ding, Li; Wang, Meilin; Yan, Hongfei; Li, Yongjun; Zhu, Shaohua.	2009	Simultaneous determination of 103 pesticide residues in tea samples by LC-MS/MS.	J. Sep. Sci., Volume 32, Issue 9, Page 1294-1301, Publication Year 2009	Findings not related to a certain test system
Inoue, Tomonori; Nagatomi, Yasushi; Kinami, Tomohisa; Uyama, Atsuo; Mochizuki, Naoki.	2010	Fate of pesticides in a distilled spirit of barley shochu during the distillation process.	Biosci., Biotechnol., Biochem., Volume 74, Issue 12, Page 2518-2522, Publication Year 2010	Observations cannot be transferred into an endpoint

Author	Year	Title	Source	Reason for not including in dossier
Ishibashi, Megumi; Izumi, Yoshihiro; Sakai, Miho; Ando, Takashi; Fukusaki, Eiichiro; Bamba, Takeshi	2014	High-throughput simultaneous analysis of pesticides by supercritical fluid chromatography coupled with high-resolution mass spectrometry	Journal of Agricultural and Food Chemistry (2014) Ahead of Print	No endpoint can be derived
Jamin, Emilien L.; Bonvallot, Nathalie; Tremblay-Franco, Marie; Cravedi, Jean-Pierre; Chevrier, Cecile; Cordier, Sylvaine; Debrauwer, Laurent	2013	Untargeted profiling of pesticide metabolites by LC-HRMS: an exposomics tool for human exposure evaluation	Analytical and Bioanalytical Chemistry Ahead of Print	Observations cannot be transferred into an endpoint
Jammer, S.; Voloshenko, A.; Gelman, F.; Lev, O.	2014	Chiral and Isotope Analyses for Assessing the Degradation of Organic Contaminants in the Environment: Rayleigh Dependence	Environmental Science and Technology (2014), 48(6), 3310-3318	Authors calculate the fenoxaprop degradation rate constant based on data from Zhang (2010; evaluated for parent compound, Table 88)
Kaiser, Y. I.; Gerhards, R.	2014	Degradation and metabolism of fenoxaprop - P - ethyl in sensitive and resistant populations of Alopecurus myosuroides.	Julius-Kuehn-Archiv (2014) , Number 443, pp. 52-59, 14 refs. ISSN: 1868-9892 Published by: Julius Kuehn Institut, Bundesforschungsinstitut fuer Kulturpflanzen, Quedlinburg Conference: Proceedings 26th German Conference on Weed Biology and Weed Control, Braunschweig, Germany, 11-13 March, 2014. URL (Availability): http://pub.jki.bund.de/index.php/JKA/issue/archive	Study design / test system used in this article is not adequate.
Kaiser, Yasmin Isabelle; Gerhards, Roland	2015	Degradation and Metabolism of Fenoxaprop and Mesosulfuron + Iodosulfuron in Multiple Resistant Blackgrass (Alopecurus myosuroides)	Gesunde Pflanzen (2015), 67(3), 109-117	Study design / test system used in this article is not adequate.
Katagi, Toshiyuki [Reprint Author]	2012	Isomerization of chiral pesticides in the environment.	Journal of Pesticide Science, (2012) Vol. 37, No. 1, pp. 1-14. ISSN: 1348-589X. E-ISSN: 1349-0923.; Journal of Pesticide Science, (2012) Vol. 37, No. 1, pp. 1-14. ISSN: 1348-589X. E-ISSN: 1349-0923.	The investigation does not report results in values reflecting agreed determinants for the hazard or exposure characterization or risk assessment under Reg. EC No 1107/2009 and information is insufficient to transfer values into such determinants
Khan, M. I.; Hassan, G.; Khan, I.; Marwat, K. B.; Khan, N. U.; Gul, R.	2011	Tolerance of chickpea (Cicer arietinum L.) cultivars to the major chickpea herbicides.	Pak. J. Bot., Volume 43, Issue 5, Page 2497-2501, Publication Year 2011	The data presented in this article is not suitable to allow contribution to risk assessment.

Author	Year	Title	Source	Reason for not including in dossier
Kobayashi, Yukari; Yoshizaki, Mayuko; Shimizu, Masanori; Maruyama, Kouichi	2014	Validation study on a multi-residue method for determination of pesticides in agricultural products by LC-MS/MS	Niigata-ken Hoken Kankyo Kagaku Kenkyusho Nenpo (2014), 29, 68-72	No endpoint can be derived
Kudsk, Per; Taberner, Andreu; De Troiani, Rosa M.; Sanchez, Teresa M.; Mathiassen, Solvejg K.	2012	Herbicide tolerance and seed survival of grain amaranth (Amaranthus sp.)	Australian Journal of Crop Science (2012), 6(12), 1674-1680	The presented data is not suitable to allow contribution to risk assessment.
Lacina, Ondrej; Zachariasova, Milena; Urbanova, Jana; Vaclavikova, Marta; Cajka, Tomas; Hajslova, Jana.	2012	Critical assessment of extraction methods for the simultaneous determination of pesticide residues and mycotoxins in fruits, cereals, spices and oil seeds employing ultra-high performance liquid chromatography-tandem mass spectrometry.	J. Chromatogr. A, Volume 1262, Page 8-18, Publication Year 2012; J. Chromatogr., A, Volume 1262, Page 8-18, Publication Year 2012	No endpoint can be derived
Lewis, D. F.; Mcelroy, J. S.; Sorochan, J. C.; Mueller, T. C.; Samples, T. J.; Breeden, G. K.	2010	Efficacy and safening of aryloxyphenoxypropionate herbicides when tank-mixed with triclopyr for bermudagrass control in zoysiagrass turf	Weed Technology (2010), 24(4), 489-494	The publication is a matter of observations for environmental responses in a region outside Europe
Loos, Martin; Krauss, Martin; Fenner, Kathrin.	2012	Pesticide Nonextractable Residue Formation in Soil: Insights from Inverse Modeling of Degradation Time Series.	Environ. Sci. Technol., Volume 46, Issue 18, Page 9830-9837, Publication Year 2012	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature (soil biological activity)
Lucini, Luigi; Molinari, Gian Pietro.	2011	Detection of the herbicide fenoxaprop-P-ethyl, its agronomic safener isoxadifen ethyl and their metabolites residue in rice.	Qual. Assur. Saf. Crops Foods, Volume 3, Issue 2, Page 63-68, Publication Year 2011	No essential use
Lucini, Luigi; Molinari, Gian Pietro.	2010	Residues of the herbicide fenoxaprop-P-ethyl, its agronomic safener isoxadifen-ethyl and their metabolites in rice after field application.	Pest Manage. Sci., Volume 66, Issue 6, Page 621-626, Publication Year 2010	Duplicate entry, This publication has been found and evaluated for the A.I, M03 and M02. The article reports on chemical synthesis or development of methods for measurements of the chemical without its application to natural samples. No essential use.
Luks, Ann-Katrin (Reprint); Wijntjes, Christiaan; Schmidt, Burkhard Luks, Ann-Katrin (Reprint) Luks, Ann-Katrin (Reprint); Schmidt, Burkhard	2016	Metabolism of the C-14-labeled herbicide clodinafop-propargyl in plant cell cultures of wheat and tobacco	JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B-PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES, (1 FEB 2016) Vol. 51, No. 2, pp. 71-80. ISSN: 0360-1234.	Study design / test system used in this article is not adequate.

Author	Year	Title	Source	Reason for not including in dossier
Matsuoka, Tomofumi; Akiyama, Yumi; Mitsuhashi, Takao.	2009	Screening method of pesticides in meat using cleanup with GPC and mini-column.	Shokuhin Eiseigaku Zasshi, Volume 50, Issue 2, Page 97-107, Publication Year 2009	No endpoint can be derived
Mehta, Ramesh; Yadav, Ashok.	2011	Residual studies of herbicide AEF-046360-8 percent + DIC-1468-14-22 percent EC in soil, wheat straw and grains by HPLC.	Environ. Ecol., Volume 29, Issue 4A, Page 2091-2093, Publication Year 2011	The publication is a matter of observations for environmental responses in a region outside Europe
Mezcua, Milagros; Malato, Octavio; Garcia-Reyes, Juan F.; Molina-Diaz, Antonio; Fernandez-Alba, Amadeo R.	2009	Accurate-Mass Databases for Comprehensive Screening of Pesticide Residues in Food by Fast Liquid Chromatography Time-of-Flight Mass Spectrometry.	Anal. Chem. (Washington, DC, U. S.), Volume 81, Issue 3, Page 913-929, Publication Year 2009	Findings not related to a certain test system
Min, Zaw Win; Hong, Su-Myeong; Yang, In-Cheol; Kwon, Hye-Young; Kim, Taek-Kyum; Kim, Doo-Ho	2012	Analysis of pesticide residues in brown rice using modified QuEChERS multiresidue method combined with electrospray ionization-liquid chromatography-tandem mass spectrometric detection	Journal of the Korean Society for Applied Biological Chemistry (2012), 55(6), 769-775	Findings not related to a certain test system
Nakamura, Sadao; Yamagami, Takashi; Ono, Yukiko; Toubou, Kenichi; Daishima, Shigeki	2013	Multi-residue analysis of pesticides in agricultural products by GC/MS using synchronous SIM/scan acquisition	Bunseki Kagaku (2013), 62(3), 229-241	No endpoint can be derived
Namikawa, Mikio; Shibata, Sayo; Shiomi, Tetsuo; Nakagawa, Tomoyuki; Ban, Soichiro; Tomita, Yoko; Semura, Shunsuke; Nakao, Yoshie; Banno, Yukinori; Kawakami, Masahiro.	2014	Simultaneous analysis of residual pesticides in fruit, vegetables, brown rice, and oolong tea by LC-MS/MS.	Shokuhin Eiseigaku Zasshi, Volume 55, Issue 6, Page 279-289, Publication Year 2014	No endpoint can be derived
Nimanthika, W. J.; Weerakoon, S. R.	2011	Impact of pre-and post-planting herbicides on growth performance and yield of Oryza genotypes in Sri Lanka.	23rd Asian-Pacific Weed Science Society Conference. Volume 1: weed management in a changing world, Cairns, Queensland, Australia, 26-29 September 2011 (2011) , pp. 405-410, 7 refs. ISBN: 978-0-9871961-0-1 Published by: Asian-Pacific Weed Science Society, Cairns Conference: 23rd Asian-Pacific Weed Science Society Conference. Volume 1: weed management in a changing world, Cairns, Queensland, Australia, 26-29 September 2011.	The article reports exactly on the same results as in Nimanthika and Weerakkoon 2012, Pakistan Journal of Weed Science Research, Volume 18, Number Special Issue, pp. 469-475 – see below

Author	Year	Title	Source	Reason for not including in dossier
Nimanthika, W. J.; Weerakoon, S. R.	2012	Impact of pre-and post-planting herbicides on growth performance and yield of Oryza genotypes in Sri Lanka. Special issue.	Pakistan Journal of Weed Science Research (2012) , Volume 18, Number Special Issue, pp. 469-475, 7 refs. ISSN: 1815-1094 Published by: Weed Science Society of Pakistan, Department of Weed Science, Peshawar URL (Availability): http://www.wssp.org.pk/si-53-2012,469-475.pdf	The data presented in this article is not suitable to allow contribution to risk assessment.
Nougadere, Alexandre; Reninger, Jean-Cedric; Volatier, Jean-Luc; Leblanc, Jean-Charles.	2011	Chronic dietary risk characterization for pesticide residues: A ranking and scoring method integrating agricultural uses and food contamination data.	Food Chem. Toxicol., Volume 49, Issue 7, Page 1484-1510, Publication Year 2011	The dietary risk assessments presented in the publication are not based on the methodology that has to be applied in a regulatory context and/or do not provide relevant information about the risks that result specifically from the representative use(s).; no data reported which might be used for environmental fate or risk assessment; all experimental data derived from other sources
Nowell, Lisa H.; Norman, Julia E.; Moran, Patrick W.; Martin, Jeffrey D.; Stone, Wesley W.	2014	Pesticide Toxicity Index-A tool for assessing potential toxicity of pesticide mixtures to freshwater aquatic organisms	Science of the Total Environment (2014), 476-477, 144-157	No data has been reported which might be used for environmental fate or risk assessment; all experimental data derived from other sources
Omote, M.; Harayama, K.; Sasaki, T.; Mochizuki, N.; Yamashita, H.	2006	Analysis of simultaneous screening for 277 pesticides in malt and beer by liquid chromatography with tandem mass spectrometry.	J. Am. Soc. Brew. Chem., Volume 64, Issue 3, Page 139-150, Publication Year 2006	Findings not related to a certain test system
Padilla, S.; Corum, D.; Padnos, B.; Hunter, D. L.; Beam, A.; Houck, K. A.; Sipes, N.; Kleinstreuer, N.; Knudsen, T.; Dix, D. J.; Reif, D. M.	2012	Zebrafish developmental screening of the ToxCast Phase I chemical library.	Reprod. Toxicol., Volume 33, Issue 2, Page 174-187, Publication Year 2012	The article is on the racemate fenoxaprop-ethyl and NOT on the substance of concern, i.e. fenoxaprop-P-ethyl.
Papadakis, Emmanouil-Nikolaos; Tsaboula, Aggeliki; Kotopoulou, Athina; Kintzikoglou, Katerina; Vryzas, Zisis; Papadopoulou-Mourkidou, Euphemia	2015	Pesticides in the surface waters of Lake Vistonis Basin, Greece: Occurrence and environmental risk assessment	Science of the Total Environment (2015), 536, 793-802	The article does not contain information related to the substance of concern

Author	Year	Title	Source	Reason for not including in dossier
Parul Chaudhary; Rahman, S. M. A.; Chaudhary, P.	2008	Screening of some agrochemicals on feeding preference of Spilarctia obliqua Walker.	Progressive Research (2008) Volume 3, Number 2, pp. 191-193, 7 refs. ISSN: 0973-6417 Published by: Society for Scientific Development in Agriculture and Technology, Jhansi	The article reports on desired effects on organisms considered as such target organisms
Patton, Aaron J.; Weisenberger, Daniel V.; Hardebeck, Glenn A.; Reicher, Zachary J.	2007	Safety of herbicides on Zenith zoysiagrass seedlings.	Weed Technol., Volume 21, Issue 1, Page 145-150, Publication Year 2007	The publication is a matter of observations for environmental responses in a region outside Europe
Petralito, S.; Zanardi, I.; Braconi, D.; Santucci, A.; Memoli, A.; Caccamo, E.; Travagli, V.	2012	Supportive use of cyclodextrins as decontamination agents for herbicides: the case of fenoxaprop-p-ethyl.	Asia-Pac. J. Chem. Eng., Volume 7, Issue S3, Page S342-S347, Publication Year 2012	The study is dealing with the question whether cyclodextrins could be used in formulations as additives to fenoxaprop. This question is not relevant for risk assessment.
Plaza-Bolanos, Patricia; Padilla-Sanchez, Juan Antonio; Garrido-Frenich, Antonia; Romero-Gonzalez, Roberto; Martinez-Vidal, Jose Luis.	2012	Evaluation of soil contamination in intensive agricultural areas by pesticides and organic pollutants: south-eastern Spain as a case study.	J. Environ. Monit., Volume 14, Issue 4, Page 1181-1188, Publication Year 2012	The investigation does not report results in values reflecting agreed determinants for the hazard or exposure characterization or risk assessment under Reg. EC No 1107/2009 and information is insufficient to transfer values into such determinants
Polgar, Laszlo; Garcia-Reyes, Juan F.; Fodor, Peter; Gyepes, Attila; Dernovics, Mihaly; Abranko, Laszlo; Gilbert-Lopez, Bienvenida; Molina-Diaz, Antonio.	2012	Retrospective screening of relevant pesticide metabolites in food using liquid chromatography high resolution mass spectrometry and accurate-mass databases of parent molecules and diagnostic fragment ions.	J. Chromatogr. A, Volume 1249, Page 83-91, Publication Year 2012; J. Chromatogr., A, Volume 1249, Page 83-91, Publication Year 2012	Duplicate entry, This publication has been found and evaluated for the A.I and M03. The article reports on chemical synthesis or development of methods for measurements of the chemical without its application to natural samples. No endpoint can be derived.
Raeppel, Caroline; Fabritius, Marie; Nief, Marie; Appenzeller, Brice M. R.; Briand, Olivier; Tuduri, Ludovic; Millet, Maurice	2015	Analysis of airborne pesticides from different chemical classes adsorbed on Radiello Tenax passive tubes by thermal-desorption-GC/MS	Environmental Science and Pollution Research (2015), 22(4), 2726-2734	No endpoint can be derived
Reyes, Y.; Infante, D.; Garcia-Borrego, J.; Pozo, E. Del; Cruz, A.; Martinez, B.; Del Pozo, E.	2012	Compatibility of Trichoderma asperellum Samuels with herbicides of more frequent use in rice crop. Compatibilidad de Trichoderma asperellum Samuels con herbicidas de mayor uso en el cultivo del arroz.	Revista de Proteccion Vegetal (2012) , Volume 27, Number 1, pp. 45-53, 22 refs. ISSN: 1010-2752 Published by: Centro Nacional de Sanidad Agropecuaria, La Habana URL (Availability): http://scielo.sld.cu/pdf/rpv/v27n1/rpv08112.pdf	The observation made in this article is based upon a route of exposure that cannot be considered representative for the intended use of the substance of concern

Author	Year	Title	Source	Reason for not including in dossier
Saito-Shida, Shizuka; Nemoto, Satoru; Matsuda, Rieko	2014	Multiresidue analysis of pesticides in vegetables and fruits by supercritical fluid extraction and liquid chromatography-tandem mass spectrometry	Shokuhin Eiseigaku Zasshi (2014), 55(3), 142-151	Findings not related to a certain test system
Sauret, Nathalie; Wortham, Henri; Strekowski, Rafal; Herckes, Pierre; Nieto, Laura Ines.	2008	Comparison of annual dry and wet deposition fluxes of selected pesticides in Strasbourg, France.	Environ. Pollut. (Oxford, U. K.), Volume 157, Issue 1, Page 303-312, Publication Year 2008	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature
Shah, Jasmin; Jan, M. Rasul; Muhammad, Mian; Shehzad, Farhat-Un-Nisa.	2010	Flow injection spectrophotometric determination of fenoxaprop-p-ethyl herbicide in different grain samples after derivatization.	J. Braz. Chem. Soc., Volume 21, Issue 10, Page 1923-1928, Publication Year 2010	Findings not related to a certain test system
Shah, Jasmin; Jan, Muhammad Rasul; Shehzad, Farhat-Un-Nisa; Muhammad, Mian.	2010	Spectrophotometric method for quantification of fenoxaprop-p-ethyl herbicide in commercial formulations and agricultural samples.	J. Chem. Soc. Pak., Volume 32, Issue 4, Page 537-541, Publication Year 2010	Duplicate entry, This publication has been found and evaluated for the A.I, M02 and M05. Findings not related to a certain test system.
Shehzad, Farhat-Un-Nisa; Shah, Jasmin; Jan, Muhammad Rasul; Muhammad, Mian.	2012	Quantification of fenoxaprop-p-ethyl herbicide in soil and vegetable samples by microwave-assisted solvent extraction and HPLC method.	J. Chem. Soc. Pak., Volume 34, Issue 6, Page 1554-1559, Publication Year 2012	Findings not related to a certain test system.
Shrila Das; Narendra Kumar; Saxena, S. C.; Das, S.; Kumar, N.	2013	In-vitro effect of herbicides on the growth of Bradyrhizobium japonicum and phosphate solubilizing bacteria.	Pantnagar Journal of Research (2013) , Volume 11, Number 1, pp. 87-91, 6 refs. ISSN: 0972-8813 Published by: G.B. Pant University of Agriculture and Technology, Pantnagar	The observation made is based upon a route of exposure that cannot be considered representative for the intended use of the substance of concern
Silva, E. R. L. [Reprint Author]; Alves, L. F. A.; Santos, J.; Potrich, M.; Sene, L.	2008	TECHNIQUES FOR EVALUATION OF THE IN-VITRO EFFECT OF HERBICIDES ON BACILLUS THURINGIENSIS BERLINER VAR. KURSTAKI. Original Title: TECNICAS PARA AVALIACAO IN VITRO DO EFEITO DE HERBICIDAS SOBRE BACILLUS THURINGIENSIS BERLINER VAR. KURSTAKI.	Arqivos do Instituto Biologico Sao Paulo, (JAN-MAR 2008) Vol. 75, No. 1, pp. 59-67.	The publication is dealing with question of compatibility with another plant protection product.
Singh, Pratap; Nepalia, V.; Tomar, S. S.	2008	Effect of herbicides and fertilizer levels on soil dehydrogenase and urease activity under soybean (Glycine max) cultivation.	Indian J. Agric. Sci., Volume 78, Issue 7, Page 638-640, Publication Year 2008	The publication is a matter of observations for environmental responses in a region outside Europe.

Author	Year	Title	Source	Reason for not including in dossier
Singh, Shashi B.; Das, Tapas K.; Kulshrestha, Gita.	2013	Persistence of herbicide fenoxaprop ethyl and its acid metabolite in soil and wheat crop under Indian tropical conditions.	J. Environ. Sci. Health, Part B, Volume 48, Issue 5, Page 324-330, Publication Year 2013	The publication is a matter of observations for environmental responses in a region outside Europe.
Slavov, Svetoslav; Gini, Giuseppina; Benfenati, Emilio.	2008	QSAR trout toxicity models on aromatic pesticides.	J. Environ. Sci. Health, Part B, Volume 43, Issue 8, Page 633-637, Publication Year 2008	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature.
Steinbach, Philipp; Schwack, Wolfgang.	2013	Experiments for miniaturization and modification of the multi-pesticide residue method EN 12393.	Trends Chromatogr., Volume 8, Page 113-129, Publication Year 2013	No endpoint can be derived.
Takeda, Hironobu; Fujimoto, Toshiko; Taniguchi, Makoto.	2011	Study of simultaneous analysis of pesticide residues in vegetables by LC/MS/MS.	Amagasaki-shiritsu Eisei Kenkyushoho, Volume 36, Page 39-44, Publication Year 2011	No endpoint can be derived.
Wang, Yanhua; Wu, Shenggan; Chen, Liping; Wu, Changxing; Yu, Ruixian; Wang, Qiang; Zhao, Xueping.	2012	Toxicity assessment of 45 pesticides to the epigeic earthworm Eisenia fetida.	Chemosphere, Volume 88, Issue 4, Page 484-491, Publication Year 2012	The study is dealing with a short version of an acute earthworm test (48h). Results are considered not relevant since acute earthworm tests were intentionally withdrawn from the EU data requirements.
Wang, Yanhua; Yu, Weihua; Yang, Lizhi; Cang, Tao; Yu, Ruixian; Wang, Qiang; Zhao, Xueping.	2012	Acute toxicity of twenty-two commonly used herbicides to earthworm (Eisenia fetida).	Shengtai Duli Xuebao, Volume 7, Issue 3, Page 317-325, Publication Year 2012	The study is dealing with acute earthworm test. Results are considered not relevant since acute earthworm tests were intentionally withdrawn from the EU data requirements.
Whiteside, Melanie; Mineau, Pierre; Morrison, Clare; Knopper, Loren D.	2008	Comparison of a score-based approach with risk-based ranking of in-use agricultural pesticides in Canada to aquatic receptors.	Integr. Environ. Assess. Manage., Volume 4, Issue 2, Page 215-236, Publication Year 2008	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature.
Wu, J. X.; Zhang, Y.; Wang, K.; Zhang, H. Y.	2015	Residue analysis and dissipation of fenoxaprop - P - ethyl and its metabolite fenoxaprop-P in rice ecosystem	Journal of Analytical Chemistry (2015), 70(7), 897-902	Duplicate entry, This publication has been found and evaluated for the A.I and M03. Test system not relevant to representative uses/GAPs; The investigation is made in field experiments in China, which cannot be considered as representative for EU, furthermore the use in rice fileds is not foreseen for the AIR of fenoxaprop-p-ethyl.
Yarpuz-Bozdogan, Nigar.	2009	Assessing the environment and human health risk of herbicide application in wheat cultivation.	J. Food, Agric. Environ., Volume 7, Issue 3 and 4, Pt. 2, Page 775-781, Publication Year 2009	The publication is a secondary source of information, e.g. review article or study that condenses information of primary nature.

Author	Year	Title	Source	Reason for not including in dossier
Zhang, Anping; Xu, Chao; Liu, Weiping	2008	Influence of toxicity and dissipation of racemic fenoxaprop and its R-enantiomer in Scenedesmus obliquus suspension by cyclodextrins	Journal of Environmental Science and Health, Part B: Pesticides, Food Contaminants, and Agricultural Wastes (2008), 43(3), 231-236	The investigation does not allow attributing the observations made to the substance of concern (e.g.mixture of substances, origin of exposure unclear).

B.7.7.2.4. Conclusion

For fenoxaprop-P-ethyl and its metabolites, a total of 1250 references were identified and evaluated for potential relevance.
For fenoxaprop-P-ethyl the publication by Zhang, Y.; Liu, D.; Diao, J.; He, Z.; Zhou, Z.; Wang, P.; Li, X.; 2010; has been identified as relevant after detailed assessment and classified as case a) according to EFSA Guidance Point 5.4.1. The article assesses the degradation behaviour of the two enantiomers of fenoxaprop-ethyl in aerobic soil. Based on the results, racemic fenoxaprop-ethyl can be degraded in soil by enantioselective hydrolysis while enantiomers of fenoxaprop ethyl esters are configurationally stable. Enantioselective degradation in soil via the R-enantiomer is also observed when the biologically inactive S-form of fenoxaprop acid is applied, while configurational stability is found when fenoxaprop-P-acid is applied to soil. The data support the results of two studies on US soils conducted by the Fenoxaprop Task Force, but also provides further information for refining the risk assessment. Thus a detailed summary is provided under B.8.1.1.1.

Beside this, 23 other publications have been identified as studies relevant after detailed assessment and classified in accordance with the EFSA Guidance Point 5.4.1. However, none of these studies indicate that a side-effect on human health, the environment and non-target species may exist, which would then need to be considered in the risk assessment of the supplementary (Annex I Renewal) dossier.

B.7.8. REFERENCES RELIED ON

Previous evaluation: responded "N.A". for NAS, "Submitted for the purpose of renewal", or "In DAR (year)", "In addendum to DAR (year)" or any other appropriate
All studies already submitted for the Annex I inclusion under Directive 91/414/EEC and evaluated in the Monograph (DAR Fenoxaprop-P-ethyl, 2005) are written in grey typeface.

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCA 6.1 /01	Fuchsbichler, G.	1993	Storage stability in wheat and validation of analytical method AL 58/86 Hoe 046360, Hoe 088406 and Hoe 054014 Universitaet Muenchen, Muenchen, Germany Bayer CropScience, Report No.: A51681, Date: 1993-07-19 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.1 /02	Neuss, B.; Werner, H. J.	2001	Stability in drinking water during a deep freeze storage up to 3 months Fenoxaprop-P-ethyl (AE F046360) AE F054015 AE F088406 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C010497, Date: 2001-01-10 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	No
KCA 6.1 /03	Ver Hey, M. E.	1992	Determination of the residue in barley grain and straw. Storage stability of Hoe 033171 or Hoe 046360 and their metabolites Hoe 053022 and Hoe 054014 Analytical Development Corporation, USA Bayer CropScience, Report No.: A49224, Date: 1992-03-12 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.1 /04	Carringer, R. D.;	1993	Field dissipation applied to soybeans in Iowa of Fenoxaprop-P-ethyl Super Whip 0.67EC (Bugle(R)	N	N		Bayer CropScience	No

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
	O'Grodnick, J. S.; Clayton, B.; Parkes, R. L.		herbicide) American Agricultural Services, Inc., USA Bayer CropScience, Report No.: A51888, Date: 1993-12-17 **...Amended: 1996-10-21** GLP/GEP: yes, unpublished **...also filed: KCA 7.1.2.2.1 /02**					
KCA 6.1 /05	Kulkarni, T. S.; Winkler, D. A.	1995	Freezer stability in poultry tissues and eggs of Fenoxaprop-ethyl (Hoe 033171) and related metabolites EN-CAS Analytical Laboratories, Winston-Salem, NC, USA Bayer CropScience, Report No.: A55153, Report includes Trial Nos.: BM-94R-07 Date: 1995-10-05 **...Amended: 1996-06-10** GLP/GEP: yes, unpublished	N	N		Bayer CropScience	Not considered in the DAR (2005). Assessed for purpose of a.s. renewal
KCA 6.2.1 /01	Wink, O.; Kuenzler, K.; Lemke, G.; Haberkorn, B.; Mueller, H. J.	1988	Metabolism and kinetics in rice plants (Oryza sativa) under field conditions Hoe 046360-chlorphenyl-U-14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A38627, Date: 1988-03-29 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /02	Buerkle, W. L.; Becker, A.	1997	Code: Hoe 046360 00 ZE98 0004 Chlorophenyl-u-14C-Hoe 046360 Inftuence of the Safener Hoe 107892 on the Metabolism of the Radiolabelled Herbicide Fenoxaprop-P-ethyl, Hoe 046360, in Barley (Hordeum vulgare) Hoechst Schering AgrEvo GmbH, Frankfurt am Main,	N	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Germany Bayer CropScience, Report No.: A58851, Date: 1997-05-22 GLP/GEP: yes, unpublished					
KCA 6.2.1 /03	Schwalbe-Fehl, M.; Schmidt, E.; Koecher, H.	1987	Metabolism and degradation kinetics in wheat (Triticum aestivum) Hoe 033171-^{14}C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A36855, Date: 1987-07-17 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /04	Wink, O.; Kuenzler, K.; Lemke, G.	1987	Residue determination in wheat (Triticum aestivum) after application of 110 g active ingredient/ha (and soil) Hoe 046360-chlorophenyl-U-14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A35778, Date: 1987-05-11 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /05	Wink, O.	1986	Racemization in soy beans and wheat of Hoe 046360-chlorophenyl-U-14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A35943, Date: 1986-05-12 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /06	Romano, M. L.; Stephenson, G. R.; Tal, A.; Hall, J. C.	1993	The effect of monooxygenase and glutathione S-transferase inhibitors on the metabolism of diclofop-methyl and fenoxaprop-ethyl in barley and wheat Journal:Pesticide Biochemistry and Physiology, Volume:46, Pages:181-189,	N	N		Public data	No, not considered necessary

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Year:1993, Report No.: A59589, GLP/GEP: n.a. published					
KCA 6.2.1 /07	Tal, A.; Romano, M. L.; Stephenson, G. R.; Schwan, A. L.; Hall, J. C.	1993	Glutathione conjugation: A detoxification pathway for Fenoxaprop-ethyl in barley, crabgrass, oat, and wheat Journal:Pesticide Biochemistry and Physiology, Volume:46, Pages:190-199, Year:1993, Report No.: A57458, GLP/GEP: n.a., published	N	N		Public data	No, not considered necessary
KCA 6.2.1 /08	Schwalbe-Fehl, M.; Schmidt, E.; Koecher, H.	1986	Residue determinations in wheat (Triticum aestivum) after application of 183 g active ingredient/ha in presence of Hoe 070542 - Fenoxaprop-ethyl Hoe 033171-14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A34525, EPA MRID No.: 40454204 Date: 1986-11-14 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /09	Wink, O.; Kuenzler, K.; Wuerz, S.	1987	Identification and characterization of the water-soluble conjugates in wheat Hoe 033171-^{14}C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A36657, EPA MRID No.: 40454203 Date: 1987-09-07 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /10	Schwalbe-Fehl, M.; Schmidt, E.; Koecher, H.	1987	Metabolism and degradation kinetics in wheat (Triticum aestivum) in presence of Hoe 070542 Hoe 033171-14C Hoechst AG, Frankfurt am Main, Germany	N	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Bayer CropScience, Report No.: A37400, Date: 1987-12-09 GLP/GEP: yes, unpublished					
KCA 6.2.1 /11	Buettner, B.; Kuenzler, K.; Lemke, G.; Mueller, H. J.	1988	Degradation behaviour in/on rice plants (Oryza sativa) under field conditions Hoe 046360-dioxyphenyl-1-^{14}C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A40366, Date: 1988-12-21 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /12	Buerkle, L. W.	2000	Identification of residues in wheat (Triticum aestivum) following treatment with ^{14}C-fenoxaprop-P-ethyl at a rate of 90 g a.s./ha Code: (U-^{14}C-chlorophenyl)-AE F046360 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C009798, Date: 2000-09-25 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.2.1 /13	Oddy, A. M.	2012	[^{14}C]-fenoxaprop-p-ethyl: Metabolism in spring wheat following post-emergence application Battelle UK Ltd., Chelmsford, Essex, United Kingdom TF- BCS-CHA, Report No.: 469 FPE, Date: 2012-08-16 GLP/GEP: yes, unpublished	N	Y	New metabolism study according to actual guidelines	TF- BCS-CHA	No, new study submitted for the purpose of renewal.
KCA 6.2.2 /01	[redacted]	1989	Distribution and excretion after repeated oral administration to laying hen of ^{14}C-Hoe 033171 [redacted] [redacted],	Y	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Report No.: A40877, Date: 1989-05-17 GLP/GEP: yes, unpublished					
KCA 6.2.2 /02	[redacted]	1994	Nature of residue in laying hens of ^{14}C-Fenoxaprop-ethyl [redacted], Report No.: A53203, Date: 1994-10-17 GLP/GEP: yes, unpublished	Y	N		Bayer CropScience	In DAR (2005)
KCA 6.2.3 /01	[redacted]	1989	Metabolism in the lactating goat following repeated oral administration Hoe 033171-^{14}C [redacted], Report No.: A41369, Date: 1989-05-01 **...Amended: 1989-08-04** GLP/GEP: yes, unpublished	Y	N		Bayer CropScience	In DAR (2005)
KCA 6.2.3 /02	[redacted]	1990	Metabolism in the lactating goat following repeated oral administration. Reply to EPA-Memorandum (Subject: PP 9F 3714, EPA Reg.No.8340-GI.) Fenoxaprop-ethyl in or on wheat CT1D 040889 Hoe 033171-14C [redacted], Report No.: A42690, Date: 1990-02-21 GLP/GEP: no, unpublished	Y	N		Bayer CropScience	In DAR (2005)
KCA 6.2.3 /03	[redacted]	1985	Nature of residues in milk and tissues of cows after dosing 50 mg/cow and day at three consecutive days Hoe 033171-14C [redacted],	Y	N		Bayer CropScience	Not considered in the DAR (2005). Assessed for purpose of a.s.

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Report No.: A30492, EPA MRID No.: 41494201, acc.73956 Date: 1985-01-17 GLP/GEP: no, unpublished					renewal
KCA 6.3.1 /01	Junker, H.; Raquet, H.; Klug, R.	1993	Fenoxaprop-P-ethyl (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in winter wheat following a single application of Hoe 046360 24 EW14 A202 Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53042, Report includes Trial Nos.: ER91DEU5300101 ER91DEU5300401 Date: 1993-12-03 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /02	Junker, H.; Raquet, H.	1993	Fenoxaprop-P-ethyi (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in spring wheat following a single application of Hoe 046360 24 EW14 A202 Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53045, Report includes Trial Nos.: ER92DEU5300401 Date: 1993-12-06 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /03	Junker, H.; Raquet, H.; Klug, R.	1993	Fenoxaprop-P-ethyl (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in winter rye following a singte application of Hoe 046360 24 EW14 A202	N	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53047, Report includes Trial Nos.: ER91DEU5320101 ER91DEU5320401 Date: 1993-12-03 GLP/GEP: yes, unpublished					
KCA 6.3.1 /04	Junker, H.; Raquet, H.	1993	Fenoxaprop-P-ethyl (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in winter rye following a single application of Hoe 046360 24 EW14 A202 Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53048, Report includes Trial Nos.: ER92DEU5320101 ER92DEU5320501 Date: 1993-12-06 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /05	Junker, H.; Raquet, H.	1993	Fenoxaprop-P-ethyl (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in winter barley following a single application of Hoe 046360 24 EW14 A202 Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53049, Report includes Trial Nos.: ER92DEU5310101 Date: 1993-12-06 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCA 6.3.1 /06	Junker, H.; Raquet, H.; Klug, R.	1993	Fenoxaprop-P-ethyl (69 g/l) and Hoe 107892 (75 g/l) - oil in water emulsion - (Code: Hoe 046360 24 EW14 A202) Investigating the residues in spring barley following a single application of Hoe 046360 24 EW14 A202 Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53050, Report includes Trial Nos.: ER91DEU5310101 ER91DEU5310301 Date: 1993-12-03 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /07	Sochor, H.	1993	Report on plant protection residue trial Hoe 046360 24 EW14 A201 Universitaet Muenchen, Muenchen, Germany Bayer CropScience, Report No.: A50817, Date: 1993-03-30 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /08	Sochor, H.	1993	Report on plant protection residue trial Hoe 046360 24 EW14 A201 Universitaet Muenchen, Muenchen, Germany Bayer CropScience, Report No.: A50818, Date: 1993-03-30 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /09	Sochor, H.	1993	Report on plant protection residue trial Hoe 046360 24 EW14 A201 (only BBA) Universitaet Muenchen, Muenchen, Germany Bayer CropScience, Report No.: A50836, Date: 1993-03-30	N	N		Bayer CropScience	In DAR (2005)

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			GLP/GEP: no, unpublished					
KCA 6.3.1 /10	Sochor, H.; Idstein, H.	1993	Report on plant protection residue trial Hoe 046360 24 EW14 A201 (only BBA) Universitaet Muenchen, Muenchen, Germany Bayer CropScience, Report No.: A50837, Date: 1993-03-30 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /11	Helgers, A.; Idstein, H.; Junker, H.	1996	Fenoxaprop-P-ethyl and Hoe 107892 oil in water emulsion 55 and 30 g/I Code: Hoe 46360 24 EW08 A802 Determination of residues of Hoe 046360 and Hoe 107892 to establish a maximum residue level foilowing one application in different wheat and Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A57042, Date: 1996-09-30 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /12	Henry, M. B.	1997	Tigress Ultra fenoxaprop-p-ethyl + diclofop-methy) + mefenpyr-diethyl oil in water emulsion 20 + 250 + 40 g/I Code: AE F023408 34 EW28 A3 (Hoe 023408 34 EW28 A3) Tigress Ultra field trials in winter wheat and barley; Residues of diclofop-me AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: A59037, Date: 1997-04-21 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	No, not considered necessary
KCA 6.3.1 /13	Fuchsbichler, G.	1997	Determination of the residues of AE F046360 (fenoxaprop-P-ethyl) in cereals AgrEvo Italia S.r.l., Milano, Italy	N	N		Bayer CropScience	No, not considered necessary

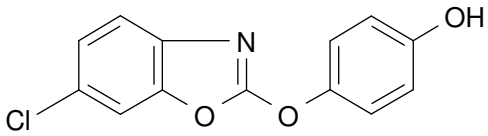
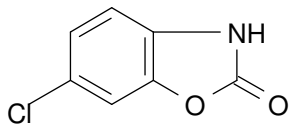
Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Bayer CropScience, Report No.: C003919, Report includes Trial Nos.: ER96ITA510 Date: 1997-06-30 GLP/GEP: yes, unpublished					
KCA 6.3.1 /14	Grolleau, G.	1997	Magnitude of the Residue of fenoxaprop-P-ethyl + HOE 107892 formulated as HOE 046360 24 EC11 A406 (AE F046360 24 EC11 A406) in Winter Wheat Raw Agricultural Commodity Northern and Southern France 1996 European Agricultural Services (EAS), Lyon, France Bayer CropScience, Report No.: A59191, Date: 1997-07-21 GLP/GEP: yes, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.3.1 /15	Schulte, G.	2015	Determination of the residues of fenoxaprop-p-ethyl and mefenpyr-diethyl in/on wheat after spray application of fenoxaprop-p-ethyl & mefenpyr-diethyl EW 144 in Germany, Belgium and the Netherlands TF- BCS-CHA, Report No.: 13-2018, Report includes Trial Nos.: 13-2018-01 13-2018-02 13-2018-03 13-2018-04 Date: 2015-05-11 GLP/GEP: yes, unpublished	N	Y	New residue trials according to actual guidelines	TF- BCS-CHA	No, new study submitted for the purpose of renewal.
KCA 6.3.1 /16	Braune, M.; van Berkum, S.	2016	Determination of the residues of mefenpyr-diethyl and fenoxaprop-p-ethyl in/on wheat after spray application of fenoxaprop-p-ethyl & mefenpyr-diethyl EW 144 in Germany, the United Kingdom and northern France TF- BCS-CHA,	N	N		TF- BCS-CHA	No, new study submitted for the purpose of renewal.

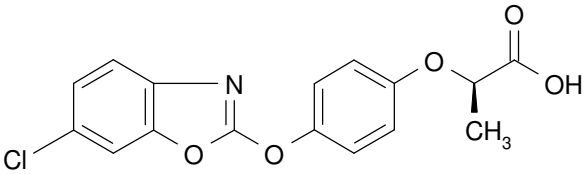
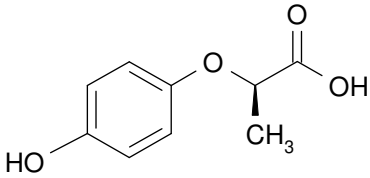
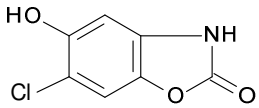
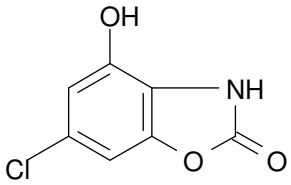
Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Report No.: 14-2006, Report includes Trial Nos.: 14-2006-01 14-2006-02 14-2006-03 14-2006-04 Date: 2016-06-15 GLP/GEP: no, unpublished					
KCA 6.3.1 /17	Schulte, G.; Reineke, A.	2011	Determination of the residues of fenoxaprop-p-ethyl and mefenpyr-diethyl in/on wheat and wheat, durum after spray application of Fenoxaprop-p-ethyl & Mefenpyr-diethyl EW 144 in the field in Spain, Portugal, southern France and Italy TF- BCS-CHA, Report No.: 10-2209, Report includes Trial Nos.: 10-2209-01 10-2209-02 10-2209-03 10-2209-04 Date: 2011-06-14 GLP/GEP: yes, unpublished	N	Y	New residue trials according to actual guidelines	TF- BCS-CHA	No, new study submitted for the purpose of renewal.
KCA 6.3.1 /18	Schulte, G.	2012	Determination of the residues of fenoxaprop-p-ethyl and mefenpyr-diethyl in/on wheat and durum wheat after spray application of fenoxaprop-p-ethyl & mefenpyr-diethyl EW 144 in the field in Spain, Portugal and Greece TF- BCS-CHA, Report No.: 11-2041, Report includes Trial Nos.: 11-2041-01 11-2041-03	N	Y	New residue trials according to actual guidelines	TF- BCS-CHA	No, new study submitted for the purpose of renewal.

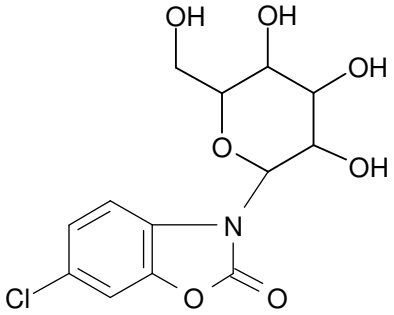
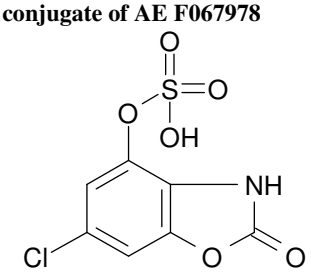
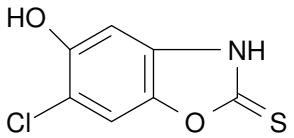
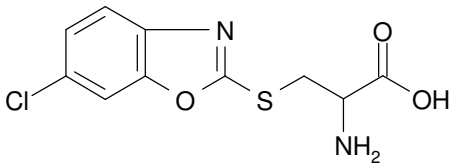
Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			11-2041-04 Date: 2012-10-31 GLP/GEP: yes, unpublished					
KCA 6.4.1 /01	[redacted]	2016	Fenoxaprop-P-ethyl: Residues of fenoxaprop-P-ethyl and its metabolites in eggs and tissues of laying hens [redacted] TF- BCS-CHA, Report No.: ENK0021, Date: 2016-06-08 GLP/GEP: yes, unpublished	Y	Y	New feeding study according to actual guidelines	TF- BCS-CHA	No, new study submitted for the purpose of renewal.
KCA 6.4.2 /01	[redacted]	1987	Ruminant feeding study code: Hoe 033171 [redacted] Report No.: A36705, EPA MRID No.: 40454207 Date: 1987-10-19 GLP/GEP: yes, unpublished	Y	N		Bayer CropScience	In DAR (2005)
KCA 6.6.1 /01	Buerkle, W. L.; Wink, O.; Koecher, H.	1987	Confined accumulation study on rotational crops sown 30 days and one year after application of 0.11 kg a.i./ha Hoe 046360 -14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A37484, EPA MRID No.: 41567706 Date: 1987-11-06 GLP/GEP: no, unpublished	N	N		Bayer CropScience	In DAR (2005)
KCA 6.6.1 /02	Schwalbe-Fehl, M.; Steinau, M.; Mueller, H. J.	1985	Confined accumulation study on rotational crops planted 111 days after treatment of the first crop Hoe 033171-14C Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A31992, Date: 1985-07-29	N	N		Bayer CropScience	In DAR (2005)

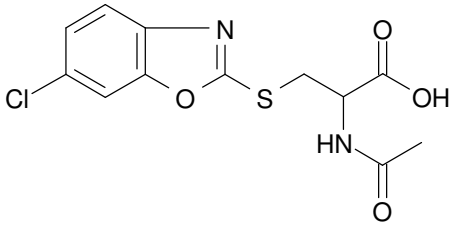
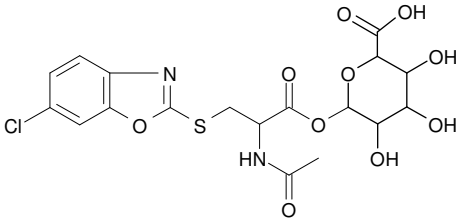
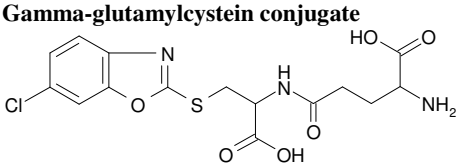
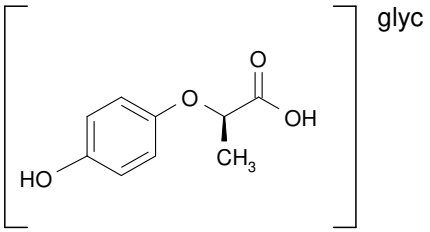
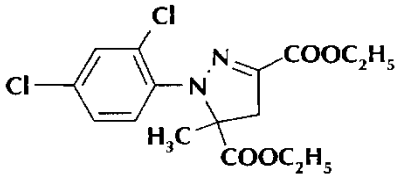
Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			GLP/GEP: no, unpublished					

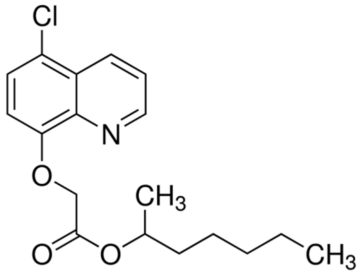
B.7.9. List Of Structures, Synonyms, Code Numbers And Occurrence

Report name **Structure** **IUPAC name** **CAS name** **[CAS registry number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
AE F046360 (parent substance) ethyl (2R)-2-{4-[(6-chloro-1,3-benzoxazol-2-yl)oxy]phenoxy}propanoate (IUPAC) Propanoic acid, 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]-, ethyl ester, (2R)-(CAS) CAS reg no: 71283-80-2	C_{18} H_{16} Cl N O_5 361.8 g/mol <u>D-Enantiomer</u>: Fenoxaprop-P-ethyl Hoe 046360 BCS-AI29180 <u>L-Enantiomer</u>: Fenoxaprop-M-ethyl Hoe 085791 AE F085791 BCS-CA37044 <u>Racemate</u>: Fenoxaprop-ethyl AE F033171 Hoe 033171 BCS-AF52457	Parent substance used as test material in all reports
AE F040356  4-[(6-chloro-1,3-benzoxazol-2-yl)oxy]phenol (IUPAC) Phenol,4-[(6-chloro-2- benzoxazolyl)oxy]-(CAS) CAS reg no: 70217-01-5	C_{13} H_8 Cl N O_3 261.7 g/mol Phenol Hoe 040356 AE B101188 BCS-AB16188	Hen
AE F054014  6-chloro-1,3-benzoxazol-2(3H)-one (IUPAC) 2(3H)-Benzoxazolone, 6-chloro- (CAS) CAS reg no: 19932-84-4	C_7 H_4 Cl N O_2 169.57 g/mol Benzoxazolone Chlorobenzoxa=zolone Hoe 054014 RP 011881 RPA 722144 RP 011811 BCS-AC79872	Wheat Barley Rice Goat Hen Rat

Report name **Structure** **IUPAC name** **CAS name** **[CAS registry number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
AE F088406  (2R)-2-{4-[(6-chloro-1,3-benzoxazol-2-yl)oxy]phenoxy}propanoic acid (IUPAC) Propanoic acid, 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]-, (2R)- (CAS) CAS reg no: 113158-40-0	$C_{16}H_{12}ClNO_5$ 333.7 g/mol <u>D-Enantiomer</u>: Fenoxaprop-P-acid Hoe 088406 BCS-BQ23896 <u>Racemate</u>: Fenoxaprop-acid AE F053022 Hoe 53022 BCS-AK65133 <u>L-Enantiomer</u>: Fenoxaprop-M-acid AE F088405 Hoe 088405 BCS-CA37049 BCS-BB40596	Wheat Barley Rice Rat
AE F096918  (2R)-2-(4-hydroxyphenoxy)propanoic acid (IUPAC) Propanoic acid, 2-(4-hydroxyphenoxy)-, (2R)- (CAS) CAS reg no: 94050-90-5	$C_9H_{10}O_4$ 182.2 g/mol HOPP-acid HPP-acid <u>D-Enantiomer</u>: BCS-CA37065 <u>Racemate</u>: AE F020686 Hoe 20686 BCS-AB96029 <u>L-Enantiomer</u>: BCS n.a. Hoe n.a.	Wheat Rice
AE F064124  6-chloro-5-hydroxy-1,3-benzoxazol-2(3H)-one (IUPAC) 2(3H)-Benzoxazolone, 6-chloro-5-hydroxy- (CAS) CAS reg no: 88412-29-7	$C_7H_4ClNO_3$ 185.6 g/mol 3-Hydroxychloro-benzoxazolone AE F064124 BCS-AU56480	Rice Goat Rat
AE F067978  6-chloro-4-hydroxy-1,3-benzoxazol-2(3H)-one (IUPAC) 2(3H)-Benzoxazolone, 6-chloro-4-hydroxy- (CAS) CAS reg no: 88412-28-6	$C_7H_4ClNO_3$ 185.6 g/mol 4-Hydroxychloro-benzoxazolone AE F067978 BCS-BB23347	Rat

Report name **Structure** **IUPAC name** **CAS name** **[CAS registry number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
N-Glucoside of AE F054014  6-chloro-3-hexopyranosyl-1,3-benzoxazol-2(3H)-one (IUPAC) CAS: n.a.	C_{13} H_{14} Cl N O_7 331.7 g/mol N-Glucoside of AE F054014 BCS-code: None	Rice
Sulfate ester conjugate of AE F067978  6-chloro-2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl hydrogen sulfate (IUPAC) CAS: n.a.	C_7 H_4 Cl N O_6 S 265.6 g/mol Sulfate ester conjugate of AE F067978 BCS-code: None	Rat
AE F080918  6-chloro-5-hydroxy-1,3-benzoxazole-2(3H)-thione (IUPAC) CAS: n.a.	C_7 H_4 Cl N O_2 S 201.6 g/mol AE F080918 BCS-AF47471	Rat
AE F0417066  S-(6-chloro-1,3-benzoxazol-2-yl)cysteine (IUPAC) L-Cysteine, S-(6-chloro-2-benzoxazolyl)- (CAS) CAS reg no: 150807-93-5 (one enantiomer only)	C_{10} H_9 Cl N_2 O_3 S 272.7 g/mol AE F0417066 Racemate: BCS-AX19709	Wheat (forage) Rat (intermediate)

Report name **Structure** **IUPAC name** **CAS name** **[CAS registry number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
AE F069225  N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine (IUPAC) CAS: n.a.	$C_{12}H_{11}ClN_2O_3S$ 298.8 g/mol AE F069225 BCS-BB24444	Barley (minor, bouquet test) Rat
Glucuronic acid conjugate  1-O-[N-acetyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteinyl]hexopyranuronic acid (IUPAC) CAS: n.a.	$C_{18}H_{19}ClN_2O_{10}S$ 490.9 g/mol Glucuronic acid conjugate of AE F069225 BCS-code: None	Rat
Gamma-glutamylcystein conjugate  gamma-glutamyl-S-(6-chloro-1,3-benzoxazol-2-yl)cysteine (IUPAC) INDEX NAME NOT YET ASSIGNED (CAS) CAS reg no: 1228473-74-2 (one diastereoisomer only)	$C_{15}H_{16}ClN_3O_6S$ 401.8 g/mol Gamma-Glutamylcystein-Conjugate M3 BCS-code: None	Wheat (postulated intermediate)
Hopp acid glycoside conjugate 	Hopp acid sugar conjugate (linkage unknown)	Wheat
Mefenpyr-diethyl (Hoe 107892)  diethyl 1-(2,4-dichlorophenyl)-5-methyl-4H-pyrazole-3,5-dicarboxylate (IUPAC) CAS : 135590-91-9	Safener $C_{16}H_{18}Cl_2N_2O_4$ 373.23 g/mol	Plant metabolism

Report name **Structure** **IUPAC name** **CAS name** **[CAS registry number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
Cloquintocet-mexyl  heptan-2-yl 2-(5-chloroquinolin-8-yl)oxyacetate (IUPAC) CAS : 99607-70-2	Safener $C_{18}H_{22}ClNO_3$ 335.828 g/mol	Plant metabolism (spring wheat)