ANNEX B

Original version January 1997, revised in March 2010

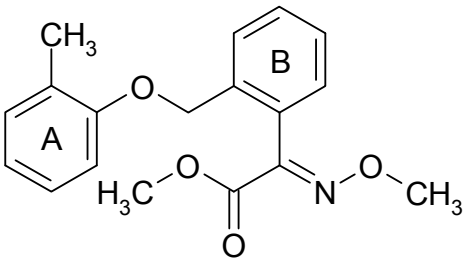
Kresoxim-methyl

B.7 Residue data

Introductory remarks

Metabolism and rotational crop studies were carried out using 2 positions for radio labelling as mentioned in the figure here below.

Kresoxim-methyl (BAS 490 F):



[phenoxy-U-^{14}C]-label (cresyl-label, A-label) and [phenyl-U-^{14}C]-label (B-label)

Position of ^{13}C label: CH3-O-*CO-*C=N-O-CH3 ([^{13}C]-Kresoxim-methyl).

The metabolism of Kresoxim-methyl in plants and animals was investigated using the active substance uniformly labelled either on the phenoxy (cresyl) ring (phenoxy-U-^{14}C)-label or on the phenyl ring (phenyl-U-^{14}C)-label.
In some cases, the ^{13}C-labelled test item was also used.

The main metabolic pathways of Kresoxim-methyl depicted respectively in rat, plants and animals are described in Appendix A to this section.
A summary of the occurrence of all the metabolites identified in the rat, plants and animals metabolism studies was also reported in the Appendix B to this section.
The summary sheets of the supervised residue trials on apples, pears, grapes and cereals are reported in an Excel file residue database attached to this document.

Added in March 2010

B.7.0 Storage stability of residue samples

-Storage Stability of BAS 490 F, BF 490-2 and BF 490-9 in Wheat Matrices (Krotzky A.J., 1994)-Interim Report
Guidelines:
IVA Guideline Residue Chemistry, Part II Storage Stability (1990)
GLP:
Yes.
Material and methods:
Test substances: BAS 490 F (Kresoxim-methyl), BF 490-9 and BF 490-2
Purity of the test substances: BAS 490 F (99.9%); BF 490-9 (99.7%); BF 490-2 (91.5%)
Experimental design:
The wheat metabolism study showed that the glycosilated metabolites BF 490-2 and BF 490-9 were relevant metabolites in green matter and straw of wheat.
-Wheat grain:
Samples were fortified with BAS 490 F at a concentration of 1 mg/kg.
-Wheat green matter:

Samples were fortified with BAS 490 F at a concentration of 1 mg/kg.
Treated field samples were used for the determination of the storage stability of the glycosilated metabolites BF 490-2 and BF 490-9.
-*Wheat straw*:
Treated field samples were used for the determination of the frozen storage stability of BAS 490 F and of the metabolites BF 490-2 and BF 490-9.

All the samples were stored under deep frozen conditions (-20°C).
Fortified samples corresponding to the day 0 were analysed immediately.
Grain samples were analysed at 0, 7, 30, 93 and 214 days.
Green matter samples were analysed at 0,7, 35 and 168 days for BAS 490 F and at 0, 35 and 168 days for the metabolites BF 490-2 and BF 490-9.
In case of wheat straw the field samples were re-analysed and 91 days after the first analysis.
Control samples were fortified either with BAS 490 F or the metabolites BF 490-2 and BF 490-9 at levels between 0.05 mg/kg and 1.0 mg/kg for procedural recoveries purposes.
Analytical procedures:
The residues of BAS 490 F in wheat grain were determined according to the BASF analytical method 351/2.
BAS 490 F was quantified by GC using ECD with a Limit of quantification of 0.05 mg/kg.
The level of residues of BAS 490 F, BF 490-2 and BF 490-9 was determined with BASF method 351/1.
The 3 analytes were fractionated by a preparative HPLC chromatography analysis. Final detection and quantification was performed by HPLC analysis (NH_2/CN column combination) and were detected with an UV-detector.
Based on the validation data package reported in Vol.3, B.5.2.1, it was demonstrated that the BASF methods 351/1 and 351/2 were suitable for the determination of the residues of BAS 490 F, BF 490-2 and BF 490-9.
Findings:
Table B.7.0-1: Determination of the recoveries for procedural recoveries samples and stored fortified samples of wheat green matter, grain and straw for Kresoxim-methyl (BAS 490 F) and the metabolites BF 490-2 and BF 490-9 in the course of the frozen storage stability study (Results expressed in percent of the nominal fortification level).
The recovered residue levels were not corrected for the procedural recoveries.

Matrix/analyte	Storage period (days)	Residue levels in frozen stored sample (% of nominal spiking level)	Procedural recovery for freshly spiked control sample (%)	
		BAS 490 F		
Wheat, green matter	**0**	92.70	88.9 89.1	93.9 98.7
	7	82.10	86.0 79.5	82.2 80.8
	35	104.10	104.1 91.4	106.5 114.5
	168	99.9	95.3	104.5
Wheat grain	**0**	77.4	73.7	81.1
	7	76.2	76.2	NA
	30	76.0	70.1	81.8
	93	72.2	72.8	71.6
	214	85.5	71.5	99.4
Wheat straw	**0**	74.0	73.1	74.8
	56	106.2	108.6	103.7
	91	95.3	102.1	88.4
		BF 490-2		
Wheat, green matter	**0**	92.7	76.8 77.3	79.7 81.6
	35	82.1	92.5	93.7

	168	104.1	74.3	NA
Wheat straw	**0**	**65.8**	**65.8**	
	56	78.5	74.7	82.3
	91	84.4	85.0	83.8
		BF 490-9		
Wheat, green matter	**0**	83.0	86.1 79.7	79.5 83.5
	35	89.7	90.2	89.2
	168	80.2	80.2	NA
Wheat straw	**0**	71.5	**64.4**	78.5
	56	81.0	89.6	72.4
	91	74.8	70.9	78.7
NA: Not analysed.				

Conclusion:
The BAS 490 F residues can be considered as stable under frozen storage stability respectively for 7 months (wheat grain), 5 months (wheat, green matter) and 3 months (wheat straw).

-Interim report: Kresoxim-methyl (BAS 490 F) and Its Metabolites BF 490-2 and BF-490-9: Frozen Storage Stability in Wheat Grain (Class T., Senciuc M., 2008)
Guidelines:
EC Directive 7032/VI/95 rev.5, Appendix H: Storage Stability of Residue Samples.
Guidance document on residue analytical methods (SANCO/3029/99 rev.4)
OECD Principles of Good Laboratory Practices.
GLP:
Yes.
Material and methods:
Test substances: BAS 490 F (Kresoxim-methyl), BF 490-9 and BF 490-2
Purity of the test substances: BAS 490 F (99.9%); BF 490-9 (99.7%); BF 490-2 (91.5%)
Fortification of the solutions:
The Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 stock solutions were diluted with methanol to obtain a mixed solution with 5.0 µg/mL for each analyte, used for fortification at the 10-times LOQ level.
The 5.0 µg/mL solution was further diluted with methanol to obtain a mixed fortification solution at 0.5 µg/mL per analyte, used for fortification at the LOQ level.
Experimental design:
The fortification level for stored samples was fixed at 0.5 mg/kg for each analyte.
For frozen storage in wheat grain, Kresoxim-methyl (BAS 490F) and its metabolites BF 490-2 and BF 490-9 were dosed simultaneously as follows:
0.5 mL of the methanolic fortification solution containing the 3 analytes, each at a concentration of 5.0 µg/mL was dosed and immediately stored frozen.
For the method validation, concurrent recovery data were generated by fortifying and extracting the control stored frozen samples that were analysed simultaneously with the stored samples.
One control sample, 2 samples fortified with the 3 analytes simultaneously at 0.5 mg/kg and 1 specimen fortified with the 3 analytes simultaneously at 0.05 mg/kg were analysed concurrently with the dosed samples stored frozen at T°≤-20°C for 0, 1, 3, 6 and 9 months period.
Analytical procedures: The analytical LC-MS/MS-based BASF method no.445/0 for the determination of Kresoxim-methyl in plant matrices was independently validated previously in a separate study.
The parent Kresoxim-methyl and its metabolites BF-490-2 and BF 490-9 were extracted with a mixture of methanol/water/2N HCl (70/25/5; v/v/v) and the extract was centrifuged. A 200 µL aliquot of the raw extract was diluted to 1.0 mL prior to the determination of the residues by LC-MS/MS analysis.
This analytical method was validated for the 3 analytes in the course of the present study with freshly fortified wheat grain samples processed and analysed concurrently with the wheat grain samples spiked and stored frozen.
Findings:

Table B.7.0-2: Concurrent method validation in wheat grain: Average recoveries and standard deviations (SD) of the BASF method n°445/0-Fortifications at the LOQ and 10 x LOQ levels.

Fortification levels (mg/kg)/analyte	Recovery results (%)	Wheat grain		
		BAS 490 F	BF 490-9	BF 490-2
0.05	Range	95; 94; 78; 84; 94	84; 104; 89; 82; 99	97; 98; 101; 91; 92
	Average	89%	92%	96%
	SD	7%	9%	4%
	Replicates (n)	5	5	5
0.5	Range	84; 77; 94; 92; 80; 76; 92; 86; 109; 110	103; 105; 101; 100; 101; 104; 99; 110; 98; 94	102; 105; 104; 99; 102; 106; 100; 95; 99; 100
	Average	90%	101%	101%
	SD	12%	4%	3%
	Replicates (n)	10	10	10

Table B.7.0-3: Amount of Kresoxim-methyl (BAS 490 F) and its metabolites BF 490-9 and BF 490-2 recovered in wheat grain found in the course of the frozen storage stability study and concurrent recoveries from freshly fortified specimens at the nominal spiking level of 0.5 mg/kg (Results expressed in mg/kg and in percent of nominal spiking level of 0.5 mg/kg).
The recovered residue levels were not corrected for the procedural recoveries.

Commodity	Analyte	Storage period (months)	Residue levels in frozen stored sample expressed in mg/kg and in % of nominal spiking level (range and mean)				Procedural recovery for freshly spiked control samples (%)	
			Mg/kg (%)	Mg/kg (%)	Mg/kg (%)	Mean (%)	Replicate 1	Replicate 2
Wheat grain	BAS 490 F	0	0.38 (76)	0.38 (76)	0.36 (73)	75	84	77
		1	0.44 (88)	0.40 (80)	0.40 (80)	83	94	92
		3	0.37 (73)	0.36 (71)	0.36 (72)	72	80	76
		6	0.42 (84)	0.44 (88)	0.41 (82)	85	92	86
		9	0.37 (74)	0.36 (73)	**0.34 (68)**	71	109	110
	BF 490-9	0	0.48 (97)	0.49 (98)	0.48 (96)	97	103	105
		1	0.48 (95)	0.45 (90)	0.44 (89)	91	101	100
		3	0.44 (88)	0.50 (99)	0.50 (99)	95	101	104
		6	0.51 (101)	0.48 (95)	0.50 (100)	99	99	110
		9	0.47 (95)	0.47 (94)	0.51 (102)	97	98	94
	BF 490-2	0	0.52 (104)	0.51 (102)	0.50 (99)	102	102	105
		1	0.48 (97)	0.43 (85)	0.49 (97)	93	104	99
		3	0.52 (104)	0.48 (96)	0.50 (100)	100	102	106
		6	0.45 (89)	0.43 (86)	0.47 (94)	90	100	95

		9	0.44 (88)	0.43 (86)	0.43 (87)	87	99	100

Conclusion:
The parent compound and its metabolites BF 490-9 and BF 490-2 were dosed together, each at the fortification level of 0.5 mg/kg in wheat grain samples stored frozen for up to 9 months.
The 3 compounds are very different and highly unlikely to be transformed into another.
The residue values were not corrected for the procedural recovery for Kresoxim-methyl and its metabolites.
The results demonstrated that Kresoxim-methyl and its relevant metabolites BF 490-9 and BF 490-2 can be considered as stable in wheat grain for 9 months.

-Kresoxim-methyl (BAS 490 F) and Its Metabolites BF 490-2 and BF 490-9: 18 Months Frozen Storage Stability in Wheat grain (Class T., Senciuc M., 2009a)
-Final Report: Kresoxim-methyl (BAS 490 F) and Its Metabolites BF 490-2 and BF 490-9: Frozen Storage Stability in Wheat grain, Soy Bean and dried Pea (Class T., Senciuc M., 2009b)
Guidelines:
EC Directive 7032/VI/95 rev.5, Appendix H: Storage Stability of Residue Samples, 22-Jul-97 ;
Guidance document on residue analytical methods (SANCO/3029/99 rev.4)
German GLP standards.
OECD Principles of good Laboratory Practice.
GLP:
Yes.
Material and methods:
Test systems: Wheat grain (dry, high in starch), dried pea (high in protein) and soy bean (oily) samples.
Analytical standards: Kresoxim-methyl, BF 490-2, BF 490-9
Experimental design:
The 3 analytes were dosed together, each at 0.5 mg/kg to the processed plant samples (powder of milled grain or seedlings) and were stored frozen for 0, 1, 3, 6, 9, 12, 18 and 24 months.
-*Stock solutions*:
Separate stock solutions were prepared from the analytical reference items to result each in concentrations of 1.00 mg/mL in methanol.
The stock solutions of Kresoxim-methyl, BF 490-9 and BF 490-2 were prepared at different sampling time points in the course of the study and then stored in a freezer prior to dilution to obtain solutions with equal concentrations.
-*Fortification solutions*:
The Kresoxim-methyl (BAS 490 F), BF 490-2 and BF 490-9 stock solutions were diluted with methanol to obtain a mixed solution with 5.0 µg/mL for each analyte, used for fortification at the 10-times LOQ level and storage stability samples.
The 5.0 µg/mL solution was further diluted with methanol to obtain a mixed fortification solution of 0.50 µg/mL per analyte, used for fortification at the LOQ level.
For method validation, concurrent recovery data were generated by fortifying and extracting blank controls and analyzing them simultaneously with the stored samples.
At each sampling point, 1 untreated blank, 2 samples freshly fortified with the 3 analytes simultaneously at 0.50 mg/kg and 1 sample freshly fortified with all the 3 analytes simultaneously at 0.05 mg/kg were processed concurrently with the 3 dosed samples stored frozen fortified at 0.50 mg/kg.
All the samples prepared for storage were stored at T°<-20°C.
Analytical procedure:
The analytical LC-MS/MS-based BASF method no.445/0 for the determination of residues of Kresoxim-methyl was considered as completely validated with a LoQ of 0.05 mg/kg (see Vol.3, point B.5.2.1).
The analytes were extracted with a mixture of methanol, water, 2N HCl and the extract was centrifuged.
A 200 µL aliquot of the raw extract was diluted to 1.0 mL with Acetonitrile/water (1:1, *v/v*) prior to the determination by LC-MS/MS.
Findings:

Table B.7.0-4: BAS method no. 445/0 was used and validated concurrently with the analysis of the stored samples with the following average recoveries and standard deviations (SD).

Fortification levels (mg/kg)	Recovery results	BAS 490 F			BF 490-9			BF 490-2		
		Wheat grain	Dried pea	Soy bean	Wheat grain	Dried pea	Soy bean	Wheat grain	Dried pea	Soy bean
0.50	Average	91%	101%	92%	100%	93%	89%	104%	97%	90%
	SD	12%	7%	8%	5%	8%	8%	4%	9%	11%
0.050	Average	89%	97%	90%	95%	91%	90%	99%	93%	87%
	SD	6%	8%	11%	9%	14%	12%	7%	11%	8%

Table B.7.0-5: Recoveries after frozen storage and concurrent recoveries from freshly fortified samples (mg/kg)- Nominal spiking level: 0.50 mg/kg

Commodity	Analyte	Storage period (months)	Mean recovery after frozen storage (% of nominal spiking level)	Procedural recovery for freshly spiked samples (%)	
Wheat grain	BAS 490 F	0	75	84	77
		1	83	94	92
		3	72	80	76
		6	85	92	86
		9	71	102	110
		12	75	94	97
		18	80	75	83
		24	102	106	111
	BF 490-9	0	97	103	105
		1	91	101	100
		3	95	101	104
		6	99	99	110
		9	97	98	94
		12	86	95	98
		18	80	96	92
		24	89	105	97
	BF 490-2	0	102	102	105
		1	93	104	99
		3	100	102	106
		6	90	100	95
		9	87	99	100
		12	95	108	109
		18	93	108	104
		24	107	110	107
Dried pea	BAS 490 F	0	84	88	91
		1	100	99	101
		3	100	106	109
		6	85	99	96
		9	85	102	102
		12	94	106	109
		18	78	96	90
		24	109	110	107

	BF 490-9	**0**	98	106	94
		1	80	92	103
		3	90	102	103
		6	88	86	87
		9	82	80	77
		12	91	98	97
		18	80	87	89
		24	105	99	93
	BF 490-2	**0**	102	105	106
		1	88	94	98
		3	95	102	107
		6	85	78	81
		9	83	84	88
		12	98	104	105
		18	86	95	96
		24	107	103	103
Soy bean	**BAS 490 F**	**0**	78	80	81
		1	87	97	100
		3	82	97	93
		6	**50**	97	82
		9	**45**	94	93
		12	**50**	88	93
		18	**65**	85	90
		24	**67**	105	104
	BF 490-9	**0**	97	98	99
		1	**53**	95	74
		2	**45**	100	95
		3	**36**	96	99
		6	**34**	91	87
		9	**28**	83	80
		12	**7**	81	87
		18	**12**	83	89
		24	**8**	80	82
	BF 490-2	**0**	96	101	103
		1	85	89	92
		3	97	104	105
		6	73	78	71
		9	75	79	84
		12	80	90	90
		18	75	70	81
		24	97	97	97

Conclusion:
Kresoxim-methyl and its 2 metabolites BF 490-2 and BF 490-9 were stable under frozen storage conditions for up to 24 months in wheat grain and dried pea.
In soybean, the level of BF 490-9 and BAS 490 F declined rapidly in the course of the storage period.
The parent BAS 490 F was stable for 3 months of frozen storage while the metabolite BF 490-9 declined within the first month of frozen storage with only 53 % of the initial residue level recovered.
The metabolite BF 490-2 remained stable during the complete course of the frozen storage stability period.

-Storage Stability of BAS 490 F in Apple (Krotzky A.J., Mackenroth C., 1994)-Interim report
-The magnitude of Kresoxim-methyl residues in apple processed fractions – 30 Day PHI program ((Wofford J.T et *al.*, 1998)-Final report regarding the storage stability data over a period of 2 years for BAS 490 F (Kresoxim-methyl) in apple.

Guidelines:
IVA Guideline Residue Chemistry, Part II Storage Stability (1990)

GLP:
Yes.
Material and methods:
Test substance: BAS 490 F (Kresoxim-methyl)
Experimental design:
Spiked samples of apple fruit were used to investigate the storage stability of BAS 490 F under freezer conditions at -20°C.
The apple samples were fortified with the test substance at a level of 1.0 mg/kg.
Other samples were used for controls and procedural recoveries purposes.
Samples were analysed at 0, 7, 30, 63, 182 and 295 days.
Analytical procedure:
The residues of BAS 490 F were determined according to BASF analytical method 351/2 using GC/ECD with a Limit of quantification of 0.05 mg/kg.
Procedural recoveries were run together with each analytical series in order to demonstrate the performance of the analytical method.
Findings:
Table B.7.0-6: Determination of the recoveries for procedural recovery samples and stored fortified samples of apple fruit for Kresoxim-methyl (BAS 490 F) in the course of the frozen storage stability study (Results expressed in percent of the nominal fortification level).
The recovered residue levels were not corrected for the procedural recoveries.

Storage period (days)	Residue levels in frozen stored sample (% of nominal spiking level)	Procedural recovery for freshly spiked control sample (%)
0	95.80	96.5; 95.2
7	85.80	81.1; 90.4
30	96.30	88.9; 103.6
63	87.90	89.0; 86.9
182	83.60	84.2; 82.9
295	90.40	82.8; 98.0
575	84.10	84.1
751	80.0	80.0

Conclusion:
Kresoxim-methyl can be considered as stable in apple fruit for more than 2 years under frozen storage conditions.

-Storage Stability of BAS 490 F and its metabolites in grapes, apples, apple juice and apple wet pomace after 12 months of freezer storage-Interim report (Movassaghi S., Riley M.E.; 1998)

This interim report included storage stability data for up to 12 months for all matrices. The following final report presented data for 26 months in grapes.

-Freezer Storage Stability of BAS 490 F (Kresoxim-methyl) and its metabolites in grapes, apples, apple juice and apple wet pomace – Final report (Jordan J., Riley M.E; 1999)
Guidelines:
EPA Pesticide Assessment Guideline, Residue Chemistry, OPPTS 860.1380 and/or 171-4(e), Storage Stability Requirement for BAS 490 F Fungicide.
GLP:
Yes.
Material and methods:
Test substances: BAS 490 F (Kresoxim-methyl), BF 490-B (Glucoside of BF 490-2) (^{14}C-uniformly labeled in the phenoxy ring), BF 490-C (Glucoside of BF 490-9) (^{14}C-uniformly labeled in the phenoxy ring). The test substances were chosen based on the outcome of the grape and apple metabolism studies that identified the parent BAS 490 F and its glycosides metabolites, BF-490-B and BF 490-C as the most predominant residues – see Vol.3, chapter B.7.1.
Characterization and purity of these analytes were determined prior the initiation of the study.

Purity of the test substances:
BF 490-F: 100.0%
BF 490-2: 97.2%
BF 490-9:99.6%
Experimental design:
Untreated control samples of grapes, apples, apple wet pomace and apple juice were obtained from the following residue trials: grapes-study No 94019, apples-study No 94154, apple wet pomace and apple juice –study No 94156. All samples were frozen at T°<-10°C.
-Control samples of grapes and apples were fortified with 1 mg/kg Kresoxim-methyl (BAS 490 F), with BF 490-B at levels ranging from 0.317 mg/kg to 0.399 mg/kg in grapes and apples, and with BF 490-C at levels of 0.469 mg/kg to 0.517 mg/kg both in grapes and apples.
-Aliquots of control apple juice and apple wet pomace were fortified with 1 mg/kg of BAS 490 F. These matrices were not analysed for the residues of the compounds BF 490-B and BF 490-C.
Aliquots of grapes and apples (RAC), apple juice and apple wet pomace samples were also used for the control and procedural recovery samples.
2 fortified samples and one control were extracted on the day of fortification for the 0 –day analysis.
After 2, 6 and 12 months of frozen storage, 2 stored fortified samples and one control aliquot were analysed for the determination of the residues of BAS 490 F, BF 490-B and BF 490-C in apples.
In apple wet pomace and juice, BAS 490 F was analysed at 2, 6 and 12 months.
In grapes, BAS 490 F was analysed at 2, 6, 12 and 26 months and the compounds BF-490-B and BF 490-C were analysed after 2, 6, 9, 12 and 26 months of frozen storage.
Each sample set consisted of 2 stored samples, the procedural fortification samples and the unfortified control sample.
Analytical procedure:
The outcome of the grape and apple metabolism studies (see Vol.3, point B.7.1) showed that the parent BAS 490 F and BF-490-B and BF 490-C were the major compounds of the terminal residues.
The analytical method BASF No 350/3-US was based on the determination of the residues of BAS 490 F as BF 490-1 and its metabolites BF 490-2 and BF 490-9.
The residues of Kresoxim-methyl (BAS 490 F) and its metabolites were extracted from grapes, apples and apple processed fractions with methanol. The glycosides of the metabolites BF 490-2 and BF 490-9 were submitted to enzymatic hydrolysis (β-glucosidase, Hisperinidase) in order to release the respective unconjugated forms.
BAS 490 F was converted into its acid form, BF 490-1, by hydrolysis with KOH. The metabolites were separated from the matrix interferences by solvent partitioning and chromatography clean-up steps.
The determination of the residues was performed by HPLC analysis using UV detector.
Molecular weight conversion factors were used to convert the residues of BF 490-1 into residues of parent BAS 490 F and the residues of BF 490-2 and BF 490-9 into residues of BF 490-B and BF 490-C, respectively.
Findings:
Table B.7.0-7: Determination of the recoveries for procedural recovery samples and stored fortified samples of grapes, apples and apple processed fractions (wet pomace and juice) for Kresoxim-methyl (BAS 490 F) and the conjugated metabolites BF 490-B and BF 490-C (glycosides of the metabolites BF 490-2 and BF 490-9) in the course of the frozen storage stability study (Results expressed in percent of the nominal fortification level).
The recovered residue levels were not corrected for the procedural recoveries.

Fortification level (mg/kg)/analyte	Storage period (months)	Residue levels in frozen stored sample (% of nominal spiking level) (range and mean)	Procedural recovery for freshly spiked control sample (%)
	BAS 490 F		
Grapes			
1.0	**0**	NA	85; 99; 67; 83 (84)
	2	72; 77 (77)	69; 93 (81)
	6	86; 85 (86)	88; 89 (89)
	12	86; 94 (90)	71; 86 (79)
	26	76	108
Apples			
1.0	**0**	NA	89; 83 (86)

	2	65; 80 (73)	81; 84 (83)
	6	67; 80 (74)	89; 95 (92)
	12	70; 70 (70)	71; 91 (81)
Apple wet pomace			
1.0	**0**	NA	90; 76 (83)
	2	80; 85 (83)	82; 79 (81)
	6	86; 81 (84)	100; 100 (100)
	12	69; 79 (74)	77; 95 (86)
Apple juice			
1.0	**0**	NA	95; 95 (95)
	2	63; 73 (**68**) [3]	83; 91 (87)
	6	85; 89 (87)	90; 76 (83)
	12	94; 87 (91)	108; 112 (110)
BF 490-B (Glucoside of BF 490-2)			
Grapes			
0.335[2]	**0**	NA	101; 82 (92)
0.393[1]**/0.335**[2]	**2**	88; 91; 117; 115 (103)	118; 113; 127; 132 (123)
0.317[1]**/0.399**[2]	**6**	72; 75; 74)	100; 98 (99)
0.393[1]**/0.341**[2]	**9**	104; 141 (123)	119; 89 (104)
0.317[1]**/**[2]	**12**	84; 82 (83)	**68**
0.258[1]	**26**	98; 75 (87)	NA
Apples			
0.393[2]	**0**	NA	113; 130 (122)
0.393[1]**/0.335**[2]	**2**	119; 106 (113)	99; 106 (103)
0.393[1]**/0.339**[2]	**6**	125; 125 (125)	114; 124 (119)
0.393[1]**/0.380**[2]	**12**	97; 100 (99)	115; 80 (98)
BF 490-C (Glucoside of BF 490-9)			
Grapes			
0.514[2]	**0**	NA	110; 115 (113)
0.504[1]**/0.514**[2]	**2**	118; 109; 115; 111 (114)	122; 121; 111; 110 (116)
0.504[1]**/0.514**[2]	**6**	108; 117 (113)	108; 105 (107)
0.504[1]**/0.517**[2]	**9**	122; 124 (123)	119; 112 (116)
0.469[1]**/0.506**[2]	**12**	102; 95 (99)	79
0.332[1]	**26**	98; 76 (87)	NA
Apples			
0.505[2]	**0**	NA	111; 113 (112)
0.504[1]**/0.514**[2]	**2**	118; 122 (120)	99; 104 (102)
0.504[1]**/0.506**[2]	**6**	108; 108 (108)	103; 110 (107)
0.504[1]**/0.506**[2]	**12**	112; 110 (111)	110; 110 (110)

NA: not analysed.
[1]: Fortification levels for BF 490-B and BF 490-C for the stored fortified samples in grapes and apples.
[2]: Fortification levels for BF 490-B and BF 490-C for the procedural recovery samples in grapes and apples.
[3]: This value is border line and considered as acceptable by RMS.

Remark:
The sugar conjugates of metabolites BF 490-2 (BF 490-B) and BF 490-9 (BF 490-C) were isolated from the metabolism studies with grapes and apples and were spiked at concentrations between 0.25 - 0.51 mg/kg. The LOQ of the applied method was validated at 0.05 mg/kg per analyte.
BF 490-C was spiked at 0.5 mg/kg.
The 0.3 mg/kg spiking level of BF490-B is equal to the 6 fold LOQ, which is in a reliable range to give precise storage data. In addition, the mean procedural recoveries of BF 490-B (glucoside of BF 490-2) in apples and grapes achieved at this fortification level, were high in a range of 92 to 123%, with one exception of 68% in grapes.

Conclusion:
Although the level of the residues of the parent BAS 490 F recovered in apples seems to have declined by 30 % after 12 months of frozen storage, it is considered that the residues of Kresoxim-methyl are still stable over 12 months frozen storage in apple, as the procedural recoveries at this latter time point was consistently lower than for the earlier time-points.
Kresoxim-methyl and the glycosides conjugates of the metabolites BF 490-2 and BF 490-9 can be considered as stable in grapes, apples and apple processed products at T°<-10°C for 26 months (grapes) and 12 months (apples).

-Freezer Storage Stability of BAS 490 F (Kresoxim-methyl) in Cucumber (Riley M.E. and Abdel-Baky S., 1998)
Guidelines:
EPA Pesticide Assessment Guideline, Residue Chemistry, OPPTS 860.1380 and/or 171-4(e), Storage Stability Requirement for BAS 490 F Fungicide.
GLP:
Yes.
Material and methods:
Test substance: BAS 490 F (Kresoxim-methyl) under its acid form B 490-1
Purity of the compound B 490-1: 99 %
Experimental design:
Untreated samples of cucumber were kept in a freezer at <-10°C until they were homogenized to a consistency appropriate for analysis at 0 month and at 2, 6 and 12 months of storage under frozen conditions.
Samples were fortified at a level of 1 mg/kg with BAS 490 F. The fortified and control samples were stored under frozen conditions at <-10°C until analysis.
At each analysis interval, 2 stored fortification samples and 3 control samples were analyzed. 2 of the control samples were fortified at 1 mg/kg of the test substance for procedural recoveries and were analyzed along with the unfortified control and the 2 stored fortified samples.
Analytical procedure:
The determination of the residues of Kresoxim-methyl in the different samples was performed using the BASF Analytical method N0350/3-US.
Residues of BAS 490 F were extracted from the cucumber samples with methanol. The glycosides of the metabolites BF 490-2 and BF 490-9, remaining after evaporation of the methanol, were subjected to enzymatic hydrolysis.
The enzymatic hydrolysis step converted the glycosides BF 490-B and BF-490-C into their unconjugated form BF 490-2 and BF 490-9, respectively.
BAS 490 F was transformed into its acid form, BF 490-1, by hydrolysis with KOH.
The metabolites were separated from the matrix interferences by solvent partitioning and chromatography clean-up steps.
The quantification of the residues was performed using HPLC/UV detector analysis.
The Limit of Quantification of the analytical method is 0.05 mg/kg for each analyte.

Table B.7.0-8: Determination of the recoveries for procedural recovery samples and stored fortified samples of cucumber for Kresoxim-methyl (BAS 490 F) in the course of the frozen storage stability study (Results expressed in percent of the nominal fortification level).
The recovered residue levels were not corrected for the procedural recoveries.

Fortification level (mg/kg)/analyte	**Storage period (months)**	**Residue level (% of nominal spiking level) (range)**
	Stored fortified cucumber samples	
1.0	**0**	80; 84
	2	78; 82
	6	85; 89
	12	**66; 60**
	Procedural fortified cucumber samples	
1.0	**0**	**73; 86**
1.0	**2**	**96; 90**

0.05	**6**	**84; 73**
1.0	**12**	**77; 78**

Notes:
-The Limit of Quantification of the method 350/3-US for BAS 490 F is 0.05 mg/kg. The Limit of Detection was set at 0.025 mg/kg for each analyte.
-The 6-month procedural samples were inadvertently fortified at the 0.05 ppm level.

Conclusion:
The residues of the parent Kresoxim-methyl can be regarded as sufficiently stable in cucumbers up to a period of 6 months under frozen storage conditions at T°<-10°C.

- Freezer Storage stability of BAS 490 F and Its Metabolites in Pecan (Thornton J.B.; 1998)
GLP:
Yes
Guidelines:
Residue Chemistry Test Guidelines - Subdivision O, Series 171-4(e) OPPTS 860.1380 Storage Stability in Raw Agricultural Commodities
Material and methods:
Test substances: BAS 490 F; ^{14}C-labeled standards of BF 490-B (glycoside of BF 490-2) and BF 490-C (glycoside of BF 490-9) (^{14}C-uniformly labeled on the phenoxy ring).
Reference standards: BF 490-1, BF 490-2 and BF 490-9.
Experimental design:
The pecan nutmeat control samples were homogenised and stored frozen. Composite control pecan samples were fortified with 1.0 ppm BAS 490 F, with 0.28 ppm BF 490-B and 0.472 ppm BF 490-C.
The glycosides metabolites standards BF 490-B and BF 490-C were radioactive and the spiking concentration was calculated from Liquid Scintillation Measurements (LSC).
Samples of pecan nutmeat were also used as control and procedural recovery samples.
The fortifications were run concurrently with control samples.
The control and the fortified samples were stored at <-10°C and were analysed at 0, 2 and 6 months of storage.
Each sample set was constituted of control samples, procedural fortified samples, samples fortified with BAS 490 F and samples fortified with BF 490-B and BF 490-C.
Analytical procedure:
The analytical method No D9611 was used to determine the level of the residues of BAS 490 F as BF 490-1 and of its glycoside metabolites BF 490-B and BF 490-C as BF 490-2 and BF 490-9, respectively.
The samples of pecan nutmeat were extracted with methanol. The methanol extract was reduced to the aqueous phase prior to enzymatic hydrolysis (Hesperidinase, β-glucosidase) that yielded the deconjugated metabolites BF 490-2 and BF 490-9. BAS 490 F was also converted into the metabolite BF 490-1 by hydrolysis with KOH.
Fractionation of the metabolites was performed by solvent partitioning followed by solid phase extraction clean-up step.
The quantification of the residues of BF 490-2, BF 490-9 and BF 490-1 was performed by HPLC analysis with UV detector.
The Limit of Quantification of the method for all samples was 0.05 mg/kg for each analyte while the Limit of Detection was determined to be 0.025 mg/kg.
Findings:
B.7.0-9: Determination of the recoveries for procedural recovery samples and stored fortified samples of Pecan nutmeat for Kresoxim-methyl (BAS 490 F) and its glycosides metabolites BF 490-B and BF 490-C in the course of the frozen storage stability study (Results expressed in percent of the nominal fortification level).
The recovered residue levels were not corrected for the procedural recoveries.

Fortification level (ppm)	**Storage period (months)**	**Recovery results for stored fortification samples (%)**	**Recovery results for procedural fortification samples (%)**
	BAS 490 F		
1.0	**0**	NA	86; 81

1.0	**2**	83; 80	82; 81
1.0	**6**	72; 79	75; 80
BF 490-B			
0.280	**0**	NA	114
0.280	**6**	85	-
0.247	**6**	-	104
BF 490-C			
0.472	**0**	NA	120
0.472	**6**	83	-
0.327	**6**	-	92
NA: not applicable. *Remark*: Fortifications were added prior to extraction and were run concurrently with the control samples.			

Conclusion:
The recoveries for the procedural fortification samples were within the acceptable recovery range.
The residues of BAS 490 F, BF 490-B and BF 490-C were shown to be stable in pecan nutmeat samples for at least 6 months under freezer storage conditions at T°<-10°C.

-Determination of the Stability of 205259 (BAS 480 F), 242009 (BAS 490 F), 285028 (BAS 505 F) and 300355 (BAS 510 F) in different Solvents (Funk H., Mackenroth C.; 2001)

In this study, the stability of 4 fungicidal active substances 205250 (BAS 480 F), 242009 (BAS 490 F), 285028 (BAS 505 F) and 300355 (BAS 510 F) in methanol, methanol/water, iso-octane and acetonitrile was determined under 2 different conditions: at 4°C in the dark and at room temperature and daylight.

This study cannot be considered as valid and is out of interest to support the investigation of the storage stability of the parent Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 in the supported uses on cereals, pome fruit and grapes.

Revised in March 2010

B.7.1 Metabolism, distribution and expression of residues in plants (Annex IIA 6.1)

B.7.1.1 Metabolism, distribution and expression of residues in apples

Remark:
The phenyl ring B was the most important ring being located in the centre of the molecule and was therefore favorised for labeling in all the apple metabolism studies.

-Plant Uptake study with ^{14}C-242 009 in apples (leaf application) (Hofmann M.; 1992a)
Guidelines:
Derived from EPA/FIFRA, § 171-4
GLP:
Yes
Material and Methods:
Test substance: [Ring B-U-^{14}C]-kresoxim-methyl.
Experimental design:
5 apple trees were treated six-fold with a 0.027% a.s. spray solution corresponding to 400 g a.s./ha (5.3 N), from the stage "beginning of flowering" (BBCH GS: 61). The spray solution was applied to run-off. Samples of fruits, leaves and branches were taken 14 days after last treatment for combustion analysis and liquid scintillation counting.
This study did not reflect the critical GAP.
Findings:

At harvest time, the following total radioactive residues were found (determined as kresoxim-methyl-equivalents):
- peel: 1.39 mg/kg
- fruit pulp: 0.061 mg/kg
- core: 0.053 mg/kg
- leaves: 18.5 mg/kg
- branches: 1.73 mg/kg

Conclusions:
The translocation of the compound from apple peel to pulp and core is very low.

-Plant Uptake study with ^{14}C-242 009 in apples (early application) (Hofmann M.; 1992b)

Guidelines:
Derived from EPA/FIFRA, § 171-4

GLP:
Yes

Material and Methods:
Test substance: [Ring B-U-^{14}C]-kresoxim-methyl.
Experimental design:
2 apple trees were treated twice with a 0.027% a.s. spray solution corresponding to 400 g a.s./ha (1.7 N). The first application was done on the stage "beginning of flowering" (BBCH GS: 59) and the second on the stage "petals fall" (BBCH GS: 69). The spray solution was applied to run-off. Samples of fruits, leaves and branches were taken at harvest time (PHI: 149 days) for combustion analysis and liquid scintillation counting.
This study did not reflect the critical GAP.

Findings:
At harvest time, the following total radioactive residues were found (determined as Kresoxim-methyl-equivalents):
- peel: 0.045 mg/kg
- fruit pulp: 0.007 mg/kg
- core: 0.039 mg/kg
- leaves: 1.03 mg/kg
- branches: 0.408 mg/kg

Conclusions:
Very low translocation was observed from the flowers to the fruits.

-Plant Uptake study with ^{14}C-242 009 in apples (fruit treatment) (Hofmann M.; 1992c).

Guidelines:
Derived from EPA/FIFRA, § 171-4

GLP:
Yes

Material and Methods:
Test substances: [Ring B-U-^{14}C]-kresoxim-methyl and [^{13}C]-kresoxim-methyl, ratio 2/1.
Experimental design:
Fruits were treated twice directly with a spray solution containing 0.054% a.s. to run-off.
Leaves and branches were protected with a foil. 14 days after the last treatment, fruits and leaves were sampled for combustion analysis and liquid scintillation counting.
This study did not reflect the critical GAP.

Findings:
The following total radioactive residues were found (determined as Kresoxim-methyl equivalents):
- peel: 5.68 mg/kg
- fruit pulp: 0.024 mg/kg
- core: 0.016 mg/kg
- leaves: 0.230 mg/kg

Conclusions:
The translocation of the compound from apple peel to pulp and core was very low.

-The metabolism of ^{14}C-242 009 (^{14}C-BAS 490 F) in apples (Grosshans F.; 1994a)

Guidelines:
EPA/FIFRA, § 171-4

GLP:
Yes

Material and Methods:
Test substances: [Ring B-U-^{14}C]-Kresoxim-methyl; [Ring B-U-^{14}C]-Kresoxim-methyl and [^{13}C]-Kresoxim-methyl, ratio 2/1.

Experimental design:
The metabolism of kresoxim-methyl in apples was investigated on samples of fruits taken in the 3 here above mentioned uptake studies (Hofmann M., 1992a, b, c).
The frozen storage stability of Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 in apple was addressed by the following studies:
-In the study: "Freezer Storage Stability of BAS 490 F (Kresoxim-methyl) and its metabolites in grapes, apples, apple juice and apple wet pomace – Final report (Riley M.E; 1999)", Kresoxim-methyl and the glycosides conjugates of the metabolites BF 490-2 and BF 490-9 were considered as stable in apples for a frozen storage period of 12 months.
-The magnitude of Kresoxim-methyl residues in apple processed fractions – 30 Day PHI program ((Wofford J.T., 1998)-Final report regarding the storage stability data over a period of 2 years for BAS 490 F (Kresoxim-methyl) in apple. In this study, the parent Kresoxim-methyl was considered to be stable for more than 2 years.

On the other hand, within the apple metabolism study, storage stability investigations were performed with apple peel from leave treatment.
At the end of the study, after 14 months of storage, stored apple peel was extracted again and the new methanol extract showed the same extractability of the stored peel sample compared to the fresh sample at the beginning of the study. In addition, HPLC chromatograms of the fresh prepared methanol extract at the beginning of the study, the stored methanol extract of fresh apple peel and the extract prepared from the stored peel sample at the end of the study showed the same relative peak intensities of the parent compound and the metabolites in all 3 chromatograms. Consequently, the storage stability of BAS 490 F and its metabolites was clearly demonstrated for the stored matrix as well as for the methanol extract.
The apple samples were stored for 14 months, corresponding to the longest storage period in this study.

Analytical procedure:
Peel and pulp were extracted separately with methanol. The extractable radioactivity was characterized by liquid-liquid partition against ethyl acetate and by TLC and HPLC analysis.
The metabolites present in the methanolic extract were isolated as far as possible by HPLC analysis and their structures were elucidated by Mass Spectrometry and/or by chromatographic comparison with reference compounds. Conjugates were treated with glucosidase.
For characterization of "bound" radioactivity, the methanol unextractable radioactive residue was treated with dilute aqueous ammonia. Fractionations for lignin and cellulose were carried out.

Findings:
Based on the calculation for the whole fruits, 94 % to 98 % of the TRR could be extracted with methanol. Between 85% (for early applications) and 95% (for late applications) of the residues contained in the methanol extract were partitioned into ethyl acetate.
The extracts of apples from all plant uptake trials qualitatively show similar metabolite patterns. The extracts contained predominantly unchanged parent kresoxim-methyl.
In total, 93.2 % of the extractable residues (88.4 % of the TRR) could be identified in apples from "leaf application". The remaining extractable radioactivity, which was split into many peaks, was too low for identification (0.002 mg/kg to 0.006 mg/kg).
It was shown that there was no marked change in the nature of radioactive residues during sample storage (13 months).
The following table gives an overview of the results of the study.

Table B.7.1.1-1: Investigation of the nature and amounts of residues of kresoxim-methyl in apples (Residues expressed as % of the TRR and in mg ^{14}C Kresoxim-methyl equiv./kg)

Type of treatment	**6 leaf applications PHI 14 days - 400 g/ha (5.3 N) Spray treatment to run-off**		**2 early applications PHI 149 days - 400 g/ha (1.7 N) Spray treatment to run-off**		**2 fruit treatments PHI 14 days - 0.054% Spray treatment to run-off**	
	mg/kg	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**
peel	2.1581	92	0.2897	89	6.3017	97.6
pulp	0.0324	8	0.0052	11	0.0231	2.4
whole apple (calculated)	0.3591		0.0407		0.8374	
Elucidation of extractable radioactive residues (ERR calculated for whole apples)						
ERR (methanol extract)	0.341	94.9	0.038	94.3	0.822	98.2
Kresoxim-methyl	0.281	78.3	0.0301	74.0	0.7788	93.0
490M0 [(1)]	0.0117	3.3	0.0005	1.2	0.0182	2.2
490M01 (BF 490-1)	0.0106	3.0	0.0008	1.9	0.0118	1.4
490M17 [(2)]	0.0057	1.6	0.0006	1.4	0.0032	0.4
Glucosides of 490M02 (BF 490-2) and 490M09 (BF 490-9)	0.0188	5.2	0.0025	6.1	0.0088	1.1
others [(3)]	0.0117	4.9 (4)	0.004	9.8 (4)	0.0014	0.4 (4)
Total identified metabolites	0.327	91.4	0.0345	84.6	0.8208	98.1
Elucidation of residual (non extractable) radioactive residues (RRR calculated for whole apples)						
RRR (not extracted residues)	0.018	5.1	0.002	5.7	0.015	1.8
Lignin	0.011	3.1				
cellulose	-	-				
ammonia extracts	0.0079	2.2				
Accountability (extracted radioactive residues and unextracted radioactive residues)						
	0.359	100.0	0.04	100.0	0.837	100.0

[(1)]: Z-isomer of the parent Kresoxim-methyl.
[(2)]: Metabolite 490M17 was not identified as such in the course of the study. The corresponding peak has however the same MS spectrum as metabolite 490M17 in the wheat study.
[(3)]: Number of peaks.

Conclusion:
The metabolic pathway of Kresoxim-methyl in apples may be established (Appendix A to this section).

The parent compound is the major constituent of the residue in apples. One metabolite was not recovered in the rat (490M17). Its toxicological significance is discussed under the point B.7.3 (Definition of the residue).

B.7.1.2 Metabolism, distribution and expression of residues in spring wheat

-Plant Uptake Study with ^{14}C-BAS 490 00 F in Spring Wheat (Hofmann M.; 1991a)
Guidelines:
Derived from EPA/FIFRA, § 171-4
GLP:
Yes
Material and Methods:
Test substance: [Ring B-U-^{14}C]-kresoxim-methyl.
Experimental design:
Spring wheat plants were treated twice (leaf application) with an application rate corresponding to 250 g a. s./ha (2N). 1st application was done at "leaf sheaths lengthen" (according to Zadock stage 29/BBCH GS 41); 2nd application was done at "first ears just visible" (according to Zadock 52/BBCH GS 51). The study was performed in a phytotron climatic chamber with Xenon arc lamps. Plants were harvested 64 days after the second application for combustion analysis and liquid scintillation counting.
This study was not performed in accordance with the critical GAP.
Findings:
At harvest time the following total radioactive residues (TRR) were determined (as kresoxim-methyl-equivalents):
- grains: 0.059 mg/kg
- glumes: 1.871 mg/kg
- straw: 12.924 mg/kg
- roots: 1.142 mg/kg
- soil: 0.038 mg/kg
Conclusion:
Some transfer occurred to the roots and (in a very limited extent) to the grains.

-Plant Uptake Study with ^{14}C-BAS 490 00 F in Spring Wheat (Hofmann M.; 1991b)
Guidelines:
Derived from EPA/FIFRA, § 171-4
GLP:
Yes
Material and Methods:
Test substances: [Ring B-U-^{14}C]-kresoxim-methyl and [^{13}C]-kresoxim-methyl, ratio 1/1
Experimental design:
Spring wheat plants were treated twice (leaf application) with an application rate corresponding to 1250 g a. s./ha (10 N). Applications were done at GS 29 and 52 (according to Zadock).The study was performed in a phytotron climatic chamber with Xenon arc lamps. Plants were harvested 63 days after the second application for combustion analysis and liquid scintillation counting.
This study was not performed in accordance with the critical GAP.
Findings:
At harvest time the following total radioactive residues (TRR) were determined (as kresoxim-methyl-equivalents):
- grains: 0.280 mg/kg
- glumes: 10.815 mg/kg
- straw: 44.799 mg/kg
- roots: 3.169 mg/kg
- soil: 0.214 mg/kg
Conclusion:
Some transfer occurred to the roots and (in a very limited extent) to the grains.

-The Metabolism of ^{14}C-BAS 490 F (^{14}C-242009) in Wheat (Grosshans F.; 1994b)

Guidelines:
EPA/FIFRA, § 171-4
GLP:
Yes
Material and Methods:
The metabolism of kresoxim-methyl in wheat was investigated on samples of forage, straw and grains taken in the 2 here above mentioned uptake studies performed in 1991 (Hofmann M., 1991 a/b).
During the radiolabelled metabolism study, the storage stability of wheat samples was proven by aid of straw and extracts thereof. Straw was the matrix containing the highest TRR and was chosen for this reason. After 21 months of storage (at the end of the study), stored straw was extracted again and the new methanol extract showed the same extractability of the stored straw sample compared to the fresh sample at the beginning of the study. In addition, HPLC chromatograms of the fresh prepared methanol extract at the beginning of the study, the stored methanol extract of fresh straw and the extract prepared from the stored straw sample at the end of the study showed the same relative peak intensities of the metabolites in all 3 chromatograms. Consequently, the storage stability of BAS 490 F and its metabolites was clearly demonstrated for the stored matrix as well as for the methanol extracts of wheat straw.
The storage stability in wheat grain was demonstrated during the storage stability study over a period of 24 months: "Kresoxim-methyl (BAS 490 F) and Its Metabolites BF 490-2 and BF 490-9: Frozen Storage Stability in Wheat Grain, Soy Bean and Dried Pea" (Class T., Senciuc M., 2009).

In the first uptake study, plants received a treatment at the double of the normal application rate (Low treatment group). In the second study, the application rate was 10 fold the normal application rate (high treatment group).
Analytical procedure:
The different plant parts were first extracted with methanol and subsequently with dilute aqueous ammonia (0.5%). The extractable radioactivity was characterized by liquid-liquid partition, by solid phase extraction, and by TLC and HPLC analysis.
The metabolites were isolated by fractionation by HPLC analysis as far as possible and their structures were elucidated by Mass Spectroscopy and/or by chromatographic comparison with reference compounds. Conjugates were treated with glucosidase.
For characterization of "bound" radioactivity, the unextractable radioactive residue was treated with enzymes, acids and bases hydrolysis. Fractionations for lignins, cellulose, protein, and starch were carried out.
Findings:
The following comments apply to the results obtained from experiments carried out on the samples from the "low treatment group". The information obtained from the "high treatment group" is qualitatively the same.
From forage more than 93 % TRR could be extracted with methanol. The extractability of radioactivity with MeOH from mature samples was lower. Only 30 % TRR could be extracted from grains and 82 % TRR from straw.
The subsequently performed extraction with dilute aqueous ammonia released an additional 31 % TRR from grains and 16 % TRR from straw. After liquid/liquid partition, the MeOH extractable radioactivity was predominantly found in the organo soluble phase (85 % to 92 % TRR).
97% of the radioactivity from the ammonia extracts could easily be isolated by chromatography on "phenyl" SPE cartridges.
The fractionation of "bound" radioactivity in straw (2.9 % TRR) indicated that 2.1 % TRR was associated with lignin and only 0.2 % TRR was incorporated into cellulose.
In grains, a large percentage of radioactivity was associated with or incorporated into starch (31.7 % TRR from which 9.4 % TRR could be converted into $^{14}CO_2$ by yeast fermentation of the glucose). Lignin accounted for 7.9 % of the total residues, proteins 6.3 % TRR and cellulose 1.6 % TRR.

The following table gives the major results of the study.

Table B.7.1.2-1: Investigation of the nature and amounts of residues of Kresoxim-methyl in spring wheat following leaf spray treatments at the total dose rate of application of 250 g/ha (2N) – (Residues expressed as % of the TRR and in mg ^{14}C Kresoxim-methyl equiv./kg)

Commodity	**forage, 55 days after 1 application**		**grain, 64 days after 2 applications**		**straw, 64 days after 2 applications**	
	mg/kg	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**
Total radioactive residues						
	1.309	100	0.064	100	9.213	100
Extractable radioactive residues						
Methanol	1.22	93.2	0.020	30.4	7.551	82.0
Aqueous ammonia	0.062	4.8	0.020	31.2	1.486	16.1
Elucidation of extractable radioactive residues						
Kresoxim-methyl	0.98	74.8	0.011	17.2	5.92	64.3
490M0 (Z-isomer)	0.016	1.2	0.0002	0.3	0.395	3.9
490M01(BF 490-1)	0.039	3.0	nd	nd	0.126	1.4
490M17 [(1)]	0.037	2.8	0.0005	0.8	0.329	3.6
490M02 (BF 490-2) glucoside	0.029	2.2	nd	nd	0.387	4.2
490M09 (BF 490-9) glucoside	0.103	7.9	0.0024	3.8	1.036	11.2
others [(2)]	0.037	5.6	0.0196	30.4	0.823	9.0
Total identified metabolites	1.204	91.9	0.0112	17.5	8.193	88.6
Residual radioactive residues						
	0.048	3.7	0.035	38.8	0.269	2.9
Elucidation of residual radioactive residues						
lignin			0.005	7.9	0.198	2.1
cellulose			0.001	1.6	0.020	0.2
proteine			0.004	6.3		
starch			0.0155	24.6		
starch work up losses			0.0045	7.0		

(1): As no reference compound was available in the study for this metabolite, its structure is not confirmed. It has been characterized by a molecular weight of 313 in GC/MS and a hydroxylation in the A-ring by NMR.
(2): The radioactivity is split into many peaks characterized by their chromatographic properties.

Commodity	forage, 55 days after 1 application		grain, 64 days after 2 applications		straw, 64 days after 2 applications	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
Nd: Not detected.						

Conclusion:
The metabolic pathway of kresoxim-methyl in wheat is presented Appendix A to this section.
The parent compound is the major constituent in forage, straw and grain, although the level of identified metabolites was rather low in wheat grain (22.1% of the TRR) and the parent compound occurred only at 17% of the total residues in grain.
No further characterization of the unidentified radioactive fraction in grain (30.4 % TRR) was attempted while the residual radioactive residues were shown to be mainly incorporated into the cellular components (lignin, cellulose, protein and starch) accounting for more than 40% of the TRR.
The postulated structure of one metabolite (490M17) is not found back in the rat metabolism. Its toxicological significance is discussed under the point B.7.3 (definition of the residue).

B.7.1.3 Metabolism, distribution and expression of residues in grapes

-Metabolism of ^{14}C-BAS 490 F in grapes (Nelsen J.; 1995).
Guidelines:
EPA/FIFRA, § 171-4 (a)
GLP:
Yes
Material and Methods:
Test substances: [Ring A-U-^{14}C]-kresoxim-methyl and [Ring B-U-^{14}C]-kresoxim-methyl.
Experimental design:
Mature vines were sprayed five times at approximately 14 day intervals at the equivalent rate of 500 g/ha of ^{14}C-BAS 490 F (6.75 N).The last application was made 14 days before harvest (14 days PHI). The applications were made separately with ^{14}C-BAS 490 F labelled in each of the aromatic rings.
After harvest, liquid scintillation counting was used for determining the total radioactive residues.
This study did not reflect the critical GAP.
Analytical procedure:
The extractability of the residues was investigated by rinsing, and subsequently extracting after homogenization grape samples with methanol.
The rinsed and extracted residues were characterized by high pressure liquid chromatography (HPLC) and thin layer chromatography (TLC).
Identification of the nature of residues was carried out by co-chromatography in HPLC and TLC systems with the reference standards.
Polar and conjugated metabolites were bulk isolated and subjected to enzyme hydrolysis with ß-Glucosidase. The hydrolysis products were separately characterized by HPLC separation and co-chromatography with reference standards. In addition, isolation and identification of released aglycones was performed by mass spectroscopy following bulk isolation of individual peaks.
Findings:
The extractability of residues with methanol was high (more than 90% of TRR for both labels). Simple rinses of the grapes surface removed 40% of the TRR.
Between 75 and 80% of the TRR could be identified. The major unidentified fractions appear to be a mixture of over 20 unhydrolysed conjugates and other polar materials all less than 0.05 mg/kg.
No major qualitative differences have been observed between the two labels.
The following table gives an overview of the results of the study.

Table B.7.1.3-1: Investigation of the nature and amounts of residues of Kresoxim-methyl in grapes after 5 leaf spray treatments at a rate of 500 g/ha of ^{14}C-BAS 490 F (6.75 N).

Label	**[Ring A-U-^{14}C]-Kresoxim-methyl**		**[Ring B-U-^{14}C]-Kresoxim-methyl**	
	mg/kg	**%TRR**	**mg/kg**	**%TRR**
Total radioactive residues				
	4.00	100	4.72	100
Extractable radioactive residues				
Methanol rinses		40		40.5
Subsequent methanol extraction		50.7		45.8
total	3.63	90.7	4.07	86.3
Elucidation of extractable radioactive residues				
Kresoxim-methyl	2.215	55.4	2.707	57.4
490M0 (Z-isomer)	0.139	3.49	0.177	3.75
490M09(BF 490-9)	0.05	1.25	0.066	1.4
other non polar compounds (3 fractions)	0.082	2.07	0.11	2.36
490M02 (BF 490-2) glucoside	0.55	13.76	0.418	8.86
490M09 (BF 490-9) glucoside	0.18	4.50	0.14	2.98
490M54 (BF 490 15) glucoside	0.083	2.07	0.064	1.37
490M01 (BF 490-1) glucoside	0.019	0.48	0.006	0.13
other polar compounds	0.150	3.74	0.236	5.05
Residual radioactive residues				
		3.8		4.1
Total recovery of residues				
		94.5		90.4

Conclusion:
The metabolic pathway of Kresoxim-methyl in grapes is presented in Appendix A to this section.
The parent compound is the major constituent of the residue. One metabolite 490M54 (BF 490 15) was not present in the rat metabolism. Its toxicological significance is discussed under the point B.7.3 (definition of the residue).

Added in March 2010

B.7.1.4 Metabolism, distribution and expression of residues in sugar beet

-Metabolism of ^{14}C-BAS 490 F (^{14}C-242009) in Sugar Beet (Veit P.; 1999)
Guidelines:
-US, EPA Residue Chemistry Test Guidelines, OPPTS 860.1300 Nature of the residue – plants, livestock.
-BBA Guidelines for the Official Examination of Pesticides, Part IV, 3-2 (Metabolism in Plants)
GLP:
Yes.
Material and methods:
Test substance: ^{14}C-BAS 490 F (^{14}C-Phenyl ring labeling)
Reference standards: BAS 490 F (Radiochemical Purity: >99 %); BF 490-1 (Purity: 99.2%); BF 490-9 (Purity: 98.5 %); BF 490-2 (Purity: 94.4 %); metabolites isolated from cell cultures: 98PM032 (Sugar conjugate of BF 490-9); 98PM031 (Sugar conjugate of BF 490-2).
Preparation of the formulation:
13.2 mg of the original test substance was dissolved in toluene. For the preparation of the application formulation, the toluene in flask was evaporated to dryness and re dissolved in acetonitrile. The acetonitrile solution was mixed with a 50 % *WG* formulation and water was added to prepare the final spray solution.
Experimental design:
The study was performed under outdoor conditions.
Sugar beets seeds were sown in a loamy sand soil in pots.
The crop was treated twice by spraying with the test substance at a total dose rate of application of 300 g a.s./ha (2 x 150 g a.s./ha). The applications took place respectively at 91 days after sowing (BBCH GS 39: Crop cover complete; leaves cover 90 % of the ground) and the second treatment occurred 3 weeks later, i.e. 28 days before harvest (DALA).
Sugar beet roots and leaves with tops were taken before and after the second application and at harvest.
All samples were stored at -18°C immediately after sampling (sugar beet roots: dry commodities/leaves with tops: high water content)
Analytical procedure:
The total radioactive residues (TRR) were determined by radio combustion analysis followed by Liquid Scintillation Counting.
HPLC analysis in different solvent systems were used either for quantification of individual peaks or for comparison because of a better separation of the polar region achieved with one system or for comparison of the storage stability (analysis at the beginning and at the end of the experimental phase).
Homogenised samples of sugar beet were extracted three times with Methanol followed by extraction with water providing respectively the methanolic and the water extracts. In some cases, an additional extraction with aqueous ammonia was carried out after the water extraction (NH_3 extracts) but without any further identification of the radioactivity.
The concentrated methanolic extracts of roots and leaves at 0 and 28 DALA were further partitioned against ethyl acetate in order to characterize the radioactive residues into organo soluble and aqueous soluble partitioned phases.
No tentative enzymatic hydrolysis was performed on the different extracts to release further radioactivity from the conjugates.
Identification of the metabolites in the organic and aqueous partitioned phases was performed by HPLC analysis in different solvent systems by chromatographic comparison of the retention times of the reference standards with those of the peaks of interest or by co-chromatography with the reference standards.
The post extraction solids phase was further extracted with an aqueous ammonia solution (NH_3 extract) to release and characterize further the radioactive residues.

All the samples were stored frozen at -18°C. Samples of sugar beet leaves at harvest (28 DALA) were analysed at the beginning and at the completion of the study, respectively at 14 days and 225 days time intervals from sampling to analysis for storage stability data.
No identification of the metabolites in sugar beet roots was attempted probably because of the very low level of radioactive residues recovered in the roots.

In the tables here below, the total radioactive residues (TRR) were reported as determined by direct combustion and calculated. The values for the TRR calculated were used.

Findings:

B.7.1.4-1: Determination of the amount and the nature of the residues in sugar beet roots and leaves at different sampling dates and at harvest after 2 spray applications of the test substance at a total dose rate of 300 g a.s./ha (2 x 150 g a.s./ha) at BBCH GS 39 and 28 days before harvest, respectively (Residues are expressed as mg ^{14}C-BAS 490 F equivalent/kg and in % of the total radioactive residues).

Matrix/days after last application (DALA)	Before 2nd treatment (3 weeks after the 1st treatment)		After 2nd treatment (0 DALA)		At harvest (28 DALA)	
	Roots	Leaves/tops	Roots	Leaves/tops	Roots	Leaves/tops
Total radioactive residues determined by direct combustion analysis (mg ^{14}C-BAS 490 F equivalent/kg)						
	0.007	0.610	0.053	1.846	0.008	1.735
Total radioactive residues calculated(1) (mg ^{14}C-BAS 490 F equivalent/kg)						
	0.007	0.543	0.024	1.434	0.009	1.255
Extractability of the radioactive residues. Residues expressed in % of the TRR and in (mg ^{14}C-BAS 490 F equivalent/kg)						
MeOH extraction phase	65.7 (0.004)	96.7 (0.526)	91.4 (0.022)	98.3 (1.409)	60.8 (0.005)	88.5 (1.110)
EtAc soluble partitioned phase	np	np	68.4 (0.017)	94.2 (1.351)	29.7 (0.003)	69.1 (0.867)
Aqueous soluble partitioned phase	np	np	10.9 (0.003)	9.0 (0.129)	37.0 (0.003)	29.2 (0.366)
Water extraction phase	10.1 (0.001)	1.0 (0.005)	1.8 (<0.001)	0.6 (0.008)	2.5 (<0.001)	2.6 (0.033)
Extractable radioactive residues (sum of MeOH and H_2O extracts) (% of the TRR)/(mg ^{14}C-BAS 490 F equivalent/kg)						
	75.8 (0.005)	97.7 (0.531)	93.2 (0.022)	98.8 (1.417)	63.3 (0.005)	91.1 (1.143)
Identification of the radioactive residues (% of the TRR)/(mg ^{14}C-BAS 490 F equivalent/kg) in the methanolic and aqueous extracted phases:						
Kresoxim-methyl (BAS 490 F)	np	96.7 (0.526)	np	98.3 (1.409)	np	88.5 (1.110)/ 67.0 (0.840) (2)
Acid metabolite (BF 490-1)		nd		0.6 (0.008)		2.6 (0.033)/9.7 (0.121) (2)
Sugar conjugate of BF 490-2(2)		nd		nd		9.2 (0.116) (2)
Unknown compounds(2)						2.6 (0.033) (2)
Total identified metabolites		96.7 (0.526)		98.9 (1.417)		91.1 (1.143)/85.9 (1.077) (2)
Unextracted radioactive residues (% of the TRR)/(mg ^{14}C-BAS 490 F equivalent/kg)						
	24.2 (0.002)	2.3 (0.012)	5.8 (0.003)(3)	1.2 (0.017)	36.6 (0.003)	8.9 (0.112)
NH_3 extraction phase		0.5 (0.003)	1.1 (0.001)(4)			2.3 (0.029)
Final NH_3 residue		0.8 (0.004)	1.2 (0.001) (4)			2.0 (0.026)
Residual radioactive residues (% of the TRR)/(mg ^{14}C-BAS 490 F equivalent/kg)						
	24.2 (0.002)	1.0 (0.005)	3.5 (0.001)	1.2 (0.017)	36.6 (0.003)	4.6 (0.057)

Accountability (ERR+URR) (% of the TRR)/(mg ^{14}C-BAS 490 F equivalent/kg)						
	100.0 (0.007)	100.0 (0.543)	100.0 (0.024)	100.1 (1.434)	100.0 (0.008)	95.4 (1.198)

Np: Not performed.
Nd: Not detected.
DALA: Days after last application.

(1): TRR calculated: Sum of the extracts (methanolic and water extracts) and the post extraction solids extract. In the course of the study TRR calculated was used for further calculations.
(2): Metabolites'investigation of the radioactive residues in the methanolic extracted phase of sugar beet leaves at harvest (28 DALA) by HPLC analysis in solvent system 2.
(3): The residue values obtained after the 1st work up accounted for 5.8 % of TRR – 0.003 mg/kg. The NH_3 extraction was performed on the 1st work-up fraction only.
Residue values obtained after the second work up on roots after the 2nd treatment: 6.8 % of TRR (0.002 mg/kg).
(4): Because of the low residue levels in the post extraction solids and some analytical problems with the ammonia solution, only low recovery levels could be achieved.
Notes:
-The applicant stated that the higher residue level observed in roots at 0 DALA (after the 2nd treatment) was due to a different sampling technique. Part of the green tops stayed on the roots and was homogenised with the roots for further analysis.

At harvest (28 DALA), the total radioactive residues in sugar beet roots were very low with up to 0.009 mg/kg while the total residues in leaves with tops accounted for 1.255 mg/kg.
The low residue levels recovered in the roots indicated that only a small amount of the applied radioactivity was translocated from the leaves to the roots.
Extractabilities with methanol of the sugar beet roots before and after the second treatment and at harvest amounted up to 91 % of the TRR while an additional extraction step with water did not increase the extractability significantly (up to 10.0 % of the TRR only).
In the sugar beet leaves, the rate of extractability with methanol was higher (up to 98% of the TRR in the leaves at 0 DALA).
Liquid-liquid partitioning of the methanolic extracts of sugar beet roots and leaves/tops at 0 DALA and at harvest (28 DALA) partitioned most of the radioactivity into the organo soluble phase (up to 68.4 % and 94.2 % of the TRR in sugar beet roots and leaves with tops, respectively).
No further metabolites investigation was attempted in sugar beet roots in the course of the study because of the very low level of recovered radioactive residues.
The rate of identification of the metabolites in the leaves/tops at different sampling intervals (before the 2nd treatment, at 0 DALA and at harvest) raised 98.9 % of the TRR.
HPLC analysis of the methanol extracts of leaves with tops before, after the second treatment and at harvest showed that the parent compound was recovered as the predominant compound of the total residues (up to 98.3 % of the TRR).
In the water extracts of leaves/tops at 0 DALA, the acid metabolite of Kresoxim-methyl was identified at a low level (0.6 – 2.6 % of the TRR).
HPLC analysis using a different solvent system showed a more efficient resolution of the radioactivity in the polar region with the identification of the parent compound (67.0 % of TRR), its acid metabolite BF 490-1 (9.7 % of TRR) and the sugar conjugate of the hydroxy metabolite BF 490-2 (9.2 % of TRR).
A comparison of the HPLC profiles of the stored methanolic extracts of sugar beet leaves at harvest (28 DALA) (for 225 days from sampling to analysis) with the HPLC results of the methanolic extracts of the samples at the beginning of the study showed an identical metabolic profile. The HPLC peak corresponding to the parent compound remained predominant in the 2 chromatograms.
The composition of the radioactivity in the methanolic extracts of the sugar beet leaves at harvest (28 DALA) remained unchanged after freezer storage (-18°C) of 225 days from sampling to analysis. No disappearance of a particular HPLC peak was observed.
Conclusion:
The metabolic pathway of Kresoxim-methyl in sugar beet leaves and tops is depicted in Appendix A to this section.

Unchanged parent compound was the most predominant component of the total residues in all the extracts of the sugar beet leaves with tops.
Additional metabolites were recovered in the leaves which corresponded to the acid metabolite BF 490-1 and the sugar conjugate of BF 490-2 after hydroxylation and sugar conjugation.
Within a storage period of 71/2 months, no change in the metabolic pattern could be observed demonstrating that the radioactive residues in the extract of sugar beet leaves were stable.

B.7.2 Metabolism, distribution and expression of residues in livestock (Annex IIA 6.2)

B.7.2.1 Metabolism, distribution and expression of residues in lactating cows or goats

-Dosing of lactating goats with (^{14}-C)-LAB 242009 (Giese U.; 1992).
-The metabolism of ^{14}C-BAS 490 F in the goat (Mayer F.; 1994)
Guidelines:
EPA/FIFRA, § 171-4
EPA Pesticide assessment guidelines, Subdivision O, Residue Chemistry &171-4.
GLP:
Yes
Material and Methods:
Test substances: [Ring B-U-^{14}C]-kresoxim-methyl, [^{13}C]-kresoxim-methyl, unlabelled kresoxim-methyl.
Experimental design:
Three goats were fed with the test substance by intubation at the following levels, labelling ratios and durations:
- Goat A: 0.25 mg/kg bw/day – (7N/2N), ratio ^{14}C/^{13}C/unlabelled: 3/0/1, 5 days;
- Goat B: 25 mg/kg bw/day - (675N/225N), ratio ^{14}C/^{13}C/unlabelled: 1/4/10, 8 days;
- Goat C: 25 mg/kg bw/day, ratio ^{14}C/^{13}C/unlabelled: 1/0/20, 8 days;

Plasma and blood level profiles were investigated in goat A. A balance of the administered dose was established for goats A and B. Levels of radioactivity in samples of tissues and excreta were measured by liquid scintillation counting.
Animals were sacrificed within 24 hours of the last administration (23 h for goat A, 4 h for goats B and C).
Samples of goat B were used for quantification, isolation and identification of metabolites.
Extraction procedure:
Milk and edible tissues were extracted with methanol and subsequently with water. Partitioning of the extracts between hexane and acetonitrile was necessary before HPLC injection. Pronase incubation and/or ammonia extraction were used to further characterize the non extractable residues.
Identification of the metabolites was carried out in urine and faeces using Mass Spectrometry analysis after fractionation by HPLC chromatography. The metabolites in milk and edible tissues were identified by chromatographic comparison of extracts with those from urine and faeces.
Findings:
The major part of the radioactivity administered was excreted with urine.
Taking into account the radioactivity eliminated with milk, urine and faeces as well as the residual radioactivity in tissues and GIT and the radioactivity from the cage cleaning, 94.5 % of the radioactivity administered were recovered from goat A and 97 % from goat B.
Kidney was the organ with the highest level of residues.
Table B.7.2.1-1 gives the balance of the administered radioactivity as well as the total residue levels in edible organs and tissues.

Table B.7.2.1-1: Balance of the administered radioactivity and total radioactive residues in edible organs and tissues (Residues expressed in mg ^{14}C kresoxim-methyl equiv./kg and in % of the TRR).

	Goat A Feeding level: 0.25 mg/kg bw/day		**Goat B Feeding level: 25 mg/kg bw/day**	
Sample	**TRR (mg/kg)**	**% of total dose**	**TRR (mg/kg)**	**% of total dose**
urine		69.51		59.31
faeces		18.08		24.52
cage cleaning		1.08		1.47
milk	0.003	0.031	0.191	0.027
liver	0.041	0.06	6.814	0.07

kidney	0.148	0.03	14.042	0.02
fat	0.001	0.01	0.327	<0.005
muscle	0.001	0.01	0.222	0.01
others (1)		5.62		11.67
Total		94.4		97.1

(1): Bile, stomach and intestin contents and urine of bladder at sacrifice.

Extractabilities with methanol and water ranged from 63 % TRR in liver to 98 % in kidney.
Table 7.2.1-2 gives an overview of the results of the identification part of the study.

Table B.7.2.1-2: Investigation of the nature and amount of residues of Kresoxim-methyl in excreta and edible tissues of the goat (**Feeding level: 25 mg/kg bw/d**) (675N/225N) – Residues expressed as % of the TRR and in mg ^{14}C kresoxim-methyl equiv./kg.

Sample	**urine**	**faeces**	**milk**	**liver**	**kidney**	**muscle**	**fat**
TRR (mg/kg)	551	88	0.19	6.61	13.5	0.23	0.36
Extractability of residues (%TRR) in methanol and water							
Methanol extracted phase	not extracted	83.5 (73.48)	101.4 (0.19)	57.8 (3.82)	96-97 (13.09)	71.8 (0.165)	70.3 (0.25)
Water extracted phase		4.7 (1) (4.13)		5.0 (0.33)	1.5-2.4 (0.32)	n.d(1)	2.3 (1) (0.008)
Elucidation of extractable radioactive residues -%TRR (mg ^{14}C kresoxim-methyl equiv./kg).							
Kresoxim-methyl	n.d.	1.5 (1.32)	n.d.	n.d.	n.d.	n.d.	6.6 (0.023)
490M01 (BF 490-1)	31.5 (173.56)	11.6 (10.2)	1.6 (0.003)	12.9 (0.85)	21.8 (2.94)	23.7 (0.054)	23.1 (0.083)
490M02 (BF 490-2)	31.7 (174.6)	12.3 (10.8)	20.4 (0.038)	8.6 (0.56)	34 (4.59)	14.2 (0.032)	24.1 (0.086)
490M06	2.1 (11.57)	3.8 (3.34)	n.d.	0.5 (0.033)	3.6 (0.48)	n.d.	8.0 (0.028)
490M09 (BF 490-9)	27.7 (152.6)	31.5 (27.7)	63.0 (0.119)	29.2 (1.93)	29.8 (4.023)	7.4 (0.017)	0.3 (0.001)
490M15 (BF 490-4)	n.d.	13.7 (12.05)	n.d.	n.d.	n.d.	n.d.	n.d.
490M18 (BF 490-8)	2.1 (11.57)	2.1 (1.84)	n.d.	1.9 (0.125)	n.d.	7.2 (0.016)	0.7 (0.0025)
490M19	0.3 (1.65)	0.9 (0.79)	n.d.	0.1 (0.0066)	n.d.	6.6 (0.015)	n.d.

490M56	0.2 (1.1)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
other characterized[(2)]	4.5 (4) (24.79)	6.1 (2) (5.36)	16.1 (5) (0.03)	3.8(15) (0.251)	5.9 (5) (0.79)	0 (0)	3.1 (7) (0.011)
Total identified and characterized radioactive residues	100.1 (551)	83.5 (73.5)	101.1 (0.19)	57 (3.76)	95.1 (12.83)	59.1 (0.135)	65.9 (0.23)
Residual radioactive residues -%TRR (mg ^{14}C kresoxim-methyl equiv./kg).							
	-	7 (6.16)	3.5 (0.006)	42.7 (2.82)	2-2.5 (0.33)	26.9 (0.048)	17.5 (0.063)
Elucidation of residual radioactive residues -%TRR (mg ^{14}C kresoxim-methyl equiv./kg).							
solubilization by pronase			-	29.1 (1.92)	1.7 (0.22)	21.3 (0.048)	11.6 (0.041)
Extractability by ammonia			-	14.1 [(3)] (0.93)	-	15.1 (0.034)	-
Accountability: extracted methanol phase+ extracted water phase + residual radioactive residues fraction -%TRR							
			104.9	105.5	100-101	98.7	90.1

n.d. = not detectable
[(1)]: fraction not used for identification
[(2)]: number of peaks
[(3)]: after separation of residues released by pronase incubation

Conclusions:
The metabolic pathway of Kresoxim-methyl in goats is presented in Appendix A to this section.
Parent compound was extensively metabolized and was recovered only in fat at a low level (6.6 % of TRR-0.023 mg/kg). Major metabolites were BF 490-1, BF 490-2, and BF 490-9, in proportions varying according to the tissue.
In milk, the major metabolite was BF 490-9 (63% of TRR-0.119 mg/kg).
In liver, major metabolites were BF 490-1 (13% of TRR-0.85 mg/kg) and BF 490-9 (29% of TRR-1.93 mg/kg).
In kidney, major metabolites were BF 490-1 (22% of TRR-2.94 mg/kg), BF 490-2 (34% of TRR-4.59 mg/kg) and BF 490-9 (30% of TRR-4.02 mg/kg).
In muscle and fat, major metabolites were BF 490-1 (respectively 24% of TRR-0.054 mg/kg and 23% of TRR-0.083 mg/kg) and BF 490-2 (respectively 14 % of TRR-0.032 mg/kg and 24 % of TRR-0.086 mg/kg).
Some metabolites were not present in the rat metabolism. 490M19 is a conjugated form of BF 490-1with glycine. 490M18 (BF 490-8) and 490M56 reflect different combinations of the reactions observed in the rat.

Added in March 2010

-The metabolism of (cresyl-^{14}C) BAS 490F (REG N0. 242009) in the goat (Kirkpatrick D., 1996)
Guidelines:
-US, EPA Subdivision O Guideline 171-4
GLP:
Yes.
Material and methods:
Test substance: ^{14}C-BAS 490 F (^{14}C-Cresyl ring labeling): [Ring A-U-^{14}C]-kresoxim-methyl
Radiochemical purity: 97.6 % (TLC and HPLC)
Specific activity: 138.7 µCi/mg
Reference standards: non-radiolabelled BF 490-1, BF 490-2, BF 490-9
Preparation of the formulation:
The labeled test substance and the non –radio labelled BAS 490F were dissolved in acetone. The solution was mixed and the solvent removed by rotary film evaporation under reduced pressure and a stream of oxygen.
Experimental design:
The animal was received nine days prior to the start of dosing.
The test substance was administered to a lactating goat by gavage once daily after milking for five consecutive days at a nominal daily dose of 18 mg ^{14}C-BAS 490F/day equivalent to a daily intake of **13.9 mg/kg in the diet as received (13N/5N)** based on the total food consumption of 6.6 kg during the dosing period.
The animal was sacrificed 23 hours after the final dose.
The goat was milked twice daily, in the morning just prior to dosing and in the afternoon.
The mean daily concentration of radioactive residues in milk was calculated as the average of the total 24 hours collection.
Excreta (urine, faeces and cage wash) were collected.
Tissue samples were also taken: liver, kidney, bile, rumen and gastrointestinal tract, muscle (foreleg, loin and rump) and fat (subcutaneous, omental and perirenal).
Analytical procedure:
The total radioactive residues were determined by radio combustion analysis and liquid scintillation counting.
-HPLC analysis was used to isolate and purify urinary metabolites, to quantify liver and kidney extracts and for co-chromatography comparison of liver and kidney extracts with reference standards or isolated urinary metabolites.
The major urinary metabolites were isolated and purified for mass spectroscopic investigation.
Samples of urine were adjusted to pH 2 with HCl and partitioned against dichloromethane to give organo soluble and aqueous soluble phases. The urine metabolites BF 490-2, BF 490-9 and BF 490-1 were isolated and quantified from the organo soluble phase by semi-preparative HPLC analysis at a level of 24.3%, 24.5% and 9.7% of the total dose, respectively. In order to confirm the identity of these 3 major metabolites, these were isolated and identified by mass spectrometry. The identification of these metabolites was also confirmed by TLC co-chromatography with the non-radiolabelled reference standards BF 490-1, BF 490-2 and BF 490-9.
-Normal and reverse phase TLC analysis in 2 different solvent systems were also used to determine the radiochemical purity of the dose solution, for the co-chromatography with unlabelled reference standards and/or co-chromatography of radioactive isolates from urine with the radioactive residues in kidney and liver extracts.
Kidney and liver samples were extracted with acetonitrile and acetonitrile:water (1:1, *v:v*) and water. The extracts were pooled and analysed by HPLC. Further aliquots of kidney and liver extracts were analysed by TLC analysis by co-chromatography with non radio labelled reference standards or with isolated radioactive urinary metabolites in different solvent systems.
The freshly extracted liver homogenates were submitted to enzymatic hydrolysis (protease digestion) without any further investigation due to the very low level of radioactivity recovered in the supernatant.
The residue left after the protease digestion was extracted twice with water: 25% ammonia (50:1, *v:v*).
Due to the low levels of radioactivity in the ammonia extracts, these fractions were not analysed further.
All the samples were stored frozen at T°<-15°C.
The period between sampling of the organs and extraction/analysis was less than 1 month.
Findings:
The health status was satisfactory and milk yields were maintained throughout the study.

23 hours after the last administration, taking into account the radioactivity eliminated with milk, urine, faeces and cage wash as well as the residual radioactivity in tissues 88.2 % of the administered radioactivity were excreted from the animal.
The major part of the radioactivity administered was excreted with urine (66.7 % of the total dose).
**Milk*: The transfer of radioactivity into milk was very low and accounted for less than 0.1 % of the total administered dose.
The residue levels plateaued on day 3 corresponding to the residue concentration of 0.003 mg/kg.
The plateau in milk was reached within the dosing period and thus accumulation of the residues in animal matrices is not expected.
**Tissues*: The residue levels in tissues were the highest in liver and kidney (respectively 0.064 and 0.052 mg ^{14}C Kresoxim-methyl equiv./kg).
The total radioactive residue levels recovered in fat , muscle and milk were too low (<0.003 mg/kg) to attempt any further metabolites'identification.

Table B.7.2.1-3 gives the balance of the administered radioactivity as well as the total residue levels in edible organs and tissues.

Table B.7.2.1-3: Balance of the administered radioactivity (percentage of the daily dose and cumulative dose administered up to the specified time period of treatment) and total radioactive residues in goat tissues (expressed as mg ^{14}C-Kresoxim-methyl equiv./kg)

Samples	Time (hours after the 1st dose)	Cumulative radioactive excretion (%)(1)	TRR (mg/kg)
Urine	0-24	52.7	-
	0-48	60.5	
	0-72	60.8	
	0-96	65.4	
	0-119	66.7	
Cagewash	0-119	1.8	-
Faeces	0-24	7.1	-
	0-48	13.4	
	0-72	18.3	
	0-96	19.3	
	0-119	19.6	
Milk		<0.1	0.003
Total excretion		***88.1***	-
Liver		0.1	0.064
Kidney		<0.1	0.052
Fat (omental, perirenal, subcutaneous)		-	<0.003
Muscle (foreleg, loin, rump)		-	<0.003
Bile		-	0.718
Whole blood		-	0.015
Plasma		-	0.021
Total recovery		**88.2**	-

(1): Radioactivity expressed as a cumulative percentage of the total administered dose on day 5.

Table B.7.2.1-4: Level and extractability of the radioactive residues in liver and kidney of goats after oral administration of (Cresyl-^{14}C) –Kresoxim-methyl at a dose rate of 13.9 mg/kg in the diet **as received** .

Tissues	**Kidney**	**Liver**
Total radioactive residues (mg ^{14}C Kresoxim-methyl equiv./kg)	0.052	0.064
Extractability of radioactive residues (Residues expressed in % of TRR and in mg ^{14}C Kresoxim-methyl equiv./kg)		
Combined solvent extraction phase[(1)]	85.5 (0.045)	42.5 (0.027)
Enzymatic hydrolysis released supernatant	np	14.4 (0.009)
Ammonia extraction phase **-1st extraction** **-2nd extraction**	np	 14.8 (0.009) 8.3 (0.005)
Elucidation of the radioactive residues (Residues expressed in % of TRR and in mg ^{14}C Kresoxim-methyl equiv./kg)		
BF 490-1	11.1 (0.006)	2.2 (0.001)
BF 490-2	34.1 (0.018)	8.5 (0.005)
BF 490-9	15.2 (0.008)	16.8 (0.011)
Compound U1[(2)]	7.5 (0.004)	7.2 (0.005)
Unknown radioactivity[(3)]	17.5 (0.009)	7.9 (0.005)
Total identified metabolites	60.4 (0.032)	27.5 (0.017)
Post extraction solids (Residues expressed in % of TRR and in mg ^{14}C Kresoxim-methyl equiv./kg)		
	14.6 (0.008)	20.1 (0.013)
Total recovery (sum of extracted radioactivity and post extraction solids)		
	100.1 (0.053)	100.1 (0.063)

Np: Not performed

(1): successive extractions of liver and kidney samples with Acetonitrile, Acetonitrile:water (1:1, *v:v*) and water.

(2): The metabolite BF 490-9 was not very stable and degraded to a component with a similar retention time to U1.

The compound U1 was a minor peak of up to 7.5 % TRR (0.004-0.005 mg/kg) in kidney and liver. Consequently, peak isolation and structure identification of the isolate was not possible. As no matching reference standard was available, the identification was not possible.

(3): Radioactivity that did not contain any discrete peaks.

Remarks:

-The results reported in table B.7.2.1-4 were corrected to 100%. Actual recoveries were 93.5 % in liver and 107.7 % in kidney.

-HPLC and TLC co-chromatography analysis of the kidney and liver extracts with the non-radio labelled reference standards and the radioactive urine isolates confirmed the metabolites as BF 490-1, BF 490-2, BF 490-9.

The total radioactivity in milk, muscle and fat samples was too low to further attempt any metabolites investigation.

-Dialysis of the liver homogenate showed that 48.4% of the TRR was recovered as free radioactivity while the rest of the radioactivity was probably bound to liver proteins or other large macromolecules. No further TLC or HPLC analysis was performed due to the low concentration of the radioactivity in the dialysate.

Combined solvent extractions allowed the solubilisation of most of the radioactivity in kidney (85.5 % of the TRR) and to a lesser extent in liver (only 42.5 % of TRR were extracted). Further 37 % of the total residues recovered in liver were released following both steps of enzymatic hydrolysis (protease digestion) and ammonia extraction.

The part of the radioactivity allocated to identified compounds accounted for 60.4 % of TRR (kidney) and only 27.5 % of TRR (liver). The post extraction solids fraction was not further characterized neither for liver (20.1% of TRR) nor for kidney (14.6 % of TRR).
The metabolite profile seen in the liver and kidney was qualitatively similar to that of urine and also similar to the metabolic profile and levels of metabolites recovered in the previous study (Mayer F., 1994).
The parent Kresoxim-methyl was not recovered in liver and kidney since it was intensively metabolized in the goat and was only detected in extracts of feces and in very small amounts in fat.
The metabolites that were identified in those matrices were BF 490-1, BF 490-2 and BF 490-9 with a predominant amount of the hydroxy metabolite 490M02 (BF 490-2) in kidney (34.1% of the TRR-0.018 mg/kg) and the hydroxy acid metabolite 490M09 (BF 490-9) in liver (16.8% of the TRR- 0.011 mg/kg).
Conclusion:
The main degradation pathway of kresoxim-methyl in lactating goats was depicted as follows:
-Cleavage of the methyl ester bond to form the free acid metabolite BF 490-1,
-Hydroxylation of the phenoxy-methyl group to form BF 490-2,
-Hydroxylation of the aromatic ring to generate the metabolite BF 490-9.

B.7.2.2 Metabolism, distribution and expression of residues in poultry

(^{14}C)-242 009: Distribution, metabolism and excretion following repeated oral administration to the laying hen (Burke A.; 1994)
The metabolism of ^{14}C-BAS 490 F (^{14}C-242 009) in laying hens (Grosshans F.; 1994e).
Guidelines:
EPA/FIFRA, § 171-4
GLP:
Yes
Material and Methods:
Test substances: [Ring B-U-^{14}C]-kresoxim-methyl, [^{13}C]-kresoxim-methyl, unlabelled kresoxim-methyl.
2 Groups of 5 and 10 laying hens received 6 daily doses by oral gavage of the test substance corresponding respectively to about 1 and 19 mg/kg bw/day.
The low dose animals were dosed at 10 mg/kg feed (dry matter) (300 N), the high dose animals were dosed at 180 mg/kg feed (dry matter) (5600N).
The labelling ratios for the 2 groups were the following:
- low dose group: ratio ^{14}C/unlabelled: 1/1
- high dose group: ratio ^{14}C/^{13}C/unlabelled: 1/4/3.
Plasma and blood level profiles were investigated in the low dose group.
Hens were sacrificed 23 (for the low dose group) and 3 (for the high dose group) hours after the last administration.
A balance of the administered dose was established for the hens of the 2 groups. Levels of radioactivity in samples of tissues and excreta were measured by liquid scintillation counting.
Hens of the high dose group were used for quantification, isolation and identification of metabolites. Excreta, eggs and edible tissues were extracted with methanol and subsequently with water. Extractable radioactivity of eggs, muscle and fat was purified by liquid/liquid partition.
Identification of metabolites was carried out in excreta using Mass Spectrometry analysis after fractionation by HPLC systems. The metabolites in eggs and edible tissues were identified by chromatographic comparison of extracts with those from excreta. Spectra of some compounds identified in the rat study were also used for chromatographic comparison.
Findings:
Plasma levels indicated a rapid absorption of the compound.
At the end of the study 88% of the total radioactivity was recovered in both groups.
Residue levels in eggs were stable in the low dose group, while they increased over the study duration from 0.10 to 0.22 mg/kg equiv. in the high dose group.

Table B.7.2.2-1 gives the balance of the administered radioactivity as well as the total residue levels in edible organs and tissues.

Table B.7.2.2-1 Balance of the administered radioactivity and total radioactive residue in edible organs and tissues – Residues expressed as % of TRR and in mg ^{14}C-kresoxim-methyl equiv./kg.

	Low dose group Feeding level: 10 mg/kg feed		High dose group Feeding level: 180 mg/kg feed	
Sample	**TRR (mg/kg)**	**% of total dose**	**TRR (mg/kg)**	**% of total dose**
excreta		82.64		71.55
cage washings		4.88		5.23
eggs	0.007-0.012	0.02	0.086-0.215	0.02
liver	0.082	0.02	6.985	0.14
kidney	0.065	0.01	0.36	0.04
fat	n.d.	-	0.758	<0.01
muscle	n.d.	-	0.204	<0.01
skin	0.009	<0.01	0.677	<0.01
G.I. tract		0.59		10.77
total		88.86		87.75

n.d. = not detected

Extractability of residues with methanol exceeded 70% in all edible tissues and eggs.
The major part of the extractable residues could be identified.

Table B.7.2.2-2 gives an overview of the results of the identification part of the study.
Comparable results were obtained after 21 months of storage.

Table B.7.2.2-2: Investigation of the nature and amount of residues of kresoxim-methyl in excreta and edible tissues of the laying hen (**Feeding level: 19 mg/kg bw/d**) – Results expressed in % of the total radioactive residues.

Sample	**excreta**	**eggs**	**liver**	**muscle**	**skin**	**fat**
TRR (mg/kg)	-	0.086-0.215	6.985	0.204	0.677	0.758
Extractability of residues (%TRR) in methanol and water						
Methanol extracted phase	83.3-87.6	76.0-82.3	75.1-79.4	72.7-81.9	78.3-83.1	88.6-93.0
Water extracted phase	-	-	3.3-5.5	2.4-2.7	3.7-4.2	1.4-1.6
Elucidation of extractable radioactive residues (%TRR) 1. Methanol extract						
Parent Kresoxim-methyl	28.1	8.3	n.d.	2.7	10.7	41.2
490M06	2.6	0.7	0.5	1.4	2.0	1.0

Sample	excreta	eggs	liver	muscle	skin	fat
TRR (mg/kg)	-	0.086-0.215	6.985	0.204	0.677	0.758
490M50/490M52	2.8	4.9	1.3	4.9	n.d.	2.6
490M51/490M66	2.8	15.7	1.0	20.0	4.0	1.9
490M63/490M67	n.d.	2.5	9.2	n.d.	n.d.	n.d.
490M25/490M26	0.3	3.3	n.d.	2.2	1.2	n.d.
490M08 (BF 490-11)/490M11	1.4	n.d.	1.0	1.1	1.2	1.2
490M55/490M65	1.4	n.d.	n.d.	n.d.	0.5	n.d.
490M16	0.1	n.d.	2.4	n.d.	n.d.	n.d.
490M60/490M20 (BF 490-14)	0.6	0.9	1.4	8.6	n.d.	n.d.
490M28	n.d.	n.d.	13.7	1.5	n.d.	n.d.
490M33/490M39	n.d.	4.2	3.0	n.d.	n.d.	n.d.
490M64	n.d.	3.1	n.d.	n.d.	n.d.	n.d.
490M56	0.8	n.d.	n.d.	n.d.	n.d.	3.2
490M02 (BF 490-2)	<0.1	n.d.	n.d.	n.d.	n.d.	n.d.
490M46	8.1	0.2	n.d.	3.9	5.6	4.5
490M57	1.6	n.d.	n.d.	1.6	1.3	0.9
490M14	n.d.	n.d.	2.7	n.d.	n.d.	n.d.
490M31	n.d.	9.7	n.d.	n.d.	n.d.	n.d.
490M09 (BF 490-9)	5.9	0.2	20.1	0.2	4.5	0.3
490M47	2.4	2.3	3.2	1.7	1.9	n.d.
490M05	0.7	0.9	4.5	3.7	2.2	n.d.
490M24	0.2	n.d.	n.d.	n.d.	1.8	1.4
490M15 (BF 490-4)	12.0	n.d.	2.6	2.4	4.1	16.6
490M58	4.0	n.d.	1.1	5.6	10.4	1.7
490M59	1.3	n.d.	0.8	2.1	7.9	0.8
490M01(BF 490-1)	n.d.	4.0	n.d.	n.d.	n.d.	n.d.
490M48 (BF 490-3)	2.1	11.4	n.d.	1.8	5.7	7.7
other characterized (1)	3.7 (21)	10.5 (9)	6.4 (7)	3.4 (4)	13.2 (9)	1.8 (3)

Sample	excreta	eggs	liver	muscle	skin	fat
TRR (mg/kg)	-	0.086-0.215	6.985	0.204	0.677	0.758
Elucidation of extractable radioactive residues (%TRR) 2. Water extract						
identified (1)			2.2 (5)			
characterized (1)			1.3 (3)			
Residual radioactive residues (%TRR)						
	15.0-15.7	16.9-24	17.0-20.1	16.0-24.9	13.1-17.0	5.9-8.1
Elucidation of residual radioactive residues (%TRR)						
Released by pronase (1)		~20 (6)	~15 (44)	~20 (6)	~10	~5

(1): number of peaks
n.d. = not detected

Conclusions:
The metabolic pathway of kresoxim-methyl is presented in Appendix A to this section.
Parent compound was extensively metabolized to a great number of degradation products, but was still present in all tissues except liver.
Several metabolites were not recovered in the rat metabolism, generally reflecting different combinations of the reactions observed in the rat. 2 Metabolites (490M58 and 490M59) present a particular structure and are discussed under the point B.7.3 (Definition of the residue).

B.7.2.3 Metabolism, distribution and expression of residues in pigs

No particular degradation pathway has been observed in goat in comparison to rats. Consequently, a pig metabolism study is not required.

Revised in March 2010

B.7.3 Definition of the residue

B.7.3.1 Definition of the residue in plant products

Plant products:
Metabolism studies were provided on apples and grapes (fruit), spring wheat (cereals) and sugar beet (root and tuber vegetables).
In each crop, the metabolic pathway of Kresoxim-methyl was similar, i.e. the parent Kresoxim-methyl was the predominant compound of the total residues in all the matrices with low levels of recovered acid BF 490-1 and the hydroxyl acid metabolites BF 490-2 and BF 490-9 mainly as glucosides.
Cleavage of the methyl ester bond of the parent molecule generated the free acid BF 490-1 which can be regarded as an intermediate that undergoes hydroxylation at the cresyl (phenoxy) ring or its methyl group resulting in metabolites BF 490-2 and BF 490-9 with a further glucoside conjugation step of these 2 metabolites.

Most of the identified metabolites were also observed in the rat metabolism and may therefore be considered as out of any toxicological relevance as they are covered by toxicological studies.
Two metabolites (490M17 in wheat grain: 0.0005 mg/kg and apple: 0.0057 mg/kg and 490M54 (BF 490-15) in grapes: 0.083 mg/kg) are different from all metabolites identified in the rat.

Metabolite 490M17 occurs in minor amount in wheat and apples. Its postulated structure involves the formation of a supplementary ring structure (lactone). A similar structure was observed in the rat (metabolite 490M20 (BF 490-14)). Metabolite 490M17 is also more polar as its structure is hydroxylated in the methylphenoxy ring which is a pathway of detoxification and excretion.
Metabolite 490M54 (BF 490-15) has a structure similar to metabolite BF 490-9 (identified in the rat) with an hydroxy group in meta position instead of para and is conjugated. In both cases (para- and meta-hydroxylation), the hydroxy-group is far away from the center of reactivity, i.e. the imino-group. The position of the hydroxy-group will have therefore no influence on the toxicological behaviour. In addition, hydroxylation normally leads to less toxic compounds. An Ames test was conducted with 490M54(BF 490-15), showing no mutagenic properties for this metabolite (Engelhardt G., 1996).
In conclusion there is no necessity to include these metabolites in the residue definition as they are considered as sufficiently addressed with regard to their toxicological pertinence.

A global residue definition is proposed for enforcement purposes as the **parent compound only**.
The residue definition for risk assessment is proposed as follows: **Kresoxim-methyl (BAS 490 F) and BF 490-2+BF 490-9, free and conjugated, expressed as parent equivalent.**

Completely validated analytical methods are available to determine the residues of Kresoxim-methyl in plant products in compliance with the residue definition both for enforcement purposes and risk assessment.

B.7.3.2 Definition of the residue in animal products

-The metabolism study in goat indicates an extensive degradation of kresoxim-methyl as observed in the rat metabolism.
The parent compound was recovered only in faeces and in fat (6.6 % of the TRR).
3 major metabolites were identified in goat matrices: the free acid BF 490-1 formed by cleavage of the methyl ester bond of the parent molecule with further hydroxylation either on the side chain of the phenoxy ring (BF 490-2) or on the phenoxy ring (BF 490-9).
A valid indicator of the level of contamination of the animal matrices differs from tissue to tissue. Several metabolites, not present in the rat metabolism were observed: 490 M18 (BF 490-8), 490 M19 and 490 M56 that was recovered only in urine. Their structure suggests that no significantly different reaction occur in comparison with rat.
In the feeding study with cows, the metabolite BF 490-1 appeared to be the major residue for liver, kidney and fat.

-An extensive metabolization of the parent compound is also observed in the laying hens. Several metabolites, not present in the rat metabolism, are also observed. Most of them don't reflect reactions different from those occurring in the rat. Two metabolites identified in laying hens (490M59 and 490M58), however reflect an oxidation of the oxime-N, what is not observed in the rat. A nitronic acid structure is proposed rather then the tautomeric nitro-group, because of the acidity of the adjacent carbon-atom.
Considering the calculated dietary burden for poultry reported in the table B.7.8-1, these metabolites are expected to be recovered at a trace level and should not be regarded as relevant for the assessment of the exposure of consumers.

The residue definition for monitoring is proposed as:
- BF 490-9 for milk, expressed as kresoxim-methyl;
- BF 490-1 for beef liver, kidney, muscle and fat, expressed as kresoxim-methyl;
- kresoxim-methyl for eggs.

The same definition applies for risk assessment.

While the parent compound is liposoluble (log K_{ow}: 3.40 at 25°C), the metabolite BF 490-1 was shown to be non fat soluble (log K_{ow} BF 490-1<3).

The analytical methods for the determination of BF 490-9 in milk (BASF method no.354/1) and BF 490-1 in beef muscle, liver, kidney and fat (BASF method no.354/2) were considered as sufficiently validated and suitable for monitoring purposes – see Vol.3, point B.5.2.2.
The analytical method for the determination of the parent Kresoxim-methyl in hen eggs was considered as valid and suitable for the residue analysis work (Analytical method 369) – see Vol.3, point B.5.2.2.

Toxicological relevance of the metabolites recovered in plants and animals:

The plant metabolites BF 490-1, BF 490-2, BF 490-9 and BF 490 -15 (490 M54) were tested in an acute oral toxicity test in the rat and/or in a bacterial mutagenicity assay (in *S. typhimurium* or *E. coli*). Only the metabolite BF 490-1 was slightly more toxic in the acute oral rat study than the parent compound itself. The LD_{50} of the ♀ was about 1090 mg/kg b.w.. This metabolite was also a major rat metabolite (BF 490-1, accounting for 4-7% of administered dose in excreta). Therefore, the toxicity was covered by existing studies, and the conclusions of the overall assessement remained unchanged. All other metabolites were not harmful by oral uptake.
All investigated metabolites were found not mutagenic in the bacterial assays.
Whereas most of these metabolites were also rat metabolites, the metabolite BF 490-15 (490 M54) was only detected in grapes. However, the latter was structurally very similar to a known rat metabolite (hydroxylated derivative of BF 490-1), more polar and therefore potentially less toxic.
It was concluded that the present metabolites do not pose a particular problem, and are likely to be covered by the toxicological package of Kresoxim-Methyl itself.

B.7.4 Use pattern

Added in March 2010

Table B.7.4-1: Representative use evaluated for kresoxim-methyl (formulation ALLEGRO, BAS 494 04 F)

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Cereals (wheat, barley, rye, triticale)	Northern & Southern Europe	BAS 494 04 F (ALLEGRO)	F	*P. herpotrichoides (Erysiphe graminis), Septoria, spp. Puccinia spp. (Fusarium spp), R. secalis P. teres*	SC	125 g/L* + 125 g/L**	foliar spray (tractor-mounted boom sprayer)	BBCH 25 – 69[1]	2 max	21 days	31.3* – 62.5* + 31.3** – 62.5**	200 – 400	125* + 125**	35	

*Kresoxim-methyl
**Epoxiconazole
[1]: 5 tillers detectable-End of flowering.

Table B.7.4-2: Representative uses of kresoxim-methyl* (formulation CANDIT, BAS 490 02 F)

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Apples, pears	Northern & Southern Europe	BAS 490 02 F (CANDIT)	F	*Venturia inequalis, Podosphaera leucotricha*	WG	500 g/kg*	foliar spray (tractor-mounted air-blast sprayer)	BBCH 53-79 (1)	1 - 4	7 – 10 days	5.6 – 62.5*	200-1800	100 – 125*	35	Rate increases with plant growth: 100 + 100 + 125 + 125
Grapes	Northern & Southern Europe	BAS 490 02 F (CANDIT)	F	*Guignardia bidwellii Phomopsis viticola Pseudopeziza tracheiphila Unicinula necator*	WG	500 g/kg*	foliar spray (tractor-mounted air-blast sprayer or hand-held equipment)	BBCH 19 – 81(2)	1 - 3	8 – 14 days	6.3 – 100*	150-1600	100 – 150*	35	Rate increases with plant growth: 100 + 120 + 150

(1): Bud burst: green leaf tips enclosing flowers visible-Fruit about 90% final size.
(2): 9 or more leaves unfolded-beginning of ripening: berries begin to develop variety-specific colour.

Note: For uses where the column "Remarks" is marked in grey further consideration is necessary.
Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

B.7.5 Identification of critical GAPs

~~For pome fruits, the critical GAP is 6-8 applications at 100 g/ha with a PHI of 35 days.~~
~~For grapes, the critical GAP is 6 applications at 100 g/ha with a PHI of 35 days.~~
~~For cereals, the critical GAP is represented by 2 applications at 125 g/ha.~~

Added in March 2010

See tables B.7.4-1/2: Use pattern

B.7.6 Residues resulting from supervised trials (Annex IIA 6.3; Annex IIIA 8.1)

Added in March 2010:

Analytical methods:

-BASF Method no.445/0: The residues of Kresoxim-methyl (BAS 490 F) were extracted from the tested plant matrices using a mixture of methanol/water/acid. A liquid/liquid partitioning against cyclohexane was used for clean-up.
The final determination of BAS 490 F was performed by LC-MS/MS.
The method was validated at the Limit of quantification of 0.05 mg/kg and was considered as suitable for the determination of the residues of Kresoxim-methyl in all the tested plants.
The initial validation report (Benz A., Mackenroth C., 2001) presented data at a LOQ of 0.05 mg/kg but in the meanwhile, a new validation study was performed (T. Schwarz, T. Class, 2007). The LOQ was lowered and validated at 0.01 mg/kg, with the exception of oilseed rapeseed, for which the original LOQ of 0.05 mg/kg was independently validated (because of significant interferences at lower level in this matrix) (see Vol.3, point B.5.2.1).

-BASF Method no.L0095/01: determined the residues of BF 490-2 and BF 490-9 (plant metabolites of Kresoxim-methyl).
Residues of BF 490-2 and BF 490-9 were extracted from plant material using methanol, the solvent was eliminated and the glycosides of the metabolites were cleaved enzymatically.
The analytes were then partitioned from the acidified aqueous extract into organic solvent and the solvent was exchanged for subsequent LC-MS/MS determination.

The enzymatic cleavage step applied in this method can be regarded as sufficiently efficient.
Reference is made to the interim report on the investigation on the efficacy of the enzymatic cleavage step of BASF Method L0095 (Kampke-Thiel, 2008-BASF DocID 2008/1044557) and reported in Vol.3, point B.5.2.1.
In addition to the ongoing investigations, the efficacy of the enzymatic cleavage was demonstrated in the course of storage stability studies with radioactive labeled sugar conjugates of metabolites BF 490-2 and BF 490-9 (isolated in the course of metabolism studies) in pecan nuts, apples and grapes:
- Jordan & Riley, 1999 (BASF DocID 1999/5006)
- Thornton, 1998 (BASF DocID 1997/5339)
A detailed evaluation of these studies is given in Vol.3, B.7.0.
The **BASF method L0095/1** (adapted BASF method 350/3) is considered to be suitable for the determination of residues of kresoxim-methyl (determined as the acid BF 490-1) and its metabolites BF 490-2 and BF 490-9 (hydroxy-acids, free and glycosilated forms) in plant matrices with high water content (e.g. apple), high acid content (e.g. grape), high fat content (e.g. soya bean) and cereals and other dry crops (e.g. wheat grain). For all matrices tested, a LOQ of 0.01 mg/kg was validated for each of the above-mentioned analytes (see Vol.3, point B.5.2.1).

-BASF Method no. 350/2:
This analytical method is technically identical to BASF Method no.350/1.

-BASF Method no. 350/1:

This analytical method was considered as suitable for the determination of Kresoxim-methyl (BAS 490 F) as well as its metabolites BF 490-2 and BF 490-9 (free and glycosilated forms) in wheat matrices.
The method was validated for the Limit of Quantification of 0.05 mg/kg for each analyte.

-BASF Method no. 351/2:
This method was used for the determination of the residues of Kresoxim-methyl (BAS 490 F) in wheat and apple matrices.
Kresoxim-methyl is extracted of the sample material in methanol 80%. After the addition of KH_2PO_4 an aliquot could be partitioned against iso-octane which will quantitatively extract parent. Following this step, the analyte is separated from matrix compounds by sequential polarity chromatography on a SPE Silica-gel column followed by a SPE C_{18} column. The analyte is detected and quantified by GC on a DB-1701 capillary connected to either a MS-detector at a mass of 206 or an ECD detector.
The method was considered as sufficiently validated for the Limit of Quantification of 0.05 mg/kg.

B.7.6.1 Residues resulting from supervised trials - Pome fruits.

- Determination of the Residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1993 – Doc.ID: 94/11751 (Schultz H.; 1994a).
- Determination of the Residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1994 - Doc.ID: 95/10054 (Schultz H.; 1995).
- Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 - Doc.ID: 95/10082 (Fuchs A.; 1995a).
- Residue behaviour of BAS 490 02 F on pome fruit under field conditions in Germany, France, Spain, Belgium, The Netherlands and Great Britain, 1994 Doc.ID: 95/10418 (Fuchs A.; 1995b).

GLP:
All submitted studies were carried out under GLP conditions.
Material and methods :
Trials are available for the North and the South of EU. The trial designs are the same for both regions: 8 to 12 applications at the rate of 0.1 kg a.s./ha, with 8 to 12 days between applications. Levels of parent compound were determined according to the methods 351/1 or 351/2. Decay curves are given with last sampling 28 to 42 days after last application.
Findings:
* North, apple, 0.1 kg/ha, 8 applic., 35 d PHI: <0.05, <0.05, <0.05, <0.05, 0.05, <0.05, <0.05, <0.05, 0.06, <0.05 (0.11 at 42 d), <0.05
North, apple, 0.1 kg/ha, 8 applic., 28 d PHI: <0.05, <0.05, <0.05, <0.05, 0.05, 0.11,
* South, apple, 0.1 kg/ha, 8 applic., 35 d PHI: <0.05, <0.05, <0.05, <0.05
South, apple, 0.1 kg/ha, 8 applic., 28 d PHI: <0.05, <0.05, <0.05, <0.05
South, apple, 0.1 kg/ha, 12 applic., 28 d PHI: <0.05, <0.05
South, pear, 0.1 kg/ha, 8 applic., 35 d PHI: <0.05, <0.05, <0.05
South, pear, 0.1 kg/ha, 8 applic., 28 d PHI: <0.05
Conclusion :
In the south, 10 trials below the LOD.
In the North 17 trials of which 5 give positive results up to 0.11 mg/kg.
MRL proposal: 0.05 or 0.1 mg/kg.

Added in March 2010:
Design of the residue trials:
One trial (pears) was available for the North of Europe and trials (apples and pears) covered the South of Europe. These were characterized respectively by 4 and 8 spay applications at dose rates of 0.100-0.150 kg a.s./ha with last application occurring at BBCH growth stages 75-86.
The determination of the residues of Kresoxim-methyl (BAS 490 F), BF 490-2 and BF 490-9 was carried out according to the following analytical BASF methods 350/3 for the determination of BAS 490 F (Kresoxim-methyl) and its metabolites BF 490-2 and BF 490-9 (free and glycosilated forms) and 351/2 for the determination of BAS 490 F (Kresoxim-methyl).
Decay curves were provided with last sampling 28 to 42 days after the last application.

Findings:
***North*:**
Pears, 0.1 kg a.s./ha, 4 applic., PHI: 35 days:
BAS 490 F (Kresoxim-methyl): <0.05 mg/kg,
BF 490-2: n.a.
BF 490-9: n.a.
***South*:**
Pears, 0.1 kg a.s./ha, 4 applic., PHI: 21 days:
BAS 490 F (Kresoxim-methyl): <0.05-<0.05 mg/kg,
Metabolite BF 490-2: n.a.-n.a.
Metabolite BF 490-9: n.a.-n.a.
Pears, 0.1 kg a.s./ha, 4 applic., PHI: 35 days:
BAS 490 F (Kresoxim-methyl): <0.05-<0.05 mg/kg,
Metabolite BF 490-2: <0.05-<0.05 mg/kg,
Metabolite BF 490-9: 0.07-<0.05 mg/kg
Apples, 0.15 kg a.s./ha, 8 applic., PHI: 35 days:
BAS 490 F (Kresoxim-methyl): <0.05 mg/kg,
Metabolite BF 490-2: <0.05 mg/kg,
Metabolite BF 490-9: <0.05 mg/kg
Conclusion:
In the North: 1 trial (pears).
In the South: 4 trials (pears) and 1 trial (apples).
The trials provided on pears were performed at a slightly under dosed seasonal rate of 0.4 kg a.s./ha (maximum seasonal rate: 0.45 kg a.s./ha).
The previous residue database could not be taken into account for MRL setting since the trials were conducted with an application rate around 50% higher than the intended one.
Additional residue trials on apples should be provided complying with the critical intended use in order to confirm the no-residue situation of Kresoxim-methyl in pome fruits and to perform a robust dietary intake risk assessment with regard to the residue levels of BF 490-2 and BF 490-9.

Provisional MRL proposal on apples, pears: 0.05* mg/kg.

B.7.6.2 Residues resulting from supervised trials - Grapes

- Study on the residue behaviour of kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 - Doc.ID: 96/10698 (Fuchs A.; 1996a).
- Study on the residue behaviour of kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France and Spain, 1995- Doc.ID: 96/10830 (Fuchs A.; 1996).
- Study on the residue behaviour of kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France, Germany and Spain, 1996 Doc.ID: 96/10890 (Meumann H.; 1996)

GLP:
All submitted studies were carried out under GLP conditions.
Material and methods:
The trials are summarized according to the usual format in the appendix to this section.
Trials are available for the North and the South of EU. In both regions, trials were made following 6 spray applications at the rate of 0.15 kg/ha. Levels of parent compound and of metabolites 490M2 and 490M9 were determined according to the method 350/3. With this method, conjugates of metabolites 490M2 and 490M9 are determined together with their free forms. Decay curves are given with last sampling 55-56 days after last application.
Findings:
* North, grapes, 0.15 kg/ha, 6 applic., 35 days:
parent: 0.25, 0.73, 0.44, 0.17, 0.20, 0.15, 0.09,0.35 mg/kg
metabolite 490M2: 0.15, 0.08, 0.11, 0.06, 0.06, 0.05, <0.05
metabolite 490M9: 0.07, 0.08, 0.05, <0.05, <0.05, 0.05, <0.05
* South, grapes, 0.15 kg/ha, 6 applic., 35 days:

parent: 0.07, 0.09, 0.18, 0.36, 0.21, <0.05, <0.05, 0.06, 0.23
metabolite 490M2: 0.27, 0.22, 0.07, 0.12, 0.28, 0.05, 0.10, 0.06, 0.06
metabolite 490M9: 0.09, 0.08, 0.06, 0.06, 0.17, <0.05, <0.05, <0.05, <0.05
Conclusions :
In the North: 7 trials - 3 x mean: 0.87 - Rber: 0.88
In the South: 9 trials - 3 x mean: 0.38 - Rber: 0.44
In the South, residues of metabolite 490M2 are at the same level as the parent compound.
MRL proposal: 0.5 mg/kg, considering that trials were conducted with an application rate 50% higher than the intended dose.

Added in March 2010

Design of the residue trials:
Trials were conducted to cover both Northern and Southern EU and were characterized by a total of 3 spray applications at a dose rate of 0.15 kg a.s./ha, the last application occurring at BBCH growth stages 75-85.
The residues of the parent (BAS 490 F) and its metabolites BF 490-2 and BF 490-9 were determined according to the following BASF analytical methods: method 445/0 for the determination of Kresoxim-methyl (BAS 490-F) and the method L0095/01 determining the residues of Kresoxim-methyl as the acid BF 490-1 and its 2 metabolites BF 490-2 and BF 490-9 (free and glycosilated forms)
The level of total BASF 490 residues was calculated by summing the residues of BAS 490 F and the metabolites BF 490-2 and BF 490-9 since the conversion factors were negligible.
Decay curves were given with last sampling 42 days after the last treatment.
Findings:
*** North, grapes, 0.15 kg/ha, 3 applic., PHI: 35 days:**
BAS 490 F (Kresoxim-methyl): 0.04-0.18 (PHI: 42 d)-0.27-0.18-0.15 (PHI: 43 d)-0.09 (PHI: 43 d)-0.11 (PHI: 42 d)-0.05 mg/kg
metabolite BF 490-2: 0.03-0.04 (PHI: 42 d)-0.03-0.05-0.04 (PHI: 43 d)- 0.02 (PHI: 43 d)-0.04 (PHI: 42 d)-0.03 mg/kg
metabolite BF 490-9: 0.02-0.03 (PHI: 42 d)-0.02-0.05-0.03 (PHI: 43 d)-0.02 (PHI: 43 d)-0.02 (PHI: 42 d)-0.02 mg/kg
*** South, grapes, 0.15 kg/ha, 3 applic., PHI: 35 days:**
BAS 490 F (Kresoxim-methyl): 0.33 (PHI: 42d)-0.02-0.06-0.04-0.19-0.02 (PHI: 41d)-0.06-0.03 mg/kg
metabolite BF 490-2: 0.03 (PHI: 42d)-0.01-0.05-<0.01-0.03-0.02 (PHI: 41d)-0.03-<0.01 mg/kg
metabolite BF 490-9: 0.03 (PHI: 42d)-0.01-0.02-0.01-0.02-0.01 (PHI: 41d)-0.04-<0.01 mg/kg
Conclusion:
-North: 8 trials – HR: 0.27 mg/kg; Rber: 0.36 mg/kg; Rmax: 0.37 mg/kg
-South: 8 trials - HR: 0.33 mg/kg; Rber: 0.315 mg/kg; Rmax: 0.44 mg/kg

MRL proposal on grapes: 0.5 mg/kg

B.7.6.3 Residues resulting from supervised trials - Cereals

- Residue behaviour of BAS 490 04 F on Cereals under field Conditions in France, 1992 –Doc.ID: 94/11003 (Becker F.; 1994).
- Study on the residue behaviour of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium, France and Germany, 1993- Doc.ID: 94/11005 (Beck J.; 1994a).
- Study on the residue behaviour of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium and Germany, 1994 - Doc.ID: 94/11004 (Beck J.; 1994b).
- Determination of the Residues of LAB 242 009 in Spring Wheat following Treatment with BAS 492 01 F under Field Conditions in Germany 1993 - Doc.ID: 95/10191 (Schultz H.;1994b).
- Determination of the Residues of LAB 242 009 in Spring Barley following Treatment with BAS 492 01 F under Field Conditions in Germany 1993 - Doc.ID: 94/11158 (Schultz H.;1994c).
-Study on the residue behaviour of BAS 490 02 F in cereals under field conditions in the Netherlands, Belgium, France, Great Britain and Germany, 1994 -Doc.ID: 95/10327 (Beck J.; 1995).

- Study on the Residue Behaviour of Kresoxim-methyl, Epoxiconazole and Fenpropimorph in Cereals after treatment with BAS 493 02 F under Field Conditions in France and Germany, 1995-Doc. ID: 96/10113 (Beck J.; 1996)

GLP:
All submitted studies were carried out under GLP conditions.
Material and methods :
The trials are summarized according to the usual format in the appendix to this section.
In total, 44 trials covering both the North and the South of EU are available for spring and winter barley, spring and winter wheat and rye. The trial designs are the same for both regions: 2 applications of 0.1 to 0.15 kg a.s./ha at stages 37-39 and 61-69. In addition, some trials were made in exaggerated conditions: 4 applications of the normal dose, or 2 applications of 3 times the normal dose.
Samples of green plants at day 0 as well as samples of ears, haulm, straw and grains at different PHIs up to normal harvest time were analysed for parent compound and metabolites 490M2 and 490M9.
Findings :
In all trials the residues of kresoxim-methyl in grain were below the LOD (0.05*).
In straw the residues of the parent compound were generally below 1 mg/kg, except in spring wheat where the mean residue on straw was 1.60 mg/kg (highest value: 3.59 mg/kg). In average, levels of metabolites 490M2 and 490M9 accounted together for about 60% of the level of the parent compound.
Conclusions :
MRL proposal for grains : 0.05*

Added in March 2010

Remark: The residue trials performed on spring/winter barley and wheat and on winter rye covering Northern Europe were already evaluated in the frame of the first Annex I listing.
Nevertheless, for sake of transparency, the complete residue values are presented here below.

Design of the residue trials:
In the frame of the re-assessment for Annex I renewal, supervised residue trials covering only Southern Europe were provided for spring wheat and barley, one trial on winter rye (NE) and complied with the critical GAP.
The trials were characterized by 2 foliar applications at a dose rate of 0.125 kg a.s./ha. The last application occurred at the BBCH growth stage 69-71.
Samples of whole plant at day 0 and samples of ears, haulm, grain and straw at different PHIs up to maturity were analysed for the parent compound as well as for the metabolites BF 490-2 and BF 490-9.
Findings:
***Spring/winter Wheat:**

***** North, 0.125 kg/ha, 2 applic., (BBCH 69-PHI: 35 days):***
***Residue values in grain*:**
BAS 490 F (Kresoxim-methyl): <0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05 mg/kg
metabolite BF 490-2:13 x na
metabolite BF 490-9:13 x na
***Residue values in straw*:**
BAS 490 F (Kresoxim-methyl): 1.46-0.36-0.58-0.59-0.74-2.42-1.51-0.65-0.24-0.06-0.09-<0.05-<0.05 mg/kg
metabolite BF 490-2: 0.15-0.16-0.14-0.14-0.06-<0.05-0.65-0.10-0.06-0.05-<0.05-0.07-<0.05 mg/kg
metabolite BF 490-9: 0.21-0.30-0.23-0.27-0.13-0.09-0.44-0.19-<0.05-0.07-<0.05-<0.05-<0.05 mg/kg

**** *South, 0.125 kg/ha, 2 applic., (BBCH 69-PHI: 35 days):***

***Residue values in grain*:**
BAS 490 F (Kresoxim-methyl): 0.02-0.01-0.01-0.06-0.02-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.05 mg/kg
metabolite BF 490-2: <0.01-<0.01-<0.01-0.01-<0.01-<0.01-<0.01-<0.01-na-na-na-<0.01-<0.01-<0.01 mg/kg
metabolite BF 490-9: <0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-na-na-na-<0.01-<0.01-<0.01mg/kg

***Residue values in straw*:**
BAS 490 F (Kresoxim-methyl): 0.45-0.11-0.10-0.21-0.52-0.10-0.25-0.38-<0.01-0.22-1.5-0.04-0.07-0.51-0.48 mg/kg
metabolite BF 490-2:0.01-0.03-0.03-0.05-0.01-0.03-0.06-na-na-na-0.04-<0.01-0.01-0.04-<0.05 mg/kg
metabolite BF 490-9:0.04-0.04-<0.01-0.05-0.05-0.03-0.05-na-na-na-0.05-<0.01-<0.01-0.04-0.09 mg/kg

***Spring/winter barley:**

***** North, 0.125 kg/ha, 2 applic., (BBCH 69-PHI: 35 days):***
Residue values in grain:
BAS 490 F (Kresoxim-methyl): <0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05-<0.05 mg/kg
metabolite BF 490-2: 16 x na
metabolite BF 490-9: 16 x na
Residue values in straw:
BAS 490 F (Kresoxim-methyl): 0.52-0.26-0.61-0.55-0.66-0.15-<0.05-0.36-0.13-<0.05-0.07-0.63-<0.05-0.75-0.28-<0.05 mg/kg
metabolite BF 490-2: 0.14-0.12-0.16-0.09-0.18-0.11-<0.05-0.12-0.08-<0.05-<0.05-0.10-<0.05-0.17-<0.05-<0.05 mg/kg
metabolite BF 490-9: 0.23-0.10-<0.05-0.10-0.30-0.10-0.06-0.07-0.12-<0.05-<0.05-0.08-0.06-0.09-0.08-<0.05 mg/kg

**** *South, 0.125 kg/ha, 2 applic., (BBCH 69-PHI: 35 days):***

Residue values in grain:
BAS 490 F (Kresoxim-methyl): 0.03-0.01-0.01-0.03-0.02-0.08-0.02-0.01-0.01-0.01-0.01-<0.01-0.02-0.04-0.01-0.03-0.02-0.01-0.05 mg/kg
metabolite BF 490-2:<0.01-<0.01-<0.01-<0.01-<0.01-0.01-<0.01- na-na-na-na-na-na-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01 mg/kg
metabolite BF 490-9:<0.01-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01- na-na-na-na-na-na-<0.01-<0.01-<0.01-<0.01-<0.01-<0.01 mg/kg
Residue values in straw:
BAS 490 F (Kresoxim-methyl): 1.24-0.57-0.09-0.89-0.36-0.43-0.09-0.15-0.44-0.04-0.22-0.13-1.06-0.41-0.87-0.17-0.43-0.32-2.14 mg/kg
metabolite BF 490-2:0.03-0.03-0.02-0.04-0.03-0.07-0.01- na-na-na-na-na-na-0.15-0.03-0.04-0.05-0.03-0.14 mg/kg
metabolite BF 490-9:0.06-<0.01-0.01-0.06-0.07-0.03-0.01- na-na-na-na-na-na-0.11-0.02-0.05-0.05-<0.01-0.20 mg/kg

***Winter rye:**

***** North, 0.125 kg/ha, 2 applic., (BBCH 69-PHI: 35 days):***
Residue values in grain:
BAS 490 F (Kresoxim-methyl): <0.05 mg/kg
metabolite BF 490-2:na
metabolite BF 490-9:na
Residue values in straw:
BAS 490 F (Kresoxim-methyl): <0.05 mg/kg
metabolite BF 490-2: 0.06 mg/kg
metabolite BF 490-9: 0.12 mg/kg

Table B.7.6.3-1: Highest and median residues values for cereal grain and straw treated with Kresoxim-methyl according to the cGAP and in accordance with the proposed residue definition for enforcement purposes and for risk assessment in plants (Residues are expressed in mg/kg).

Spring/winter wheat					
North EU					
	Grain			**Straw**	
	HR	**STMR**	**Rmax/Rber**	**HR**	**STMR**
BAS 490 F	<0.05	<0.05	-	2.42	0.58
Sum of BAS 490-F and met. BF 490-2+BF490-9, free and conjugated expressed as parent[1]	Np[2]	np[2]	-	3.51	0.82
South EU					
BAS 490 F	0.06	0.01	-	1.5	0.215
Sum of BAS 490-F and met. BF 490-2+BF490-9, free and conjugated expressed as parent[1]	0.08	0.03	-	2.4	0.31
Spring/winter barley					
North EU					
	Grain			**Straw**	
	HR	**STMR**	**Rmax/Rber**	**HR**	**STMR**
BAS 490 F	<0.05	<0.05	-	0.75	0.27
Sum of BAS 490-F and met. BF 490-2+BF490-9, free and conjugated expressed as parent[1]	Np[2]	np[2]	-	1.14	0.445
South EU					
BAS 490 F	0.08	0.02	-	2.4	0.41
Sum of BAS 490-F and met. BF 490-2+BF490-9, free and conjugated expressed as parent[1]	0.1	0.04	-	2.48	0.53

[1]**:** The residue definition for risk assessment in plants was established as follows: Kresoxim-methyl (BAS 490 F) and BF 490-2+BF 490-9, free and conjugated, expressed as parent equivalent.
The level of total BASF 490 residues was calculated by summing the residues of BAS 490 F and the metabolites BF 490-2 and BF 490-9 since the conversion factors were negligible.
[2]: The calculation was not performed since the residue levels of respective metabolites BF 490-2 and BF 490-9 were not determined.
The levels of BF 490-2 and BF 490-9 had not been measured in these EU-N trials because the measured levels of the parent were below the LOQ of 0.05 mg/kg and based on the wheat metabolism study (B.7.1.2), the level of these metabolites is expected to be below the level of the parent compound in cereal grain.

MRL proposal on cereal grain (barley, wheat, rye, triticale): 0.1 mg/kg (according to extrapolation Table 4 of the current EU guidance document SANCO 7525/VI/95 rev.8).

B.7.7 Effects of industrial processing and/or household preparation on the residue (Annex IIA 6.5; Annex IIIA 8.4)

B.7.7.1 Effects on the nature of the residues

Added in March 2010

-Hydrolysis of BAS 490 F at 90°C, 100°C and 120°C (Hassink J., 2008c)
Guidelines:
Council Directive 91/414/EEC
EC document 7035/VI/95 rev.5

OECD Draft Test Guideline 507-Nature of the Residues in Processed Commodities – High Temperature hydrolysis

GLP:

Yes.

Material and methods:

Test substances: (Benzyl-ring-U-^{14}C) BAS 490 F (Kresoxim-methyl) – Radiochemical purity: 99.2%

Unlabelled reference standards: Kresoxim-methyl (BAS 490 F), BF 490-1, BF 490-2

Experimental design:

The test item was suspended in aqueous buffer solutions of different pH-values.

Labelled stock solutions:

About 5 mg of the labelled test item was brought to volume with 5 mL toluol, which results in a concentration for the test item solution of 1.1729 mg/mL.

The radiochemical purity of the labelled test item dissolved in acetonitrile was checked before the start of the experiment using HPLC-analysis.

Buffer solutions:

All buffer solutions were prepared with commercially available buffers.

Application solutions:

-pH 4 and 90°C – pasteurisation:

A determined volume of the stock solution was given in a flask and the solvent toluol was evaporated and the residue was dissolved in acetonitrile. 10 mL buffer solution pH 4 was added and the concentration of the test substance was determined by Liquid Scintillation Counting (LSC) before and after pasteurisation.

The test solutions were treated under reflux at 90°C for 20 min.

The pH value remained constant throughout the entire test.

-pH 5 and 100°C – baking, brewing, boiling:

A similar procedure was followed as for the pasteurisation with buffer solution pH 5.

The test solutions were treated under reflux at 100°C for 60 min.

The pH value remained constant throughout the entire test.

-pH 6 and 120°C – Sterilisation:

A similar procedure was followed as for the pasteurisation with buffer solution pH 6.

Sterilisation of the samples was performed at about 120°C/20 min.

The pH value remained constant throughout the entire test.

The samples were taken before starting the test and at the end of the test for LSC analysis of the solution.

Additionally, samples for HPLC analysis were taken before and at the end of the test for the purity check.

Analytical procedure:

The level of radioactivity in the samples was determined by Liquid Scintillation Counting followed by HPLC analysis by co-chromatography with reference standards for identification of metabolites in the test solutions.

Findings:

Table B.7.7.1-1: Recovery of the total applied radioactivity in samples before and after the test (Recovered residues expressed as µg/mL and (% TAR)[1]

Test	**Pasteurisation (pH 4, 90°C, 20 min.)**	**Baking, brewing, boiling (pH 5, 100°C, 60 min.)**	**Sterilisation (pH 6, 120°C, 20 min.)**
Before test[2]	0.104 µg/mL (100.0% TAR)	0.082 µg/mL (100.0% TAR)	0.103 µg/mL (100.0% TAR)
After test	0.103 µg/mL (99.2% TAR)	0.082 µg/mL (99.9% TAR)	0.102 µg/mL (98.9% TAR)

[1]:TAR: Total applied radioactivity
[2]:Actual concentration determined in the application solutions by LSC before each test.

Table B.7.7.1-2: Identification of the total applied radioactivity in samples before and after the tests (Residues expressed in % of the total applied radioactivity)

Test	BF 490-1	BF 490-2	BAS 490 F
Pasteurisation (pH 4, 90°C, 20 min.)			
Before test	n.d.	n.d.	100.0
After test	n.d.	n.d.	99.2
Baking, brewing, boiling (pH 5, 100°C, 60 min.)			
Before test	n.d.	3.2	96.8
After test	7.9	2.4	89.6
Sterilisation (pH 6, 120°C, 20 min.)			
Before test	n.d.	n.d.	100.0
After test	70.8	4.6	23.5

Table B.7.7.1-1 showed that no loss of radioactivity occurred after each test (98.9 to 99.9 % of the total applied radioactivity).
The results from the hydrolysis study showed that Kresoxim-methyl was only stable under the processing conditions of pasteurization. At higher temperature conditions and pH 5 (simulated processing conditions of baking, brewing and boiling) or pH 6 (simulated processing conditions of sterilization) the hydrolytic degradation of Kresoxim-methyl resulted in degradation to metabolites BF 490-1 and BF 490-2. The major degradation product formed at pH 5 and 6, accounting for 8-71% of the recovered radioactivity, was identified as BF 490-1. BF 490-2 was a minor degradation product, mostly present at pH 6 at a level of 4.6% of the TRR.
Conclusion:
Kresoxim-methyl (BAS 490 F) was shown to be stable during the simulation of pasteurisation and baking, brewing and boiling processes.
During the simulation of the sterilisation processing, the parent compound degraded significantly with the formation of mainly the acid metabolite BF 490-1.
The applicant proposed a different residue definition for monitoring for apple and grapes processed commodities based on the following rationale: In the course of the processing studies in apples and grapes, the applied analytical method detected all residues of BAS 490 F (kresoxim-methyl) and BF 490-1 simultaneously as the acid BF 490-1. Consequently, a differentiation between both components is not possible, as only BF 490-1 was determined. In case of a parent only residue definition for monitoring, it is very likely, that less than 25% of the Kresoxim-methyl residue in fruit juices is detected. For this reason, the following residue definition is recommended for processed commodities:
Kresoxim-methyl (BAS 490 F) and BF 490-1, expressed as parent equivalent.

However, RMS considers that the parent Kresoxim-methyl remains a valid indicator of the total radioactive residues in processed commodities and the residue definition for monitoring and risk assessment purposes in the processed commodities is proposed to be the same as in the raw agricultural commodities (see point B.7.3.1).

B.7.7.2 Effects on the level of residues

Processing studies were carried out for pome fruits and grapes.
These studies are summarized according to the usual format in the appendix to this section.

B.7.7.2.1 Effects on the level of residues - Pome fruits

-Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 (Fuchs A.; 1995a)

Three processing trials were realised on a kitchen production scale. Apple juice and apple sauce were produced after washing of fruits.

Raw apples contained residues of kresoxim-methyl ranging from 0.08 to 0.19 mg/kg before processing. Washing had no clear influence on the residue level. Residues in juice and sauce were below the LOD (0.05*) in each case, and were recovered in wet pomace.

Revised in March 2010:
Guidelines:
BBA –Richtlinie Teil IV, 3-3 (Jan.1990)
Evaluation of Residue Behaviour – General Guideline for Planning, Design and Performance of Residue Trials.
GLP:
Yes.
Material and methods:
Test substance: Kresoxim-methyl-Former LAB 242 009 (BAS 490 F)
Experimental design:
The test substance was applied 8 times , sprayed at 10 day interval at application rates ranging between 0.084 and 0.112 kg a.s./ha.
The apple samples were collected just after the last application as well as 6, 14, 21 and 28 days later.
For processing of apples to sauce and juice, samples taken 14 days after last application were used.
Apple juice and sauce were produced from washed apples.
The time interval of storage between the last application and the analysis accounted for approximately 9 months.
Analytical procedure:
The determination of the residues of Kresoxim-methyl was performed using BASF method no.351/2 with a Limit of Quantification of 0.05 mg/kg in raw apples and processed apple juice and sauce.
Findings:
Table B.7.7.2.1-1: Recovered residue levels of Kresoxim-methyl in raw apples, washed apple, apple juice, wet pomace and apple sauce and derived Processing Factors (PF)- 14 DALA (mg/kg)

Trial	Raw Apple	Washed apple		Apple juice		Wet pomace		Apple sauce	
			PF		PF		PF		PF
DU1/12/93	0.16	0.19	1.18	<0.05	0.26	<0.05	0.26	<0.05	0.26
DU2/52/93	0.19	0.07	0.36	<0.05	0.71	0.09	1.28	<0.05	0.71
DU3/36/93	0.08	0.16	2.0	<0.05	0.31	0.17	1.06	<0.05	0.31

Conclusion:
After washing, one sample showed a decrease of the residue level while in the 2 other trials, a tendency of residue level increase was observed. The database was too small to draw any reliable conclusion on the actual effect of washing on the residue behaviour in apple.
A similar situation occurred in wet pomace. In 2 residue trials, a slight concentration of the residues as expected occurred while in the third trial no residues of Kresoxim-methyl were recovered.
No residue above the Limit of Quantification of the analytical method was recovered in apple juice and sauce.

Added in March 2010:

-The magnitude of Kresoxim-methyl residues in apple processed fractions – 30 Day PHI program ((Wofford J.T., 1998)
Guidelines:
Residue Chemistry Test Guidelines Subdivision O, 171-4(1) OPPTS 860.1520
Magnitude of the Residue – Processed Food/Feed
GLP:
Yes.
Material and methods:
Test substance: Kresoxim-methyl (BAS 490 F)
Experimental design: Apple trees at a site in Washington (US) received 4 foliar spray applications of the test substance at 7 day intervals.
One plot was treated at the dose rate of 0.224 kg a.s./ha and the 2 other plots were treated at an exaggerated dose rate of 0.672 kg a.s./ha and 1.12 kg a.s./ha, respectively.

Whole apples were collected at maturity (30 DALA) and were processed to simulate industrial practices as closely as possible in washed apples, wet pomace and fresh juice.
Analytical procedure:
Whole apples (RAC), wet pomace and juice were analysed for the determination of the residues of BAS 490 F as its acid form BF 490-1, BF 490-2 and BF 490-9 according to BASF method number 350/3-US (Limit of quantification:0.05 mg/kg for each analyte).
The storage interval (<-10°C) between harvest and analysis of the apple samples and between the production of the processed fractions and final analysis was 3.5 months.
Findings:
Table B.7.7.2.1-2: Recovered residue levels of BAS 490 F (Kresoxim-methyl), BF 490-2 and BF 490-9 in whole apple, apple juice and wet pomace (mg/kg) – Samples from the plot treated at a rate of 1.12 kg a.s./ha

Matrix	**BAS 490 F (mg/kg)**	**BF 490-2 (mg/kg)**	**BF 490-9 (mg/kg)**	**Processing factors**		
				BAS 490 F (mg/kg)	**BF 490-2 (mg/kg)**	**BF 490-9 (mg/kg)**
Whole washed apple	0.82	<0.05	<0.05	NA	NA	NA
Apple juice	0.08	<0.05	<0.05	<1	NA	NA
Wet pomace	2.31	<0.05	<0.05	2.8	NA	NA
NA: Not applicable						

Conclusion:
Apple juice and wet pomace were produced from washed apples. The residue levels on raw apples were not provided and no conclusion can be drawn on the actual effect of washing on the residue level.
Kresoxim-methyl did not concentrate in juice.
No metabolite BF 490-2 and BF 490-9 were detected above the LOQ of the method (0.05 mg/kg) in any whole washed apple, apple juice and wet pomace.

B.7.7.2.2 Effects on the level of residues - Grapes

Study on the residue behaviour of kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 (Fuchs A.; 1996a).

Four processing trials for the production of wine were realised according to the commercial practice.
In wine, residues of parent compound were always below the limit of determination (0.05*). In one trial, measurable levels of metabolites 490M2 and 490 M9 were observed in wine (respectively 0.11 and 0.05 mg/kg).
Residues of parent compound and of metabolites 490M02 (BF 490-2) and 490M09 (BF 490-9) were mainly recovered in wet pomace. The concentration factor between grapes and wet pomace is about 2 for kresoxim-methyl and metabolite 490M09 (BF 490-9) and 3 for the metabolite 490M02 (BF 490-2). In average, levels of metabolites 490M02 (BF 490-2) and 490M09 (BF 490-9) accounted together for about 50% of the level of the parent compound in the wet pomace.

Revised in March 2010:

Material and methods:
Experimental design:
The test substance BAS 490 F was applied 6 times in spray intervals of 9-15 days at an application rate of 0.150 kg a.s./ha.
Grape samples were collected just after the last application and 34, 42, 49 and 56 days later.
The fruit samples from the 34 DALA were used for processing.
Grape samples were processed into must, rosé/white/red wine and pomace, wet.
Analytical procedure:
The samples were analysed with BASF method no.350/3 for the determination of the parent Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 with a Limit of Quantification of 0.05 mg/kg for each analyte.
Findings:

Table B.7.7.2.2-1: Residue levels of BAS 490 F (Kresoxim-methyl), BF 490-2 and BF 490-9 in grapes and its processed commodities (mg/kg)

Matrix	DALA[1]	BAS 490 F (mg/kg)	BF 490-2 (mg/kg)	BF 490-9 (mg/kg)	Processing factor[4]
Trial DU2/03/95					
					BAS 490 F
Grapes, white	0	0.50	0.11	0.07	NA
Grapes	34	0.25	0.15	0.07	NA
Must, cold[2]	34	<0.05	0.05	<0.05	0.32
Must, heated[3]	34	<0.05	<0.05	<0.05	0.32
Pomace, wet	34	0.57	0.42	0.19	2.51
White wine	34	<0.05	<0.05	<0.05	0.32
White wine	34	<0.05	<0.05	<0.05	0.32
Fruit	42	0.35	0.16	0.09	NA
Fruit	49	0.19	0.15	0.07	NA
Fruit	56	0.16	0.15	0.07	NA
Trial DU2/04/95					
Grapes, red	0	0.64	0.10	0.06	NA
Grapes	35	0.73	0.08	0.08	NA
Must, cold[2]	35	0.19	<0.05	<0.05	0.32
Must, heated[3]	35	0.06	0.10	0.06	0.24
Pomace, wet	35	1.40	0.33	0.18	2.14
Wine rosé	35	<0.05	0.05	<0.05	0.16
Wine red	35	<0.05	0.11	0.05	0.23
Fruit	42	0.40	0.15	0.10	NA
Fruit	49	0.93	0.15	0.10	NA
Fruit	56	0.31	0.10	0.07	NA
Trial DU3/01/95					
Grapes, white	0	0.63	0.11	0.05	NA
Grapes	35	0.44	0.11	0.05	NA
Must, cold[2]	35	0.08	<0.05	<0.05	0.3
Must, heated[3]	35	0.07	<0.05	<0.05	0.28
Pomace, wet	35	0.38	0.21	0.08	1.11
White wine	35	<0.05	<0.05	<0.05	0.25
White wine	35	<0.05	<0.05	<0.05	0.25
Fruit	41	0.16	0.07	<0.05	NA
Fruit	49	0.18	0.08	<0.05	NA
Fruit	56	0.33	0.09	<0.05	NA
Trial DU3/02/95					
Grapes	0	0.39	0.07	<0.05	NA
Grapes	35	0.17	0.06	<0.05	NA
Must, cold[2]	35	0.09	0.06	<0.05	0.71
Must, heated[3]	35	<0.05	0.07	<0.05	0.6
Pomace, wet	35	0.52	0.11	<0.05	2.42
Wine rosé	35	<0.05	<0.05	<0.05	0.53
Wine red	35	<0.05	<0.05	<0.05	0.53
Fruit	41	0.14	0.06	<0.05	NA
Fruit	49	0.20	0.05	<0.05	NA
Fruit	56	0.23	0.06	<0.05	NA

[1]: Days after last application
[2]: Shortly after pressing
[3]: after short heating up
[4]: The processing factors were calculated for the sum of Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 in compliance with the residue definition for risk assessment in plant products.

Conclusion:
No residues above the LoQ (0.05 mg/kg) were recovered in wine and no increase of the residue level in must was observed.
A concentration of the residues of both the parent Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 was observed in wet pomace.

B.7.8 Livestock feeding studies (Annex IIA 6.4; Annex IIIA 8.3)

~~Intake calculations for livestock (according to appendix G of the "Guidelines for the establishment of Community Maximum Residue Levels (MRLs) of Plant Protection Products in Food and Feedingstuffs of Plant and Animal Origin") are presented herebelow~~

~~Table B.7.8-1 : Intake calculations for dairy cattle (maximum daily intake of dry matter: 20 kg for 550 kg body weight).~~

~~Material~~	~~% of total DM/day~~	~~intake of DM from material (kg/animal/d)~~	~~% dry matter in material~~	~~intake of material (kg/animal/d)~~	~~residue in material (mg/kg)~~	~~residue intake (mg/animal/d)~~
~~grape wet pomace~~	~~10~~	~~2~~	~~25 (1)~~	~~8~~	~~1 (2)~~	~~8~~
~~cereal grains~~	~~40~~	~~8~~	~~86~~	~~9.3~~	~~0.05~~	~~0.5~~
~~Cereal straw~~	~~20~~	~~4~~	~~86~~	~~4.7~~	~~4 (3)~~	~~19~~
~~Total~~						~~27.5~~

~~(1): estimation~~
~~(2): residue in wet pomace is calculated for a MRL in grapes of 0.5 mg/kg with a concentration factor of 2. It can be considered that the presence of residues of metabolites 490M2 and 490M9 is covered.~~
~~(3): maximum value found in straw of spring wheat for the sum of parent and of metabolites 490M2 and 490M9: 3.90 mg/kg~~

~~The potential intake of residues of kresoxim-methyl and its metabolites 490M2 and 490M9 by dairy cattle is 0.05 mg/kg body weight.~~

Table B.7.8.2 : Intake calculations for beef cattle (maximum intake of dry matter: 15 kg for 350 kg body weight).

Material	% of total DM/day	intake of DM from material (kg/animal/d)	% dry matter in material	intake of material (kg/animal/d)	residue in material (mg/kg)	residue intake (mg/animal/d)
grape wet pomace	30	4.5	25 (1)	18	1 (2)	18
cereal grains	20	3	86	3.5	0.05	0.2
cereal straw	50	7.5	86	8.7	4 (3)	34.8
Total						53

(1): estimation
(2): residue in wet pomace is calculated for a MRL in grapes of 0.5 mg/kg with a concentration factor of 2. It can be considered that the presence of residues of metabolites 490M2 and 490M9 is covered.
(3): maximum value found in straw of spring wheat for the sum of parent and of metabolites 490M2 and 490M9: 3.90 mg/kg

The potential intake of residues of kresoxim-methyl and its metabolites 490M2 and 490M9 by beef cattle is 0.15 mg/kg body weight.

Table B.7.8.3 : Intake calculations for pig (maximum intake of dry matter: 3 kg for 75 kg body weight).

Material	% of total DM/day	intake of DM from material (kg/animal/d)	% dry matter in material	intake of material (kg/animal/d)	residue in material (mg/kg)	residue intake (mg/animal/d)
cereal grains	80	2.4	86	2.8	0.05	0.14
Total						0.14

The potential intake of residues of kresoxim-methyl and its metabolites 490M2 and 490M9 by pig can be considered as negligible (0.002 mg/kg body weight).

~~Table B.7.8.4 : Intake calculations for chicken (maximum intake of dry matter: 0.12 kg for 1.9 kg body weight).~~

~~Material~~	~~% of total DM/day~~	~~intake of DM from material (kg/animal/d)~~	~~% dry matter in material~~	~~intake of material (kg/animal/d)~~	~~residue in material (mg/kg)~~	~~residue intake (mg/animal/d)~~
~~cereal grains~~	~~70~~	~~0.084~~	~~86~~	~~0.098~~	~~0.05~~	~~0.005~~
~~Total~~						~~0.005~~

~~The potential intake of residues of kresoxim-methyl and its metabolites 490M2 and 490M9 by chicken can be considered as negligible (0.003 mg/kg body weight).~~

Added in March 2010

Livestock can be exposed to significant residues of Kresoxim-methyl via treated feed items, i.e. cereal straw and grain and apple pomace.

Grape pomace is not considered relevant for the calculation of the dietary burden.

As relevant intake, the residues of the parent Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9, both free and conjugated were used.

B.7.8-1: Maximum dietary burden for livestock animals (Residues of Kresoxim-methyl and BF 490-2 +BF 490-9, free and conjugated expressed as parent equivalent)

Crop/Commodity	% dry matter	Residue mg/kg (STMR or HR)	Chicken					Dairy Cattle					Beef Cattle					Pig				
			1,9 kg bw			0,12 kg MS		550 kg bw			20 kg MS		350 kg bw			15 kg MS		75 kg bw			3 kg MS	
			% intake	intake to 100%	total MS (%)	fresh weight	residue intake	% intake	intake to 100%	total MS (%)	fresh weight	residue intake	% intake	intake to 100%	total MS (%)	fresh weight	residue intake	% intake	intake to 100%	total MS (%)	fresh weight	residue intake
I - Green Forage (Incl. Hay)																						
Grasses	20				-	-	-	100		-	-	-	100		-	-	-			-	-	-
Alfalfa/Clover	20				-	-	-	40		-	-	-	40		-	-	-	15		-	-	-
Forage Rape	14				-	-	-			-	-	-	35		-	-	-	15		-	-	-
Kale/Cabbage	14		5		-	-	-	35		-	-	-	35		-	-	-	15		-	-	-
Sugar Beet Leaves/Tops	16				-	-	-	30		-	-	-	30		-	-	-	25		-	-	-
Silage (Clover, Grasses)	20				-	-	-	100		-	-	-	100		-	-	-	15		-	-	-
Silage (Maize)*	35				-	-	-	100		-	-	-	100		-	-	-			-	-	-
Fruit Pomace (Apple, Citrus)	23	0,42[1]			-	-	-	10		**10**	8,7	**3,7**	30		**30**	19,6	**8,2**			-	-	-
Hay	85				-	-	-	100		-	-	-	100		-	-	-	15		-	-	-
II - Grains																						
Grains (except maize)	86	0,04[2]	70		**70**	0,098	**0,0039**	40		**40**	9,3	**0,372**	80	20	**20**	3,5	**0,1**	80		**80**	2,8	**0,11**
Maize	86		70		-	-	-	30		-	-	-	30		-	-	-	40		-	-	-
Bran (Wheat and Rye)	89		15		-	-	-	20		-	-	-	20		-	-	-	20		-	-	-
III - Straws (cereals)	86	3,51[3]			-	-	-	20		**20**	4,7	**16,326**	50		**50**	8,7	**30,6**			-	-	-
IV - Pulses	86		30		-	-	-	20		-	-	-	20		-	-	-	40		-	-	-
V - Root and Tubers																						
Potatoes	15		20		-	-	-	30		-	-	-	60		-	-	-	60		-	-	-

Swede/turnips	10		20		-	-	-	30		-	-	-	60		-	-	-	60		-	-	-
Sugar and Fodder beet	20		20		-	-	-	30		-	-	-	60		-	-	-	60		-	-	-
VI - Oil seed (Meal Cake)																						
Soya,Peanut,Rape,sunflower	86		10		-	-	-	30		-	-	-	30		-	-	-	20		-	-	-
% total MS intake (must be <100 %)			**70**					**70**					**100**					**80**				
mg/animal/day							**0,0039**					**20,3498**					**38,9674**					**0,112**
mg/kg bw/day			**Chicken**				**0,0021**			**Dairy Cattle**		**0,0370**			**Beef Cattle**		**0,1113**			**Pig**		**0,001**
mg/kg DM/day							**0,0326**					**1,0175**					**2,5978**					**0,037**

(1): Highest residue value (HR) of 0.15 mg/kg calculated on the residue database on apple and the highest transfer factor of 2.8 from washed whole apple to wet pomace.
(2): STMR value for cereal grain (see table B.7.6.3-1).
(3): HR value for cereal straw (see table B.7.6.3-1).

B.7.8.1 Livestock feeding studies in lactating cows or goats

BAS 490F Residues in milk and tissues of dairy cows (Redgrave V.; 1994).
Guidelines :
Codex Committee on Pesticide Residues, ALINORM 87/24, Appendix IV, Annex I 1986
US EPA Pesticide Assessment Guidelines, Subdivision O, Part 171-4
GLP :
yes
Material and Methods :
Test substance: Kresoxim-methyl, unlabelled
Groups of 3-5 dairy cows were fed with oral doses of kresoxim-methyl for 28/29 days at dosages of 120, 360 and 1200 mg/cow/day (corresponding to about 0.23 (6N/2N), 0.65 (18N/6N) and 2.19 (60N/20N) mg/kg body weight/day). The substance was incorporated in the ration.
Animals were sacrificed 16-24 hours after the final dose, except 2 cows of the high dose group, sacrificed 2 and 7 days after the end of the dosing period to provide depletion data.
Milk, cream and skim milk, as well as edible tissues were analyzed for metabolites 490M01 (BF 490-1), 490M02 (BF 490-2) and 490M09 (BF 490-9) according to methods No 354/1 (milk) and No 354/2 (tissues).
The method no. 354/1 fulfills the standard requirements for a residue analytical method for a Limit of quantification of 0.002 mg/kg for each metabolite BF 490-2 and BF 490-9.
The method No 354/2 fulfills the criteria and can be used in residue analysis work with a Limit of quantification of 0.01 mg/kg for each metabolite BF 490-1, BF 490-2, BF 490-9 in liver, kidney, muscle and fat.
Findings :
* Milk residues:
All samples of whole milk, cream and skim milk from the 3 groups were below the limit of determination of the analytical method (0.002 mg/kg) for metabolites 490M02 (BF 490-2) and 490M09 (BF 490-9) (metabolite 490M01 (BF 490-1) is not relevant for this matrix).
* Tissue residues:
The following table gives a summary of the results obtained from the analyses of tissues of cows sacrificed within 16-24 hours after the last dose. Figures in this table are the means of the 3 cows of each group.

Table B.7.8.1-1: Residues of metabolites of kresoxim-methyl in cow tissues after feeding 120/360/1200 mg/kg/d.

Metabolite	Dose level	Group mean residue concentration (mg/kg)				
	mg/cow/day	liver	kidney	muscle	subcut. fat	periton. fat
490M01 (BF 490-1)	120	nd	0.030	<0.01	<0.01	<0.01
	360	0.027	0.102	<0.01	<0.01	0.028
	1200	0.032	0.264	<0.01	0.024	0.089
490M02 (BF 490-2)	120	(*)	nd	<0.01	nd	nd
	360	(*)	<0.01	nd	nd	nd
	1200	(*)	<0.01	<0.01	<0.01	<0.01
490M09 (BF 490-9)	120	nd	<0.01	(*)	nd	nd
	360	0.013	0.014	(*)	nd	nd
	1200	0.013	0.030	(*)	<0.01	<0.01

(*): metabolite not relevant for this matrix
nd: below limit of detection
<0.01: below limit of determination

Results for cows of the high dose group killed after 2 and 7 days withdrawal demonstrated that depletion/elimination of residues occurred on cessation of treatment. Only residues of 490M01 (BF 490-1) were still present in liver and kidney after 2 days, at respective concentrations of 0.014 and 0.044 mg/kg. After 7 days, the residues of 490M01 (BF 490-1) were 0.025 mg/kg in kidney and below the limit of determination in liver.

Conclusions :
The low dose group can be considered as representative of the residue level that may occur in the feedingstuff of beef cattle. Residues of metabolite 490M01 (BF 490-1) only are present at a quantifiable level in kidney considering the calculated dietary burden. The following MRLs can be proposed respectively for metabolite BF 490-9 (milk) and metabolite 490M01 (BF 490-1) (tissues):
- milk : 0.002* mg/kg;
- meat, liver, fat : 0.01* mg/kg;
- kidney : 0.05 mg/kg.

-Residues in Milk and Tissues of Dairy Cows (Maxwell J.G., 1996)
Guidelines:
-US, EPA Subdivision O Guideline 171-4
GLP:
Yes.
Material and methods:
In section B.5.2.2, the BASF method no. 354/1 (milk) fulfils the standard requirements for a residue analytical method. The average recovery is in the range of 70% to 110% and the relative standard deviation is lower than 20%.
The BASF method no. 354/2 (tissues) was also considered to fulfil the criteria and can be used in residue analysis work.
In the previous study "BAS 490 F, Residues in Milk and Tissues of Dairy Cows" (Redgrave V.; 1994), the procedural recoveries of the metabolites BF 490-1, BF 490-2 and BF 490-9 from fat samples obtained with 3 analytical sample sets were less than 50 %. This result could not be justified.
Contamination of a fourth set was suspected. In addition, the mean recoveries from the validation data obtained at 1mg/kg for BF 490-2 and BF 490-9 in fat were below the trigger value of 70 %.
Consequently, in order to confirm the results obtained for the samples analysed in these sets, re-analysis of the relevant samples from the original feeding study was undertaken under the following ruminant feeding study (Maxwell J.G., 1996).
This study details the methods used and results obtained from the determination of the levels of BAS 490 F metabolites in subcutaneous and peritoneal fat and in whole milk from dairy cows.
Analytical procedure:
The analytical method used for the determination of BF 490-2 and BF 490-9 in milk was BASF method 354/1 with modifications.
The analytical method used for the determination of BF 490-1, BF 490-2 and BF 490-9 in beef muscle, liver, fat and kidney was BASF method 354/2 with modifications.
In the frame of this study, these metabolites were quantified in subcutaneous/peritoneal fat matrices.
The analytical methods involved an initial extraction using acetone (milk matrices) or methanol (tissues), clean-up of the extracts using combinations of precipitation, partition and identification and quantification of the metabolites BF 490-1, BF 490-2 and BF 490-9 by HPLC analysis on a SPE/CN NH_2 column using spectrophotometric (UV) detection.
These analytical methods were validated for a Limit of Quantification of 0.002 mg/kg for milk matrices for each metabolite BF 490-2 and BF 490-9 and 0.010 mg/kg for tissues, for each analyte BF 490-1, BF 490-2 and BF 490-9, respectively.

The maximum storage period of samples from milking and sacrifice to the initiation of the analysis was 399 days for whole milk and 415 days for tissues (subcutaneous fat and peritoneal fat).

Storage stability data under frozen conditions (-20°C) of the metabolites BF 490-1 and BF 490-9 in whole milk, liver, kidney, skeletal muscle and fat from dairy cows were not provided to cover this storage period.

This is a minor issue in the frame of Annex I renewal since the residue levels of BF 490-9 (milk) and BF 490-1 (tissues) are below the limit of quantification of the analytical methods at the calculated dietary burden.
This point should be reconsidered if in the future, additional feed items are envisaged.

Findings:
The low recoveries of the metabolites BF 490-1, BF 490-2 and BF 490-9 from fat samples, as observed in the validation study (see Table B.5.2-16), were also apparent in the dairy cow feeding study evaluated here above (point B.7.8.1) (Redgrave V., 1994), where procedural recovery values were below 50% and a definite reason for this recovery loss could not be identified.

In this study, the samples from the original cow feeding study were re-analysed, by using the methods 354/1 (milk) and 354/2 (tissues) modified in order to confirm the initial results. Procedural recoveries determined in this new study were found to be within acceptable range (70 – 110%), as shown in the table here below.

Table B.7.8.1-2: Recovery data for the metabolites BF 490-1, BF 490-2 and BF 490-9 in whole milk and in fat (subcutaneous/peritoneal)

Matrix	***Fortification level (mg/kg)***	**Procedural recoveries (%)**		
		BF 490-1	**BF 490-2**	***BF 490-9***
Whole milk	0.005	-	96.6 / 96.5 (n=2)	107 / 109 (n=2)
Subcutaneous fat	0.01 / 0.05 / 0.1	104 / 75.5 / 84.0	93.0 / 86.9 / 105	101 / 79.3 / 92.7
Peritoneal fat	0.01 0.1 1	104 / 108 (n=2) 107 / 99.9 (n=2) 105.2 (± 7.8)(*) (n=6)	109 / 114 (n=2) 116 / 110 (n=2) 103.7 (± 3.5)(*) (n=6)	131 / 103 (n=2) 133 / 107 (n=2) 106.4 (± 8.4)(*) (n=6)

(*) mean recovery (± RSD) [%]

Conclusion:
Although a limited number of recovery experiments were performed per fortification level, the procedural recoveries obtained suggest that the **modified** method 354/2 is able to extract the analytes from high fat level tissue samples to an adequate extent. However, it should be noted that quite some modifications were made to the original analytical procedure of BASF method 354/2 and thus, it seems that those modifications are responsible for the better recoveries achieved. It is mentioned that this 'modified' method was already validated at the contract lab, i.e. under HRC studies no BSF 528 (HRC report no 943038) and BSF 532 (HRC report no 942413), but the applicant BASF stated that no validation report is available to them.

B.7.8.2 Livestock feeding studies in poultry

The residues in cereal grains after an application according to the proposed recommendations are below the LOD of 0.05 mg/kg (see point B.7.6). Therefore there is no requirement for a feeding study in hens.
The MRL of the parent compound for egg can be fixed at 0.01* mg/kg.

B.7.8.3 Livestock feeding studies in pigs

A metabolism study in pigs was not required as metabolic pathways in rat and goat can be considered as similar. For the same reason, a livestock feeding study in pigs is not required. Moreover, intake calculations for pigs indicate that no significant exposure can be expected.

B.7.9 Residues in succeeding or rotational crops (Annex IIA 6.6; Annex IIIA 8.5)

-Rotational Crop Study with ^{14}C-labelled 242009 (Hofmann M.; 1993a).

Guidelines :
BBA, IV, 3-10
GLP :
yes
Material and Methods :
Test substance: [Ring B-U-^{14}C]-kresoxim-methyl
Prior to seeding or planting of representative crops (spring wheat, green beans, carrots, and lettuce), the active ingredient corresponding to a rate of use of 300 g a.s./ha had been aerobically aged in the soil for 29 days. The aged soil was then mixed with untreated soil in a ratio of 1:9 in order to simulate ploughing. Seeding and planting were done on the following day, 30 days after soil treatment.
Soil and plant samples were dosed by combustion analysis.
Findings :
After soil treatment and after the ageing period the following total radioactive residues (TRR expressed in mg kresoxim-methyl equiv./kg) were determined:
- soil, after treatment: 0.918 mg/kg
- soil, after ageing and dilution: 0.049 mg/kg
After harvest of rotational crops, the following TRR (expressed in mg kresoxim-methyl equiv./kg) in plants and plant parts were determined:
- spring wheat, plants (42 days after sowing): 0.067 mg/kg
- spring wheat, straw (124 days after sowing): 0.119 mg/kg
- spring wheat, grains (124 days after sowing): 0.006 mg/kg
- beans, plants (26 days after sowing): 0.361 mg/kg
- beans, plants (77 days after sowing): 0.210 mg/kg
- beans, green beans (77 days after sowing): 0.009 mg/kg
- carrot, tap roots (52 days after sowing): 0.052 mg/kg
- carrot, tap roots (89 days after sowing): 0.005 mg/kg
- carrot, green (89 days after sowing): 0.056 mg/kg
- carrot, tap roots (111 days after sowing): 0.006 mg/kg

- lettuce, plant (26 days after planting): 0.053 mg/kg
- lettuce, head (56 days after planting): 0.028 mg/kg
- lettuce, head (66 days after planting): 0.010 mg/kg

Samples of soil taken after harvest of the different rotational crops still contained residue levels of 0.032 to 0.050 mg kresoxim-methyl equiv./kg

Conclusions :

The enrichment of edible plant parts of leafy vegetables, root vegetables and cereals, installed as succeeding crops, with kresoxim-methyl or its metabolites is not sufficient to reach measurable levels in monitoring.

-Crop Rotation Study with ^{14}C-labelled 242009 (Hofmann M.; 1993b).

This study was initiated in order to generate more sample material for the characterization of residues in a subsequent study.

Guidelines :

BBA, IV, 3-10

GLP :

yes

Material and Methods :

Test substance: [Ring B-U-^{14}C]-kresoxim-methyl

Prior to seeding or planting of representative crops the active ingredient corresponding to a rate of use of 300 g a.s./ha had been aerobically aged in the soil for 30 days. The aged soil was then mixed with untreated soil in a ratio of 1:9 in order to simulate ploughing.

Soil and plant samples were dosed by combustion analysis.

Findings :

After the soil treatment and after the ageing period the following total radioactive residues (TRR expressed in mg kresoxim-methyl equiv./kg) were determined:

- soil, after treatment: 0.833-1.046 mg/kg
- soil, after ageing and dilution: 0.063-0.066 mg/kg

In plant samples, the following TRR were determined (expressed in mg kresoxim-methyl equiv./kg):

- spring wheat, plants (61days after sowing): 0.232 mg/kg
- spring wheat, straw (125 days after sowing): 0.068 mg/kg
- spring wheat, grains (125 days after sowing): 0.007 mg/kg
- beans, bines (75 days after sowing): 0.067 mg/kg
- beans, green beans (75 days after sowing): 0.004 mg/kg
- carrot, plants (50 days after sowing): 0.025 mg/kg
- carrot, tap roots (90 days after sowing): 0.003 mg/kg
- carrot, green material (90 days after sowing): 0.010 mg/kg
- lettuce, leaves (30 days after planting): 0.051 mg/kg
- lettuce, head (49 days after planting): 0.020 mg/kg

Samples of soil taken after harvest of the different rotational crops still contained residue levels of 0.028 to 0.034 mg kresoxim-methyl equiv./kg

Conclusions :

The conclusions of the first study are confirmed.

-The Characterization of radioactive Residues in Wheat, Beans, Carrots and Lettuce from a rotational Crop Study with ^{14}C-BAS 490 F (^{14}C-242 009) (Grosshans F.; 1994d)

Guidelines :

BBA, IV, 3-10

GLP :

yes

Material and Methods :

Test substance: [Ring B-U-^{14}C]-kresoxim-methyl

The nature of the radioactivity in wheat straw, in bean forage, in carrot forage and in lettuce (head) was examined. The sample material was extracted first with MeOH and then with aqueous ammonia. The extractable radioactivity was characterized by liquid/liquid partition and analyzed by HPLC. The metabolites were isolated by HPLC, conjugates were cleaved by enzymes and the structure of isolated metabolites and aglycones were elucidated by chromatographic comparison with reference compounds.

Findings :
The extractability of the plant samples is given in the following table.

Table B.7.9-1 : Extractability of residues in plant samples of the rotational crop study (expressed in % of TRR).

	wheat straw	bean forage	carrot forage	lettuce
Methanol	45.2-58.9	61.6-82.0	54.3-57.1	71.4-76.7
Aqueous ammonia	24.8-39.7	8.3-26.3	11.9-34.3	7.0-20.0
Unextracted fraction	12.9-23.5	8.0-22.5	14.3-39.6	13.3-16.3

In extracts of bean forage, carrot forage and lettuce, the conjugate fraction was the predominant radioactive residue. These conjugate fractions accounted for 36.7% of TRR in bean forage, 43.6% TRR in carrot forage and 41.5% TRR in lettuce. Enzymatic cleavage of these conjugates afforded mainly the aglycones 490M02 (BF 490-2) and 490M09 (BF 490-9). The rest of extractable radioactivity in these samples was composed of several radioactive peaks. Lettuce contained 9.4% TRR of unchanged parent and carrot forage 12.7% TRR of 490M01 (BF 490-1).
The extract of wheat straw contained an unknown peak representing 12.5-26.5% of TRR, more polar than the conjugate fraction (representing 8.9-11.6% of TRR and yielding aglycones 490M02 (BF 490-2) and 490M09 (BF 490-9) after cleavage). The rest of extractable radioactivity consisted of several polar peaks and of the free hydroxy metabolites 490M02 (BF 490-2) and 490M09 (BF 490-9) (together 3.4-8.5% of TRR). Unchanged parent was present in very small amount.
The unknown peak was characterized by cleavage and derivatization attempts. Cleavage with acid did not change its polarity. Diazomethane formed an unpolar derivative.
Conclusions :
The metabolic pathway of kresoxim-methyl in succeeding crops is presented in Appendix A to this section.

B.7.10 Proposed pre-harvest intervals, re-entry intervals or withholding periods to minimize residues in crops, plants, plant products, treated areas or spaces (Annex IIA 6.8; Annex IIIA 8.7)

Added in March 2010

The products BAS 490 02 F and BAS 494 04 F containing 500 g/l and respectively 125 g/l active substance BAS 490 F (Kresoxim-methyl) are provided for the use in grapes and pome fruits, as well as in cereals.

-Pre-harvest interval (in days) for each relevant crop

Cereals: 35 days
Grapes: 35 days
Pome fruits: 35 days

-Re-entry period (in days) for livestock, to areas to be grazed
Because Kresoxim-methyl is not intended for use in areas to be grazed, no re-entry period for livestock has to be defined. In order to avoid residues above the MRLs proposed for products of animal origin, a withholding period for cereal green matter to be used as feeding stuff is not needed, as the highest residues in forage after application are still covered by the 1x dose level of the animal feeding study in lactating cows.
The withholding period for grains and straw is given by the intended use.

-Re-entry period for man to crops, buildings or spaces treated
Workers should not enter treated areas until the spray has dried.

-Withholding period (in days) for animals feeding stuffs

Animal feeding stuffs are not treated directly with formulations containing Kresoxim-methyl. Therefore, no specific withholding periods are required. However, straw from treated cereals may be used as animal feed. In this instance, the proposed PHI of 35 days will cover this use and no additional time interval between treatment and use as animal fodder needs to be defined. No new animal feeding study was triggered.

-Waiting period between last application and sowing or planting

This point is not relevant since Kresoxim-methyl is applied directly to the crop and not as a pre-emergence treatment.

-Waiting periods between application and handling treated products

This point is not relevant since Kresoxim-methyl is not used as a post-harvest treatment. Furthermore, a PHI of 35 days is proposed for cereals, grapes and pome fruits. Thus, there is no need for workers to handle recently treated produce and no specific waiting period needs to be established.

-Waiting period before sowing/planting succeeding crops

No waiting period is necessary.

Due to the fact that no relevant accumulation of Kresoxim-methyl or its degradation products were observed in the confined rotational crop study (see point B.7.9), no limited plant back interval concerning the succeeding crops is necessary for the use in cereals. In the parts of plants used for human food or animal feed consumption, e.g. lettuce, the concentration of parent was $\leq$ 0.009 mg/kg. The levels of individual metabolites present were below 0.009 mg/kg.

Grapes and pome fruits are permanent crops.

B.7.11 Estimates of the potential and actual exposure through diet and other means (Annex IIA 6.9; Annex IIIA 8.8)

Added in March 2010

B.7.11.1 Chronic dietary intake risk assessment:

Table B.7.11-1: Chronic dietary intake risk assessment according to EFSA PRIMo rev.2a

The chronic dietary intake risk assessment was performed according to the established residue definition for risk assessment for both plant and animal matrices (see point B.7.3).

Kresoxim-methyl									
Status of the active substance:				Code no.					
LOQ (mg/kg bw):				proposed LOQ:					
Toxicological end points									
ADI (mg/kg bw/day):	**0,4**			ARfD (mg/kg bw):	**/**				
Source of ADI:	**DRAR**			Source of ARfD:	**/**				
Year of evaluation:	**2010**			Year of evaluation:	**/**				
Chronic risk assessment									
TMDI (range) in % of ADI minimum - maximum									
0	1								
No of diets exceeding ADI:	---								
Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)	
0,8	DE child	0,5	Apples	0,2	Table and wine grapes	0,1	Wheat		
0,6	FR all population	0,5	Table and wine grapes	0,1	Wheat	0,0	Apples		

0,6	WHO Cluster diet B	0,3	Table and wine grapes	0,2	Wheat	0,0	Apples
0,5	NL child	0,3	Apples	0,1	Wheat	0,1	Table and wine grapes
0,5	PT General population	0,3	Table and wine grapes	0,1	Wheat	0,0	Apples
0,4	WHO cluster diet E	0,2	Table and wine grapes	0,1	Wheat	0,0	Apples
0,4	DK child	0,1	Wheat	0,1	Rye	0,1	Apples
0,3	IE adult	0,1	Table and wine grapes	0,1	Wheat	0,0	Apples
0,3	DK adult	0,2	Table and wine grapes	0,1	Wheat	0,0	Apples
0,3	WHO cluster diet D	0,2	Wheat	0,1	Table and wine grapes	0,0	Apples
0,3	WHO Cluster diet F	0,1	Table and wine grapes	0,1	Wheat	0,0	Apples
0,2	NL general	0,1	Table and wine grapes	0,1	Wheat	0,1	Apples
0,2	IT kids/toddler	0,2	Wheat	0,0	Apples	0,0	Pears
0,2	FR toddler	0,1	Apples	0,1	Wheat	0,0	Table and wine grapes
0,2	UK Toddler	0,1	Wheat	0,1	Apples	0,0	Table and wine grapes
0,2	UK Adult	0,1	Table and wine grapes	0,0	Wheat	0,0	Apples
0,2	ES child	0,1	Wheat	0,0	Apples	0,0	Pears
0,2	UK vegetarian	0,1	Table and wine grapes	0,1	Wheat	0,0	Apples
0,2	SE general population 90th percentile	0,1	Wheat	0,0	Apples	0,0	Table and wine grapes
0,2	ES adult	0,1	Wheat	0,1	Table and wine grapes	0,0	Apples
0,2	WHO regional European diet	0,1	Wheat	0,0	Table and wine grapes	0,0	Apples
0,2	FR infant	0,1	Apples	0,0	Wheat	0,0	Pears
0,2	IT adult	0,1	Wheat	0,0	Apples	0,0	Table and wine grapes
0,1	UK Infant	0,1	Apples	0,1	Wheat	0,0	Pears
0,1	LT adult	0,1	Apples	0,0	Rye	0,0	Wheat
0,1	PL general population	0,1	Apples	0,0	Table and wine grapes	0,0	Pears
0,1	FI adult	0,0	Table and wine grapes	0,0	Wheat	0,0	Apples

Conclusion:
The chronic dietary intake of residues of Kresoxim-methyl through the consumption of pome fruit, grapes and cereals does not pose any safety concern for the consumers'health.

B.7.12 Community MRLs and MRLs in EU Member States (Document E-4)

Added in March 2010

According to Regulation (EC) No149/2008, the current EU MRLs for Kresoxim-methyl are:
-Pome fruit: 2 mg/kg,
-Grapes: 1 mg/kg,
-Cereals: 0.05* mg/kg

B.7.13 Proposed MRLs and justification for the acceptability of those residues (Annex IIA 6.7; Annex IIIA 8.6)

Revised in March 2010

Table B.7.13-1 : Proposed MRLs

Expression of the residue	Products	MRL (mg/kg)
Kresoxim-methyl	Apple, pears	0.05* (provisional)
Kresoxim-methyl	grapes	0.5
Kresoxim-methyl	Cereals (Barley, wheat, rye and triticale)	0.1
490M9 : (2-[2-(4-hydroxy-2-methylphenoxymethyl)phenyl]-2-methoxy-iminoacetic acid), expressed as kresoxim-methyl	milk	0.002*
490M1 (2-methoxyimino-2-[2-(o-tolyloxymethyl)phenyl]acetic acid), expressed as kresoxim-methyl	meat, liver, fat	0.01*
490M1 (2-methoxyimino-2-[2-(o-tolyloxymethyl)phenyl]acetic acid), expressed as kresoxim-methyl	kidney	0.05
kresoxim-methyl	eggs	0.01*

B.7.14 Summary and evaluation of residue behaviour

Added in March 2010

Metabolism in plants and livestock:

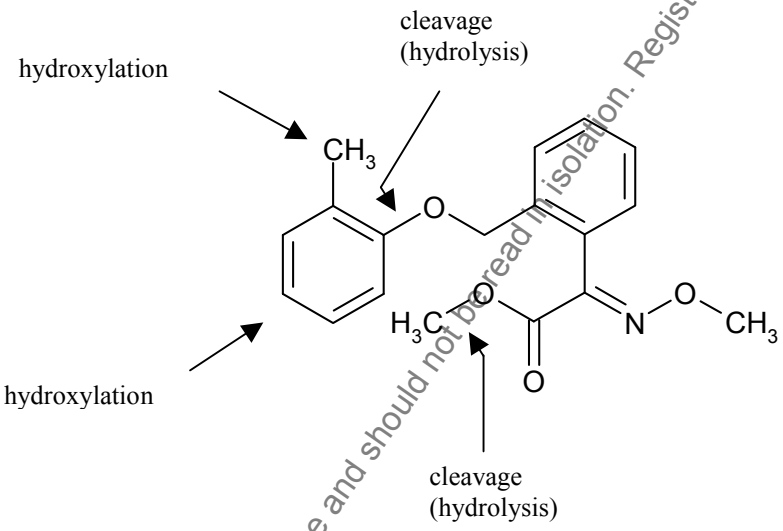
Plant products:
Metabolism studies were provided on apples and grapes (fruit), spring wheat (cereals) and sugar beet (root and tuber vegetables).
In each crop, the metabolic pathway of Kresoxim-methyl was similar, i.e. the parent Kresoxim-methyl was the predominant compound of the total residues in all the matrices with low levels of recovered acid BF 490-1 and the hydroxyl acid metabolites BF 490-2 and BF 490-9 mainly as glucosides.
Cleavage of the methyl ester bond of the parent molecule generated the free acid BF 490-1 which can be regarded as an intermediate that undergoes hydroxylation at the cresyl (phenoxy) ring or its methyl group resulting in metabolites BF 490-2 and BF 490-9 with a further glucoside conjugation step of these 2 metabolites.

Livestock products:
The metabolic pathway of Kresoxim-methyl was investigated in lactating goats and laying hens.
-The metabolism study in goat indicates an extensive degradation of kresoxim-methyl as observed in the rat metabolism.
The parent compound was recovered only in faeces and in fat (6.6 % of the TRR).
3 major metabolites were identified in goat matrices: the free acid BF 490-1 formed by cleavage of the methyl ester bond of the parent molecule with further hydroxylation either on the side chain of the phenoxy ring (BF 490-2) or on the phenoxy ring (BF 490-9).

A valid indicator of the level of contamination of the animal matrices differs from tissue to tissue.
-An extensive metabolization of the parent compound is also observed in the laying hens. Several metabolites, not present in the rat metabolism, were also observed. Most of them did not reflect reactions different from those occurring in the rat.

The toxicological relevance of the metabolites recovered in plants and animals was discussed under point "B.7.3. Definition of the residue".
It was concluded that the identified metabolites do not pose a particular problem, and are likely to be covered by the toxicological package of Kresoxim-Methyl itself.

The sites of metabolic attack in the Kresoxim-methyl molecule in plants and animals are depicted in the figure here below.



Supervised field residue trials:
-Apples:
Additional residue trials on apples should be provided complying with the critical intended use in order to confirm the no-residue situation of Kresoxim-methyl in pome fruits and to perform a robust dietary intake risk assessment with regard to the residue levels of BF 490-2 and BF 490-9.
Provisional MRL proposal on apples, pears: 0.05* mg/kg.
-Grapes:
A complete residue database was provided in accordance with the critical GAP.
MRL proposal on grapes: 0.5 mg/kg
-Cereals:
Sufficient supervised residue trials were provided on spring/winter wheat and barley covering Northern and Southern Europe.
MRL proposal on cereal grain (barley, wheat, rye, triticale): 0.1 mg/kg (according to extrapolation Table 4 of the current EU guidance document SANCO 7525/VI/95 rev.8).

Effect of industrial processing on the nature and the level of the residues in processed commodities

-Effect on the nature of the residues:
Kresoxim-methyl (BAS 490 F) was shown to be stable during the simulation of pasteurisation and baking, brewing and boiling processes.
During the simulation of the sterilisation processing, the parent compound degraded significantly with the formation of mainly the acid metabolite BF 490-1.

-Effect on the level of the residues:
-*Apple*: Apple juice and wet pomace were produced from washed apples. The residue levels on raw apples were not provided and no conclusion can be drawn on the actual effect of washing on the residue level.
Kresoxim-methyl did not concentrate in juice.
No metabolite BF 490-2 and BF 490-9 were detected above the LoQ of the method (0.05 mg/kg) in any whole washed apple, apple juice and wet pomace.
-*Grapes*: No residues above the LoQ (0.05 mg/kg) were recovered in wine and no increase of the residue level in must was observed.
A concentration of the residues of both the parent Kresoxim-methyl and its metabolites BF 490-2 and BF 490-9 was observed in wet pomace.

Livestock feeding studies:
-Ruminants:
All samples of whole milk, cream and skim milk from the 3 groups were below the limit of determination of the analytical method (0.002 mg/kg) for metabolites 490M02 (BF 490-2) and 490M09 (BF 490-9).
Residues of metabolite 490M01 (BF 490-1) only are present at a quantifiable level in kidney considering the calculated dietary burden.
The following MRLs can be proposed for metabolite BF 490-9 (milk) and metabolite BF 490-1 (tissues):
- milk : 0.002* mg/kg;
- meat, liver, fat : 0.01* mg/kg;
- kidney : 0.05 mg/kg.
-Poultry:
Nor required.

Rotational crop studies:
The enrichment of edible plant parts of mainly lettuce and wheat (straw) installed as succeeding crops, with kresoxim-methyl or its metabolites was sufficient to reach residue levels of 0.01 mg/kg.
A metabolism study on rotational crops showed a similar metabolic pathway of Kresoxim-methyl as for the primary crops.

Chronic dietary intake risk assessment:
The chronic dietary intake of residues of Kresoxim-methyl through the consumption of pome fruit, grapes and cereals does not pose any safety concern for the consumers'health.

B.7.15 References relied on *[revised in March 2010]*

B.7.15.1 Active substance (BAS 490 F)

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.1.1/1 *[Added in March 2010]*	Mackenroth C., Krotzky A.J.	1994	Storage stability of BAS 490 F in apple BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11097 Yes unpublished	Y	BASF
II A 6.1.1/2 *[Added in March 2010]*	Krotzky A.J.	1994	Storage stability of BAS 490 F, BF 490-2 and BF 490-9 in wheat matrices BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11176 Yes unpublished	Y	BASF
II A 6.1.1/3 *[Added in March 2010]*	Class T., Senciuc M.	2008	Interim report: Kresoxim-methyl (BAS 490 F) and its metabolites BF 490-2 and BF 490-9 - Frozen storage stability in wheat grain PTRL Europe GmbH; Ulm; Germany Fed.Rep. 2008/1014862 Yes unpublished	Y	BASF
II A 6.1.1/4	Class T., Senciuc M.	2009a	Kresoxim-methyl (BAS 490 F) and its metabolites BF 490-2 and BF 490-9: 18 months frozen storage stability in wheat Grain PTRL Europe GmbH; Ulm; Germany Fed.Rep. 2009/1018683 Yes unpublished	Y	BASF
II A 6.1.1/5	Class T., Senciuc M.	2009b	Final Report: Kresoxim-methyl (BAS 490 F) and Its Metabolites BF 490-2 and BF 490-9: Frozen Storage Stability in Wheat grain, Soy Bean and dried Pea BASF Study ID 280744 BASF DocID 2009/1018683 PTRL Europe Study No. P 1204 G PTRL Europe Report No. B 1204–3 G	Y	BASF
II A 6.1.1/6 *[Added in March 2010]*	Jordan J., Riley M.E.	1999	Freezer storage stability of BAS 490F (Kresoxim-methyl) and its metabolites in grapes, apples, apple juice and apple wet pomace BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1999/5006 Yes unpublished	Y	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.1.1/7 *[Added in March 2010]*	Movasaghi S., Riley M.E.	1998	Storage stability of BAS 490 F and its metabolites in grapes, apples, apple juice, and apple wet pomace after twelve months of freezer storage BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1998/5027 Yes unpublished	Y	BASF
II A 6.1.1/8 *[Added in March 2010]*	Abdel-Baky S., Riley M.E.	1998	Freezer storage stability of BAS 490 F (Kresoxim-methyl) in cucumber BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1998/5189 Yes unpublished	Y	BASF
II A 6.1.1/8 *[Added in March 2010]*	Thornton J.B.	1998	Freezer storage stability of BAS 490 F and its metabolites in pecan BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1997/5339 Yes unpublished	Y	BASF
IIA 6.2.1	Grosshans F.	1994c	The metabolism of ^{14}C-BAS 490 F (^{14}C-242 009) in wheat BASF Aktiengesellschaft, Limburgerhof, Germany BASF Reg. Doc. #94/10685 Yes unpublished	N	BASF
II A 6.2.1/1	Hofmann M.	1992a	Plant uptake study with 14C-242 009 in apples (leaf application) BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1992/11332 Yes unpublished	N	BASF
II A 6.2.1/2	Hofmann M.	1992b	Plant uptake study with 14C-242 009 in apples (early application) BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1992/11618 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.2.1/3	Hofmann M.	1992c	Plant uptake study with 14C-242 009 in apples (fruit treatment) BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1992/11760 Yes unpublished	N	BASF
II A 6.2.1/4	Grosshans F.	1994a	The metabolism of 14C-242 009 (14C-BAS 490 F) in apples BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/10265 Yes unpublished	N	BASF
II A 6.2.1/5	Grosshans F.	1994b	The metabolism of 14C-242 009 (14C-BAS 490 F) in apples BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/10466 Yes unpublished	N	BASF
II A 6.2.1/6	Hofmann M.	1991a	Plant uptake study with 14C-BAS 490 00 F in spring wheat BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1991/10607 Yes unpublished	N	BASF
II A 6.2.1/7	Hofmann M.	1991b	Plant uptake study with 14C-BAS 490 00 F in spring wheat BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1991/10608 Yes unpublished	N	BASF
II A 6.2.1/8	Grosshans F.	1994d	The metabolism of 14C-BAS 490 F (14C-242 009) in wheat BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/10685 Yes unpublished	N	BASF
II A 6.2.1/9	Nelsen J.M. et al.	1995	Metabolism of 14C-BAS 490 F in grapes BASF Corporation Agricultural Products Center; Research Triangle Park, NC 27709-3528; United States of America 1995/5001 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.2.1/10 *[Added in March 2010]*	Veit P.	1999	Metabolism of 14C-BAS 490 F (14C-242009) in sugar beet BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1999/10740 Yes unpublished	N	BASF
II A 6.2.2/1	Burke A.B.	1994	14C-242 009: Distribution, metabolism and excretion following repeated oral administration to the laying hen Hazleton Europe; Harrogate North Yorkshire HG3 1PY; United Kingdom 1994/11102 Yes unpublished	N	BASF
II A 6.2.2/2	Grosshans F.	1994e	The metabolism of 14C-BAS 490 F (14C-242 009) in laying hens BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11103 Yes unpublished	N	BASF
II A 6.2.3/1	Giese U.	1992	Dosing of lactating goats with (14C)-LAB 242 009 NATEC - Institut fuer naturwissenschaftlich-technische Dienste GmbH; Hamburg; Germany Fed.Rep. 1992/10545 Yes unpublished	N	BASF
II A 6.2.3/2 *[Added in March 2010]*	Jonas W.	1992	Addendum 1: Dosing of lactating goats with (14-C)-LAB 242 009 NATEC - Institut fuer naturwissenschaftlich-technische Dienste GmbH; Hamburg; Germany Fed.Rep. 1992/10883 Yes unpublished	Y	BASF
II A 6.2.3/3	Mayer F.	1994	The metabolism of 14C-BAS 490 F in the goat BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11104 Yes unpublished	N	BASF
II A 6.2.3/4 *[Added in March 2010]*	Kirkpatrick D.	1996	The metabolism of (cresyl-14C) BAS 490 F (Reg.No. 242 009) in the goat Huntingdon Life Sciences Ltd.; Huntingdon Cambridgeshire PE18 6ES; United Kingdom 1996/10074 Yes unpublished	Y	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.2.5/1 *[Added in March 2010]*	Mayo B.C.	1994	14C-BAS 490 F (14C-Reg.No. 242 009): The bioaccumulation and metabolism in rainbow trout Huntingdon Research Centre Ltd.; Huntingdon Cambridgeshire PE18 6ES; United Kingdom 1994/10725 Yes unpublished	Y	BASF
II A 6.3.1/1 *[Added in March 2010]*	Schroth E., Martin T.	2008c	Study on the residue behavior of BAS 490 F, BSA 480 F and BAS 421 F on barley and wheat after the application of BAS 493 05 F, BAS 480 31 F and BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2007 Agrologia SL; Palomares; Spain 2008/1043814 Yes unpublished	Y	BASF
II A 6.3.1/2	Schroth E., Martin T.	2009a	Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on barley after the application of BAS 494 04 F, under field conditions in France (South), Greece, Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1090698 Yes unpublished	Y	BASF
II A 6.3.1/3	Schroth E., Martin T.	2009b	Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on wheat after the application of BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1090699 Yes unpublished	Y	BASF
II A 6.3.1/4	Beck J. et al.	1995	Study on the residue behaviour of BAS 494 02 F in cereals under field conditions in the Netherlands, Belgium, France, Great Britain and Germany, 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10327 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.3.1/5	Beck J. et al.	1996	Study on the residue behaviour of Kresoxim-Methyl, Epoxiconazole and Fenpropimorph in cereals after treatment with BAS 493 02 F under field conditions in France and Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10113 Yes unpublished	N	BASF
II A 6.3.1/6	Krotzky A et al.	1994	Residue behaviour of BAS 490 04 F on cereals under field conditions in France, 1992 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11003 Yes unpublished	N	BASF
II A 6.3.1/7	Beck J. et al.	1994	Study on the residue behavior of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium and Germany, 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11004 Yes unpublished	N	BASF
II A 6.3.1/8	Beck J., Fegert A.	1994	Study on the residue behavior of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium, France and Germany, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11005 Yes unpublished	N	BASF
II A 6.3.1/9	Schulz H.	1994a	Determination of the residues of LAB 242 009 in spring wheat following treatment with BAS 492 01 F under field conditions in Germany 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11080 Yes unpublished	Y	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.3.1/10	Schulz H.	1994b	Determination of the residues of LAB 242 009 in spring wheat following treatment with BAS 492 01 F under field conditions in Germany 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11080 Yes unpublished	N	BASF
II A 6.3.1/11	Schulz H.	1994c	Determination of the residues of LAB 242 009 in spring barley following treatment with BAS 492 01 F under field conditions in Germany 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11158 Yes unpublished	N	BASF
II A 6.3.1/12 *[Added in March 2010]*	Schroth E., Martin T.	2008a	Interim report: Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on barley after the application of BAS 494 04 F, under field conditions in France (South), Greece, Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1043812 Yes unpublished	Y	BASF
II A 6.3.1/13 *[Added in March 2010]*	Schroth E., Martin T.	2008b	Interim report: Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on wheat after the application of BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1047529 Yes unpublished	Y	BASF
II A 6.3.2/1 *[Added in March 2010]*	Schulz H.,	2008a	Study on the residue behaviour of BAS 490 F in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern and Southern France, Italy and Spain 2007 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2008/1014860 Yes unpublished	Y	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.3.2/2	Schulz H.	2009	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern France, Southern France, Italy, Greece and Spain, 2008 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2009/1018523 Yes unpublished	Y	BASF
II A 6.3.2/3	Fuchs A. et al.	1996a	Study on the residue behaviour of Kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10698 Yes unpublished	N	BASF
II A 6.3.2/4	Fuchs A. et al.	1996b	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France and Spain, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10830 Yes unpublished	N	BASF
II A 6.3.2/5	Meumann H. et al.	1996	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France, Germany and Spain, 1996 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10890 Yes unpublished	N	BASF
II A 6.3.2/6 *[Added in March 2010]*	Schulz H.	2008b	Interim report: Study on the residue behaviour of BAS 490 F in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern and Southern France, Italy and Spain, 2008 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2008/1043811 Yes unpublished	Y	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.3.2/7 *[Added in March 2010]*	Wofford J.T., Riley M.E.	1998	Magnitude of Kresoxim-Methyl residue in grapes - Additional sites in CA, NY, ID, and OR BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1998/5134 Yes unpublished	Y	BASF
II A 6.3.2/8 *[Added in March 2010]*	Jackson S. et al.	1996	Magnitude of BAS 490 F residues in grapes BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1996/5219 Yes unpublished	Y	BASF
II A 6.3.3/1 *[Added in March 2010]*	Paleohorinos E., Rabe U.	1999	Kresoxim-methyl water dispersible granule 500 g/kg (BAS 490 02 F): Study on the residue behaviour of Kresoxim-methyl in apples after 8 treatment with BAS 490 02 F in Greece, 1997 Hoechst Schering AgrEvo Hellas SA; Maroussi; Greece 1999/10647 Yes unpublished	N	BASF
II A 6.3.3/2	Schulz H.	1994d	Determination of the residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11751 Yes unpublished	N	BASF
II A 6.3.3/3	Schulz H.	1995	Determination of the residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1994 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1995/10054 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.3.3/4	Fuchs A. et al.	1995	Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10082 Yes unpublished	N	BASF
II A 6.3.3/5	Fuchs A., Schulz H.	1995	Residue behaviour of BAS 490 02 F on pome fruit under field conditions in Germany, France, Spain, Belgium, The Netherlands and Great Britain 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10418 Yes unpublished	N	BASF
II A 6.3.3/6 *[Added in March 2010]*	Schulz H.	2000	Determination of the residues of BAS 490 F in pears following treatment with BAS 490 02 F under field conditions in Italy 1999 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 2000/1000235 Yes unpublished	Y	BASF
II A 6.3.3/7 *[Added in March 2010]*	Perny A.	2000	Determination of Kresoxim-methyl residues in pears following treatment with the preparation BAS 490 02 F under field conditions in France in 1999 Anadiag SA; Haguenau; France 2000/1000239 Yes unpublished	Y	BASF
II A 6.3.3/8 *[Added in March 2010]*	Meumann H., Benz A.	2000	Study on the residue behaviour of Kresoxim-methyl in pears after treatment with BAS 490 02 F under field conditions in France BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 2000/1000240 Yes unpublished	Y	BASF
II A 6.4.2/1	Redgrave V.A.	1994	BAS 490 F - Residues in milk and tissues of dairy cows Huntingdon Research Centre Ltd.; Huntingdon Cambridgeshire PE18 6ES; United Kingdom 1994/10960 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.4.2/2 *[Added in March 2010]*	Maxwell J.G.	1996	BAS 490 F - Residues in milk and tissues of dairy cows Huntingdon Life Sciences Ltd.; Huntingdon Cambridgeshire PE18 6ES; United Kingdom 1996/10146 Yes unpublished	Y	BASF
II A 6.5.1/1 *[Added in March 2010]*	Hassink J.	2008c	Hydrolysis of BAS 490 F at 90° C, 100° C and 120° C BASF SE; Limburgerhof; Germany Fed.Rep. 2008/1014942 Yes unpublished	Y	BASF
II A 6.5.3/1 *[Added in March 2010]*	Fuchs A. et al.	1996a	Study on the residue behaviour of Kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10698 Yes unpublished	Y	BASF
II A 6.5.3/2 *[Added in March 2010]*	Fuchs A. et al.	1995	Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10082 Yes unpublished	Y	BASF
II A 6.5.3/3 *[Added in March 2010]*	Wofford J.T. et al.	1998	The magnitude of Kresoxim-methyl residues in apple processed fractions - 30 day PHI program BASF Corporation Agricultural Products Center; Research Triangle Park, NC 27709-3528; United States of America 1998/5021 Yes unpublished	Y	BASF
II A 6.6/1	Hofmann M.	1993a	Rotational crop study with 14C-labelled 242 009 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1993/10500 Yes unpublished	N	BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
II A 6.6/2	Hofmann M.	1993b	Crop rotation study with 14C-labelled 242 009 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1993/11533 Yes unpublished	N	BASF
II A 6.6/3	Grosshans F.	1994d	The characterization of radioactive residues in wheat, beans, carrots and lettuce from a rotational crop study with 14C-BAS 490 F (14C-242 009) BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/10860 Yes unpublished	N	BASF

B.7.15.2 Plant protection products ALLEGRO (BAS 494 02 F) and BAS 494 04 F

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.1.2/1 *[Added in March 2010]*	Funk H., Mackenroth C.	2001	Determination of the stability of 205 259 (BAS 480 F); 242 009 (BAS 490 F), 285 028 (BAS 505 F) and 300 355 (BAS 510 F) in different solvents BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 2000/1014856 Yes unpublished		BASF
III A 8.3.1/1 *[Added in March 2010]*	Schroth E., Martin T.	2008c	Study on the residue behavior of BAS 490 F, BSA 480 F and BAS 421 F on barley and wheat after the application of BAS 493 05 F, BAS 480 31 F and BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2007 Agrologia SL; Palomares; Spain 2008/1043814 Yes unpublished		BASF
III A 8.3.1/2	Schroth E., Martin T.	2009a	Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on barley after the application of BAS 494 04 F, under field conditions in France (South), Greece, Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1090698 Yes unpublished	Y	BASF
III A 8.3.1/3	Schroth E., Martin T.	2009b	Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on wheat after the application of BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1090699 Yes unpublished	Y	BASF
III A 8.3.1/4	Beck J. et al.	1995	Study on the residue behaviour of BAS 494 02 F in cereals under field conditions in the Netherlands, Belgium, France, Great Britain and Germany, 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10327 Yes unpublished		BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.1/5	Beck J. et al.	1996	Study on the residue behaviour of Kresoxim-Methyl, Epoxiconazole and Fenpropimorph in cereals after treatment with BAS 493 02 F under field conditions in France and Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10113 Yes unpublished		BASF
III A 8.3.1/6	Krotzky A et al.	1994	Residue behaviour of BAS 490 04 F on cereals under field conditions in France, 1992 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11003 Yes unpublished		BASF
III A 8.3.1/7	Beck J. et al.	1994	Study on the residue behavior of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium and Germany, 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11004 Yes unpublished		BASF
III A 8.3.1/8	Beck J., Fegert A.	1994	Study on the residue behavior of BAS 490 04 F and BAS 492 01 F in cereals under field conditions in the Netherlands, Belgium, France and Germany, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1994/11005 Yes unpublished		BASF
III A 8.3.1/9	Schulz H.	1994a	Determination of the residues of LAB 242 009 in spring wheat following treatment with BAS 492 01 F under field conditions in Germany 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11080 Yes unpublished		BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.1/10	Schulz H.	1994b	Determination of the residues of LAB 242 009 in spring barley following treatment with BAS 492 01 F under field conditions in Germany 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11158 Yes unpublished		BASF
III A 8.3.1/11 *[Added in March 2010]*	Schroth E., Martin T.	2008d	Interim report: Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on barley after the application of BAS 494 04 F, under field conditions in France (South), Greece, Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1043812 Yes unpublished		BASF
III A 8.3.1/12 *[Added in March 2010]*	Schroth E., Martin T.	2008e	Interim report: Study on the residue behavior of BAS 480 F (Epoxiconazole) and BAS 490 F (Kresoxim-methyl) on wheat after the application of BAS 494 04 F, under field conditions in France (South), Italy and Spain, 2008 Agrologia SL; Utrera; Spain 2008/1047529 Yes unpublished		BASF

B.7.15.3 Plant protection product CANDIT (BAS 490 02 F)

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.1/1 *[Added in March 2010]*	Schulz H.	2008	Study on the residue behaviour of BAS 490 F in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern and Southern France, Italy and Spain 2007 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2008/1014860 Yes unpublished		BASF
III A 8.3.1/2	Schulz H.	2009	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern France, Southern France, Italy, Greece and Spain, 2008 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2009/1018523 Yes unpublished	Y	BASF
III A 8.3.1/2	Fuchs A. et al.	1996a	Study on the residue behaviour of Kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10698 Yes unpublished		BASF
III A 8.3.1/3	Fuchs A. et al.	1996b	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France and Spain, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10830 Yes unpublished		BASF
III A 8.3.1/4	Meumann H. et al.	1996	Study on the residue behaviour of Kresoxim-methyl in grapes after treatment with BAS 490 02 F under field conditions in France, Germany and Spain, 1996 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10890 Yes unpublished		BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.1/5 *[Added in March 2010]*	Schulz H.	2008	Interim report: Study on the residue behaviour of BAS 490 F in grapes after treatment with BAS 490 02 F under field conditions in Germany, Northern and Southern France, Italy and Spain, 2008 SGS Institut Fresenius GmbH; Taunusstein; Germany Fed. Rep. 2008/1043811 Yes unpublished		BASF
III A 8.3.1/6 *[Added in March 2010]*	Wofford J.T., Riley M.E.	1998	Magnitude of Kresoxim-Methyl residue in grapes - Additional sites in CA, NY, ID, and OR BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1998/5134 Yes unpublished		BASF
III A 8.3.1/7 *[Added in March 2010]*	Jackson S. et al.	1996	Magnitude of BAS 490 F residues in grapes BASF Corp. Agricultural Products Center; Research Triangle Park NC; United States of America 1996/5219 Yes unpublished		BASF
III A 8.3.2/1 *[Added in March 2010]*	Paleohorinos E., Rabe U.	1999	Kresoxim-methyl water dispersible granule 500 g/kg (BAS 490 02 F): Study on the residue behaviour of Kresoxim-methyl in apples after 8 treatment with BAS 490 02 F in Greece, 1997 Hoechst Schering AgrEvo Hellas SA; Maroussi; Greece 1999/10647 Yes unpublished		BASF
III A 8.3.2/2	Schulz H.	1994	Determination of the residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1993 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1994/11751 Yes unpublished		BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.2/3	Schulz H.	1995	Determination of the residues of LAB 242 009 in apples following treatment with BAS 490 02 F under field conditions in Italy 1994 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 1995/10054 Yes unpublished		BASF
III A 8.3.2/4	Fuchs A. et al.	1995	Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10082 Yes unpublished		BASF
III A 8.3.2/5	Fuchs A., Schulz H.	1995	Residue behaviour of BAS 490 02 F on pome fruit under field conditions in Germany, France, Spain, Belgium, The Netherlands and Great Britain 1994 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10418 Yes unpublished		BASF
III A 8.3.2/6 *[Added in March 2010]*	Schulz H.	2000a	Determination of the residues of BAS 490 F in pears following treatment with BAS 490 02 F under field conditions in Italy 1999 Institut Fresenius Chemische und Biologische Laboratorien GmbH; Taunusstein; Germany Fed. Rep. 2000/1000235 Yes unpublished		BASF
III A 8.3.2/7 *[Added in March 2010]*	Perny A.	2000a	Determination of Kresoxim-methyl residues in pears following treatment with the preparation BAS 490 02 F under field conditions in France in 1999 Anadiag SA; Haguenau; France 2000/1000239 Yes unpublished		BASF

OECD data point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
III A 8.3.2/8 *[Added in March 2010]*	Meumann H., Benz A.	2000a	Study on the residue behaviour of Kresoxim-methyl in pears after treatment with BAS 490 02 F under field conditions in France BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 2000/1000240 Yes unpublished		BASF
III A 8.5.3/1	Fuchs A. et al.	1996a	Study on the residue behaviour of Kresoxim-methyl in grapes and grape process fractions after treatment with BAS 490 02 F under field conditions in Germany, 1995 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1996/10698 Yes unpublished		BASF
III A 8.5.3/2	Fuchs A. et al.	1995	Residue behaviour of BAS 490 02 F on pome fruit and its processing products under field conditions in Germany, France, Belgium, The Netherlands and Spain, 1993 BASF AG Agrarzentrum Limburgerhof; Limburgerhof; Germany Fed.Rep. 1995/10082 Yes unpublished		BASF
III A 8.5.3/3 *[Added in March 2010]*	Wofford J.T. et al.	1998	The magnitude of Kresoxim-methyl residues in apple processed fractions - 30 day PHI program BASF Corporation Agricultural Products Center; Research Triangle Park, NC 27709-3528; United States of America 1998/5021 Yes unpublished		BASF

ANNEX B

Kresoxim-methyl

APPENDIX A: Metabolic pathways in plants and animals

Figure 1: Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in rats

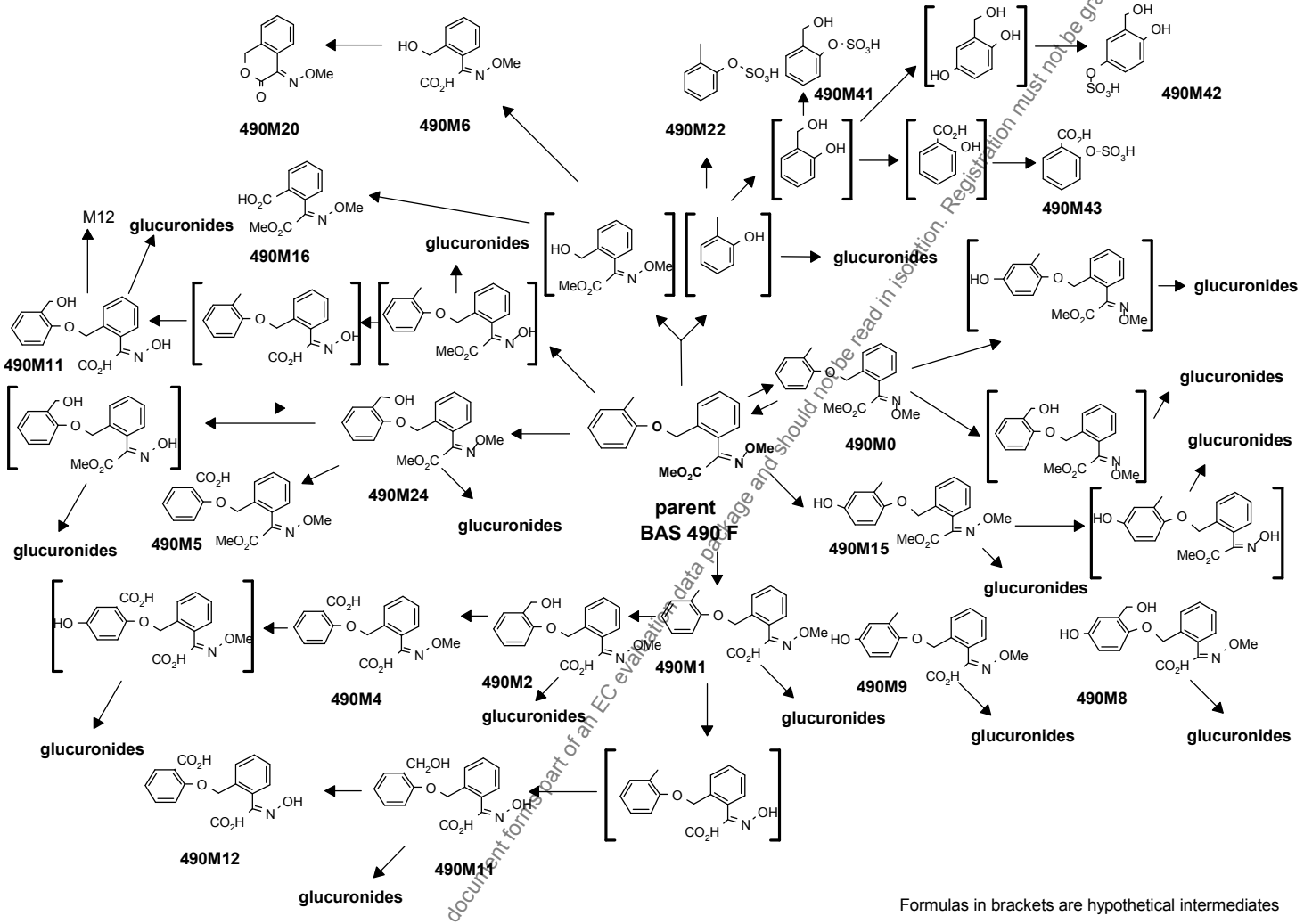


Figure 2 : Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in treated plants

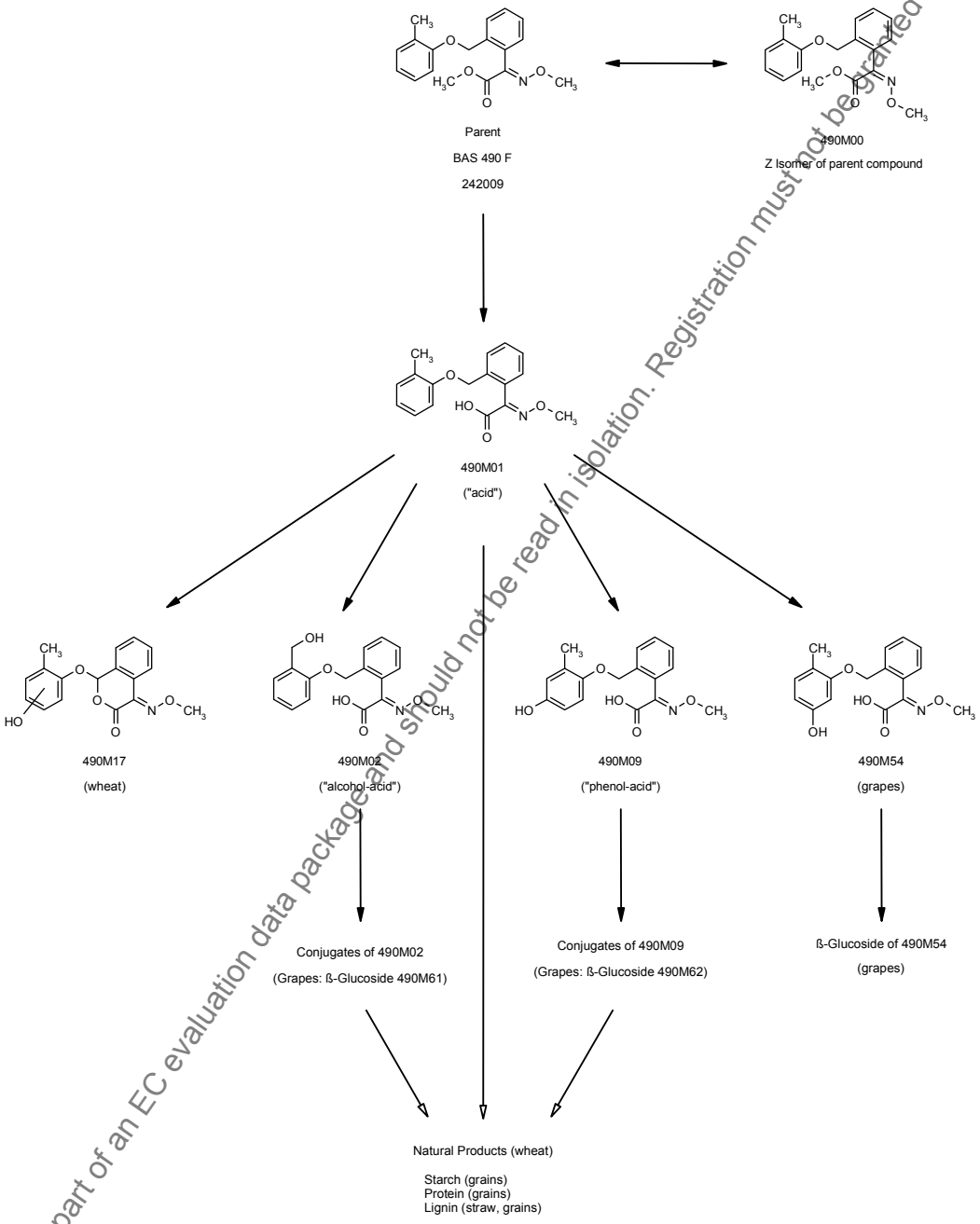


Figure 3 : Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in sugar beet

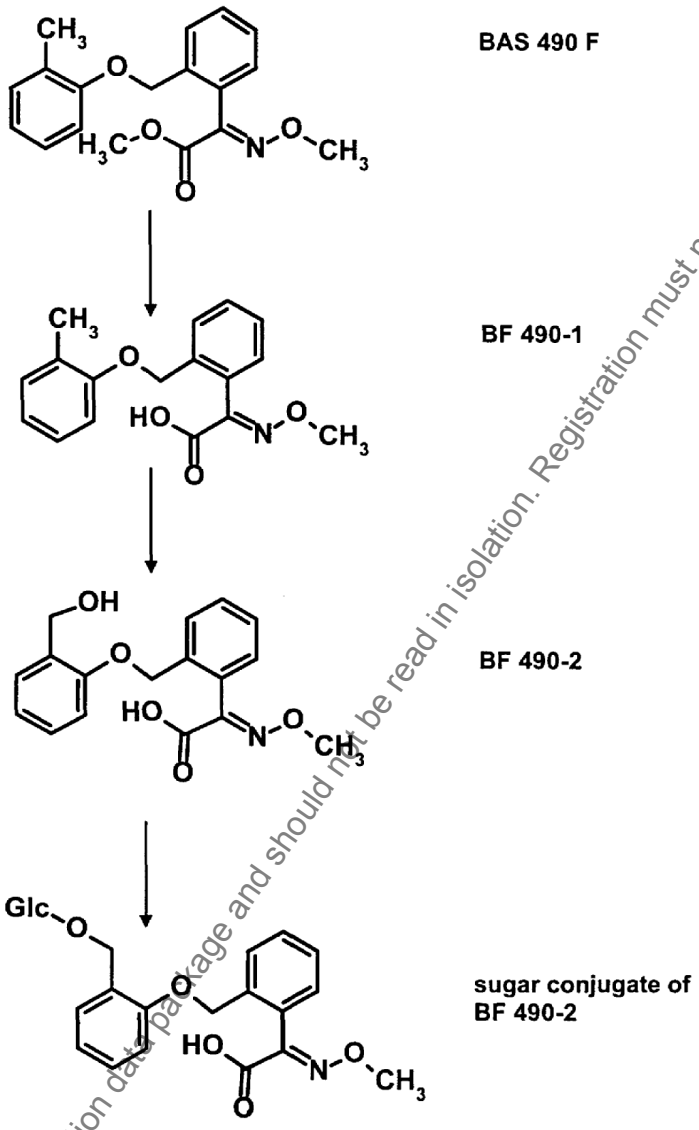


Figure 4: Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in succeeding crops

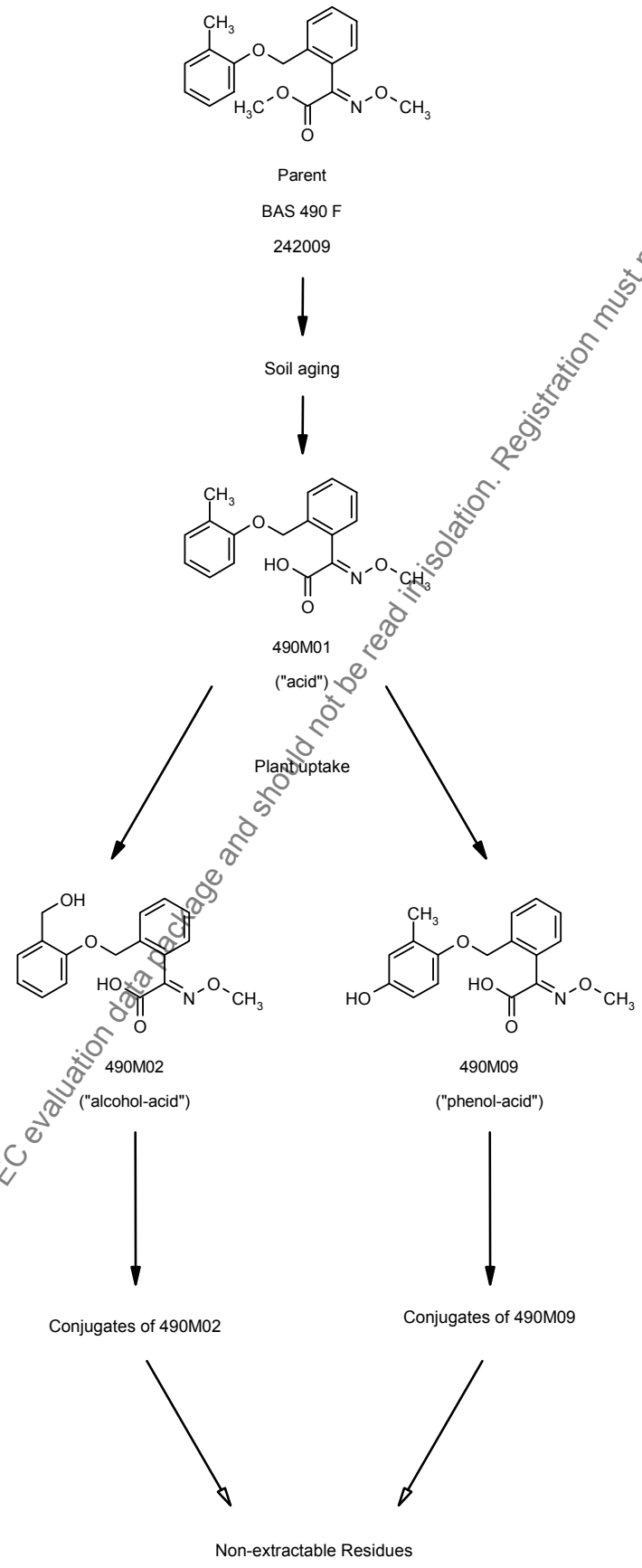
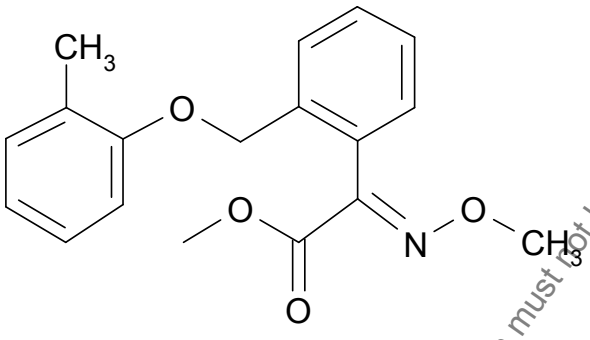
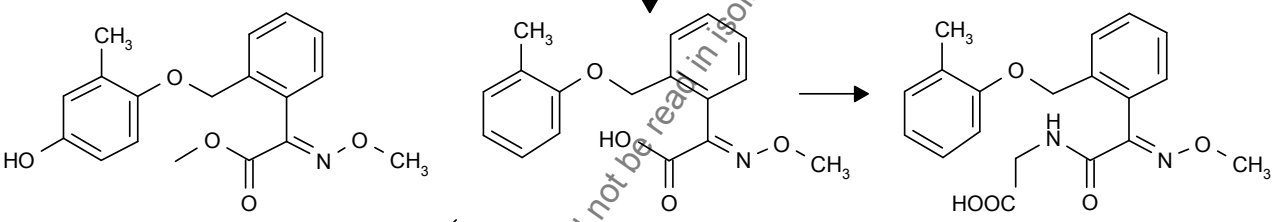


Figure 5 : Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in lactating goats.

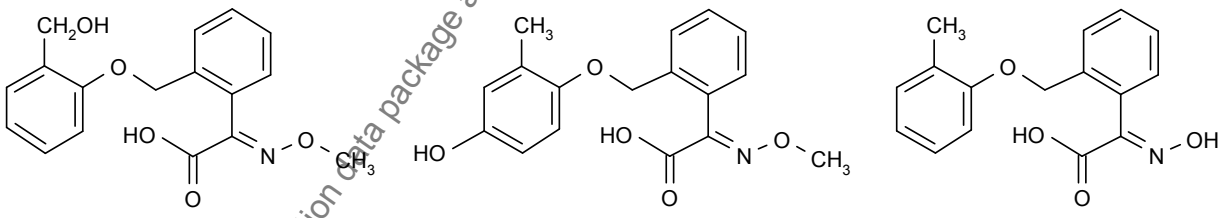


BAS 490 F

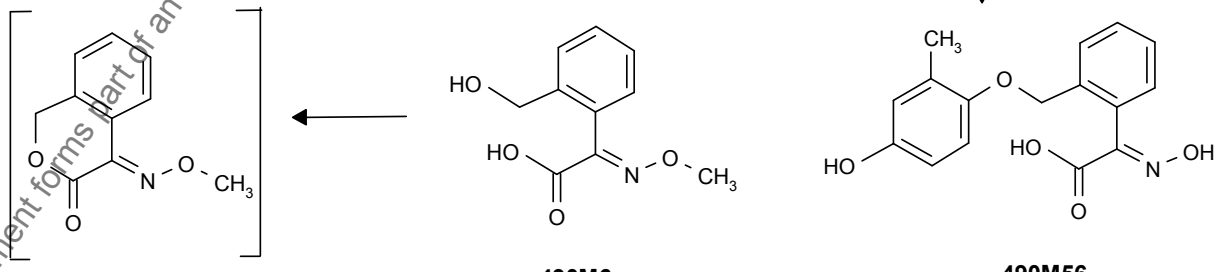
Fat



490M15 **490M1** **490M19**



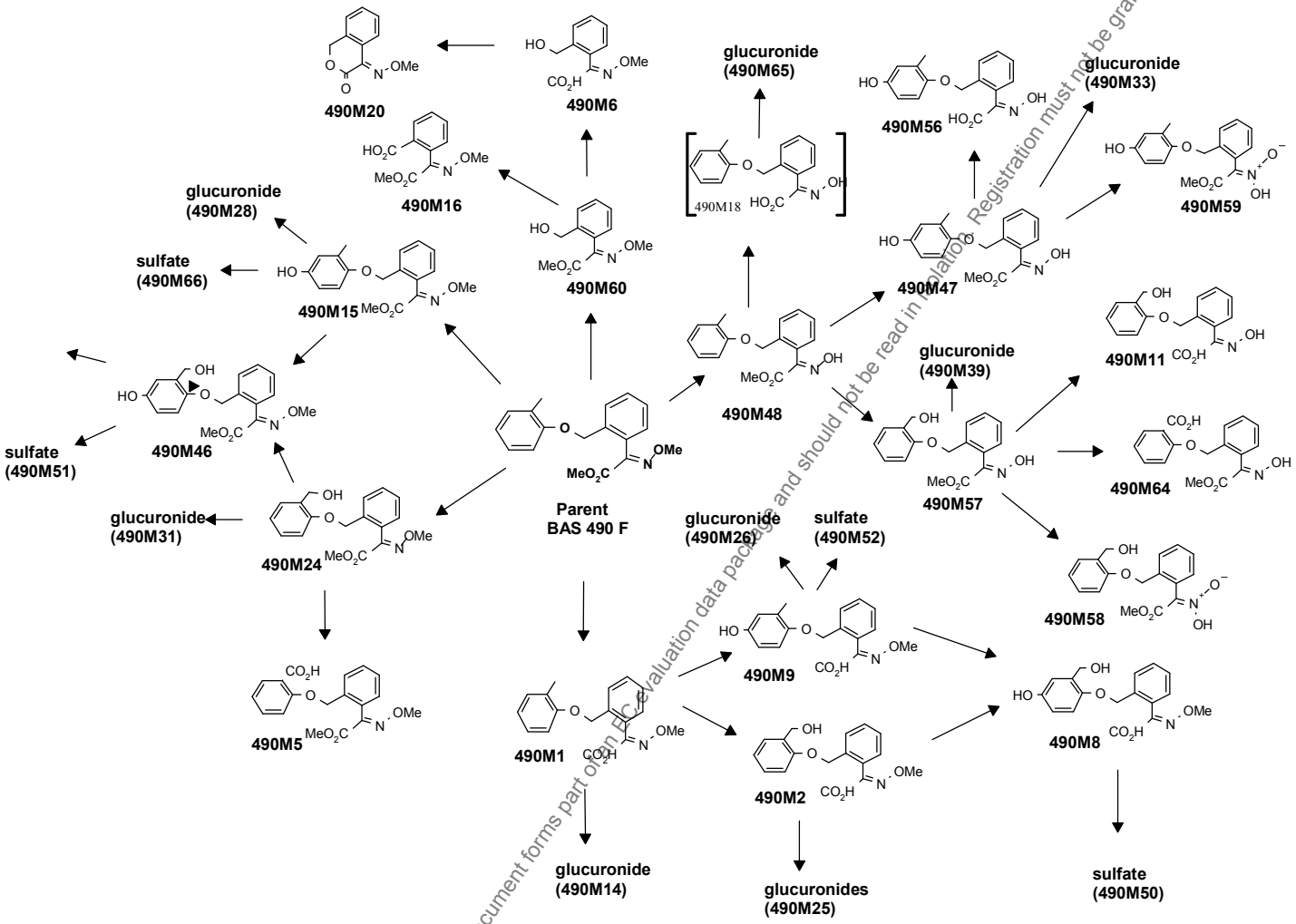
490M2 **490M9** **490M18**
(E/Z isomers)



490M20
(formed during work-up)

490M6 **490M56**

Figure 6 : Proposed metabolic pathway of Kresoxim-methyl (BAS 490 F) in laying hens.

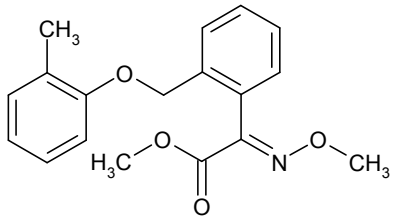
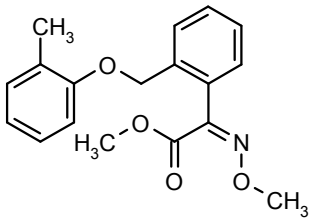
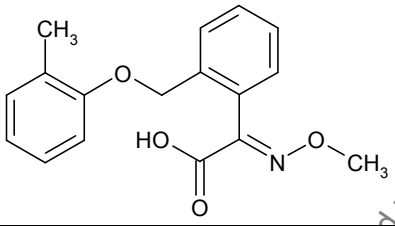
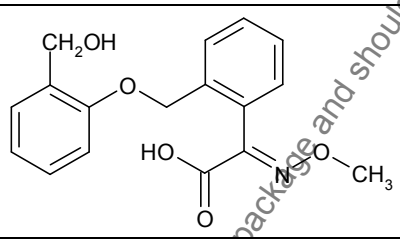
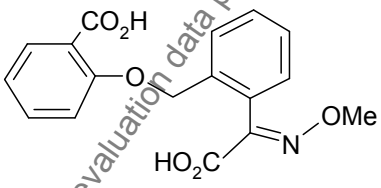
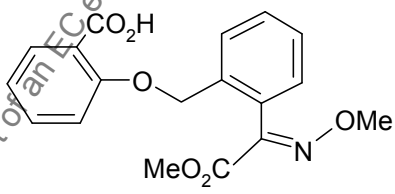


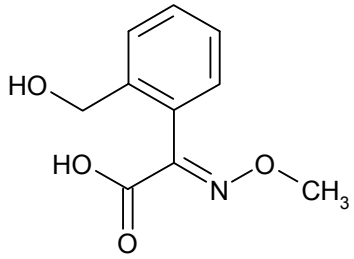
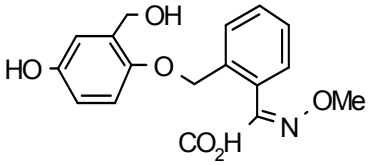
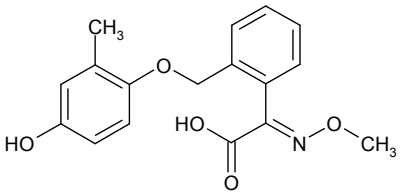
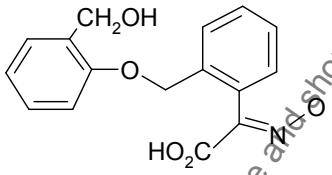
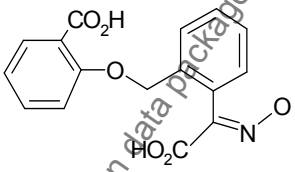
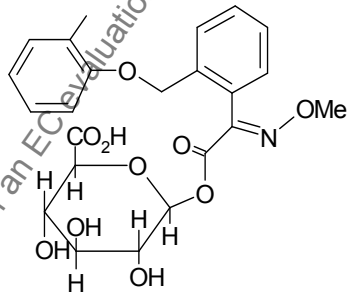
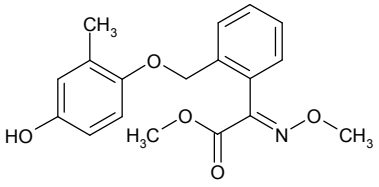
ANNEX B

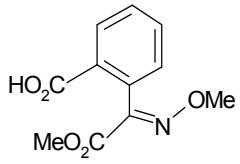
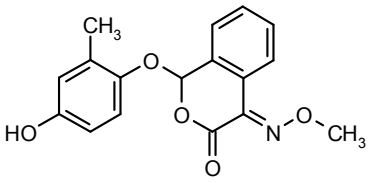
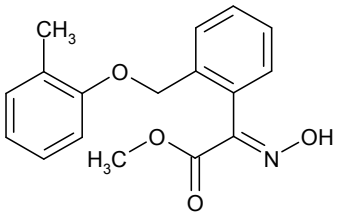
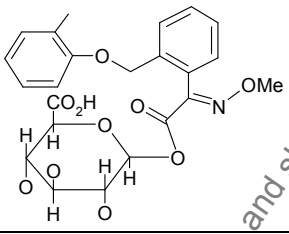
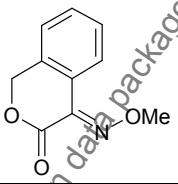
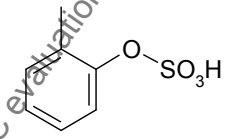
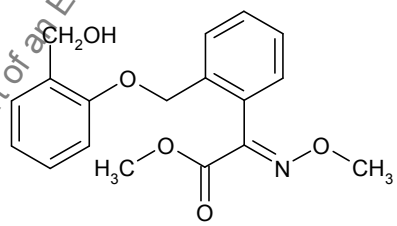
Kresoxim-methyl

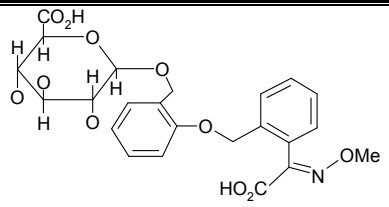
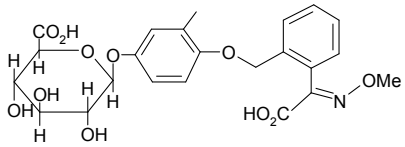
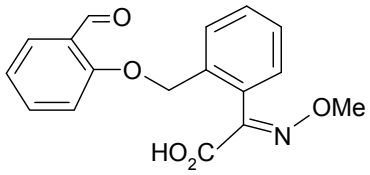
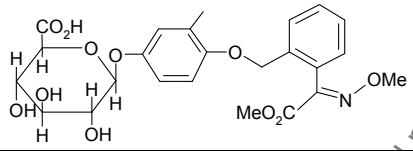
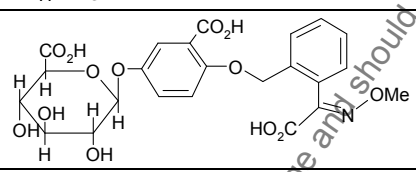
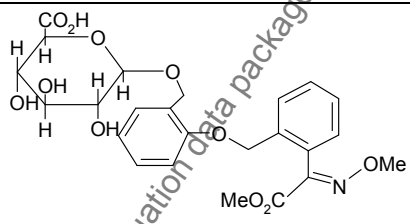
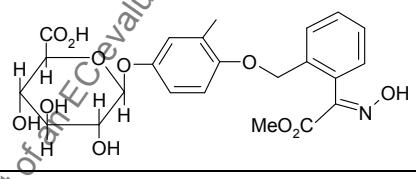
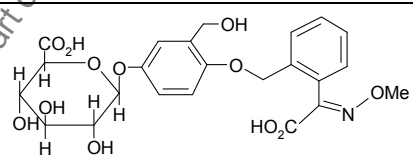
APPENDIX B:

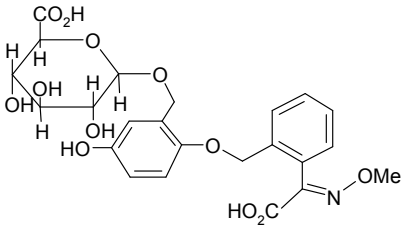
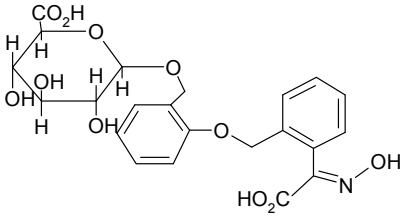
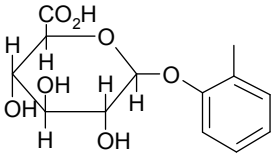
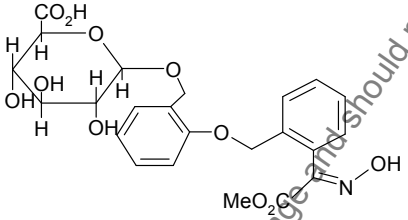
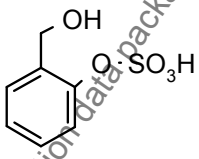
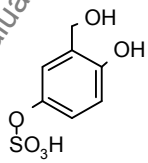
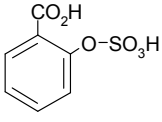
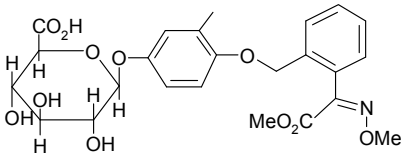
Occurrence of the metabolites identified in plant and animal metabolism studies

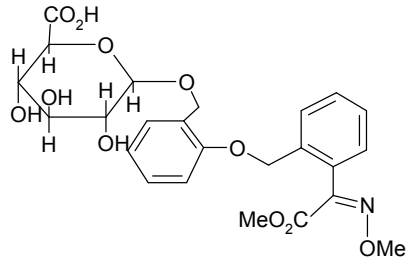
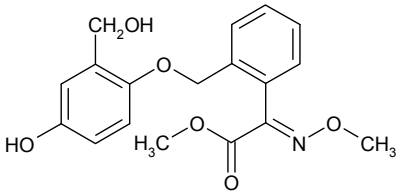
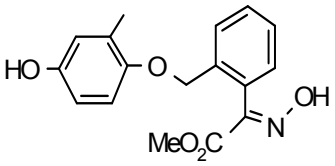
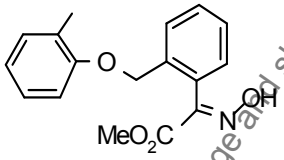
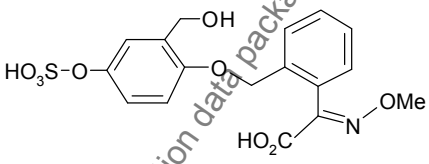
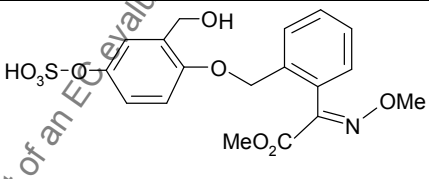
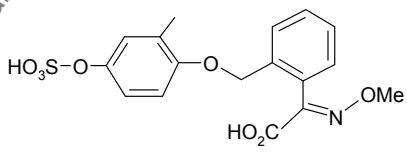
Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
Active ingredient BAS 490 F (Reg. No.: 242009)		+	+	+	+	+	+	+	(+)	+
490M00 (Reg. No.: 242010)		+			+	+				
490M01 BF 490-1 (Reg. No.: 262451)		+	+	+	+	+	+	+	+	+
490M02 BF 490-2 (Reg. No.: 291685)		+	+		+	+	+	+	+	+
490M04 BF 490-5 (Reg. No.: 286404)		+								
490M05		+		+						

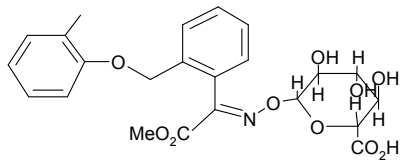
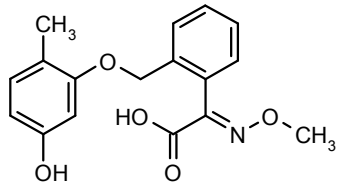
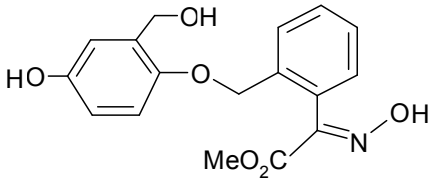
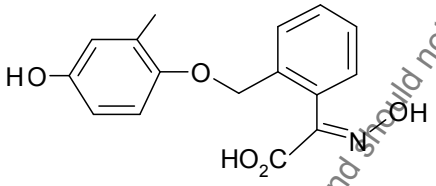
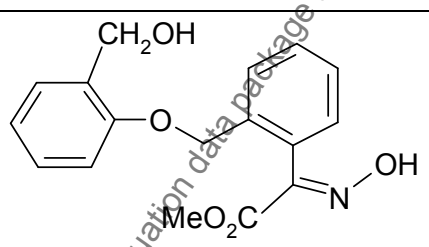
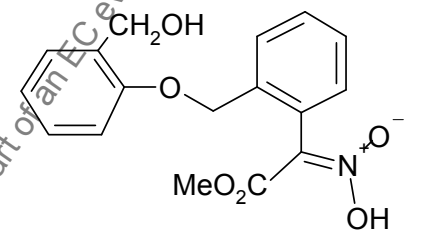
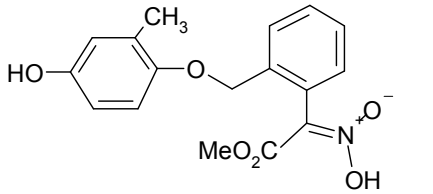
Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M06		+	+	+						
490M08 BF 490-11 (Reg. No.: 303218)		+		+						
490M09 BF 490-9 (Reg. No.: 292932)		+	+	+	+	+	+		+	
490M11		+		+						
490M12		+								
490M14		+		+						
490M15 BF 490-4 (Reg. No.: 299446)		+	+	+						

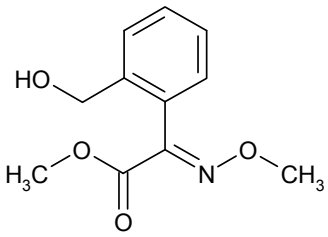
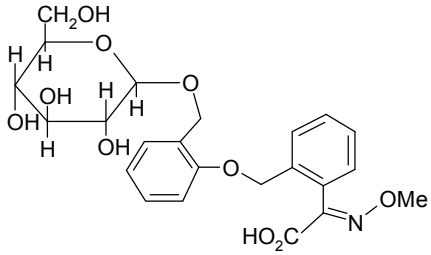
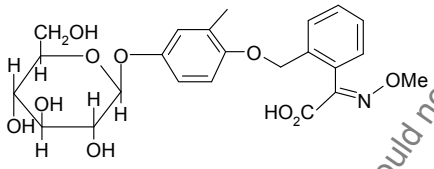
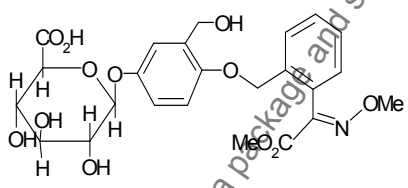
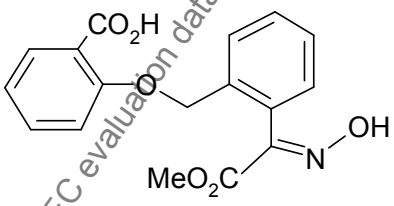
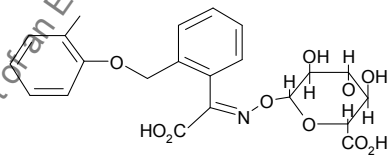
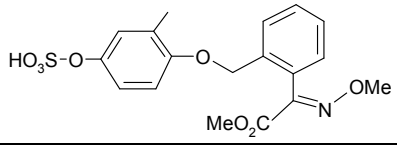
Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M16		+		+						
490M17					+					
490M18 BF 490-8 (Reg. No.: 299153)			+							
490M19			+							
490M20 BF 490-14 (Reg. No.: 271247)		+	+	+						
490M22		+								
490M24		+		+						

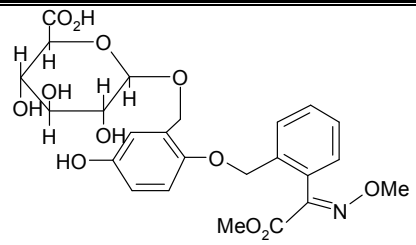
Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M25		+		+						
490M26		+		+						
490M27		+								
490M28		+		+						
490M29		+								
490M31		+		+						
490M33		+		+						
490M34		+								

Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M35		+								
490M36		+								
490M37		+								
490M39		+		+						
490M41		+								
490M42		+								
490M43		+								
490M44		+								

Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M45		+								
490M46				+						
490M47				+						
490M48 BF 490-03 (Reg. No.: 266042)				+						
490M50				+						
490M51				+						
490M52				+						

Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M53		+								
490M54 BF 490-15 (Reg. No.: 339774)							+			
490M55				+						
490M56			+	+						
490M57				+						
490M58				+						
490M59				+						

Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M60				+						
490M61							+			
490M62							+			
490M63				+						
490M64				+						
490M65				+						
490M66				+						

Metabolite: M-Code BF-Code (Reg. No.)	Structure	Rat	Goat	Hen	Wheat	Apple	Grape	Sugar beet	Confined Rot Crop	Hydro-lysis
490M67				+						

ANNEX B

Kresoxim-methyl

APPENDIX C:

Supervised Field Residue Trials – Summary sheets

An Excel file residue database on apples, pears, grapes and cereals is attached to this document.