Metiram

Amendment to the AIR dossier

NEGLIGIBLE EXPOSURE ASSESSMENT

Compiled by:

[redacted]

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number
29/Feb/2016	CA 6.1/1: Interim report 2014/1000228 replaced by final report 2015/1260660.	BASF Doc Id 2016/1051893
20/Jul/2018	CA, 6.2: detailed study summaries of plant and animal metabolism have been added; CA 6.5.3: information on storage interval period before analysis of grape processed commodities has been inserted; CA 6.6: scientifical sounded argumentation has been added; CA 6.10.1: assessment of relevance of metiram and its relevant degradation products in pollen and nectar has been reported	BASF Doc Id 2018/1102493
May 2019	Section MCA 6 has been modified, to demonstrate negligible exposure for potato use	BASF DocID 2019/1075956

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

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CA 6 RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED AND PLANT METABOLISM

During AIR 3 process, EFSA concluded on metiram ED properties. Despite the fact that BASF SE does not agree with EFSA conclusion, BASF SE has anyhow submitted an amendment to dossier to demonstrate that the use of metiram leeds to negligible exposure in the case of the representative formulated product on potato.

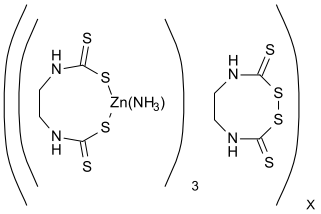
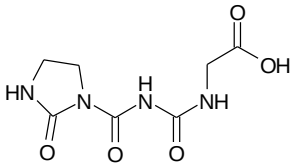
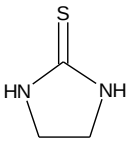
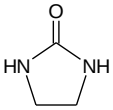
With focus on the representative formulated product with potato as the target crop (applications according to GAP), the dietary exposure to metiram was evaluated. Residue level in treated potato are expected to be lower than the LOQ. Therefore, dietary exposure can be expected to be negligible. In order to provide an **indicative estimation**, dietary exposure calculations were done using the LOQ as a worst case, yet unlikely, residue level. These calculations result in very low values chronic and acute exposure (maximal values are % ADI, 2% ARfD). To be noted, these numbers are theoretical calculations with various worst case assumptions: in practice, the realistic dietary exposure is well below these numbers (for details see Table 6.9- 3 in appendix)

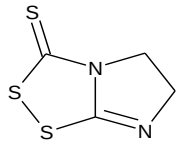
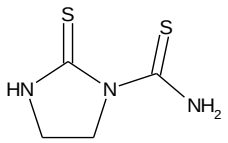
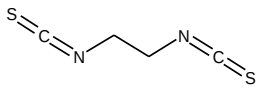
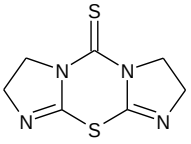
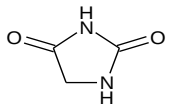
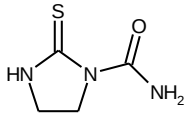
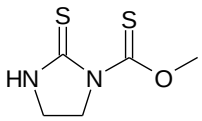
In addition, occurrence of the metiram metabolite ETU (resulting from GAP compliant use on potato) has been confirmed to be very low as well (see section 6.3, overview is provided in Table 6.3.1- 4), in 23 GAP compliant residue trials with STMR <0.01 mg/kg, thus below the LOQ. Residues in potato for consumption are expected to be even lower, since ETU is not stable over extended storage. Therefore, absence of ETU in potatoes as food commodities is expected. In conclusion, calculation of dietary exposure is not providing meaningful information and therefore was not done in the present dossier on negligible exposure.

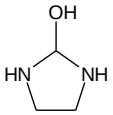
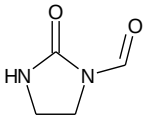
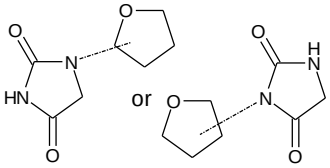
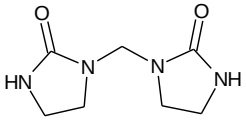
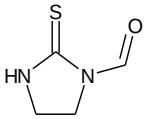
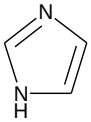
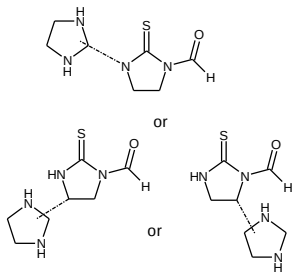
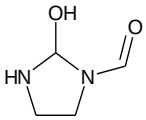
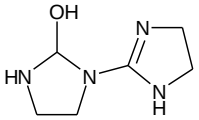
➔ Taken together, for potato as target crop, negligible exposure to metiram and its relevant metabolites is expected when considering the available data.

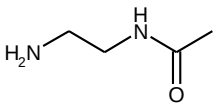
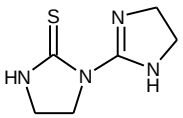
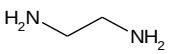
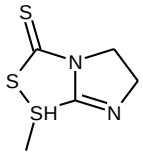
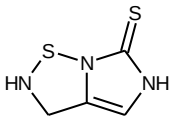
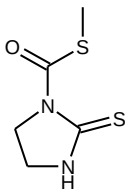
A concordance list of structures and designations of reference compounds used during Consumer Safety studies is given below.

An overview of metabolites identified during consumer safety studies is given below.

Code Numbers			Description	Compound found in	Structure
Substance/ Metabolite Code	**Reg No.**	**Synonyms/ Old nomenclature**	**Chemical Name CAS-No.**		
BAS 222 F	250284	M222F000 Metiram Metiram TK = Metiram TK 85 = Metiram Premix 95 = Metiram–Complex 95% = BAS 222 29 F	Zinc ammoniate ethylenebis (dithiocarbamate) – poly(ethylenethiouram disulfide) 9006-42-2		
M222F001	Not assigned	None	2-[(2-oxoimidazolidine-1-carbonyl)carbamoylamino]acetic acid No CAS available	Rotational Crop	
M222F002	146099	BF222-ETU ETU	2-IMIDAZOLIDINETHIONE; 4,5-Dihydro-1H-imidazol-2-thione 96-45-7	Plant, Animal	
M222F003	27270	BF222-EU EU	Imidazolidine-2-one ETHYLENEUREA 120-93-4	Plant, Animal	

Code Numbers			Description	Compound found in	Structure
Substance/ Metabolite Code	Reg No.	Synonyms/ Old nomenclature	Chemical Name CAS-No.		
M222F004	243959	BF 222-EBIS EBIS ETM	5,6-Dihydro-3H-imidazo-[2,1-c]-1,2,4-dithiazole-3-thione, DIDT Ethylene-bis-(isothiocyanate) sulfide Ethylenethiuram monosulfide, 33813-20-6	Plant, Animal	
M222F005	251072	BF222-Carbimid Carbimid ETT	2-thioxo-imidazolidinyl-thiocarboxamide 695-76-1		
M222F006	247214	BF222-EBIT EBIC	Ethylenediisothiocyanate 3688-02-08		
M222F007	4670450	TDIT M212	2,3,7,8-tetrahydrodiimidazo[2,1-b:1',2'-e][1,3,5]thiadizine-5-thione 75676-85-6	Plant	
M222F008	132345	Hydantoin	2,4-Imidazolidinedione 461-72-3	Plant, Animal,	
M222F009	Not assigned	None	2-thioxoimidazolidine-1-carboxamide No CAS available		
M222F010	Not assigned	None	O-methyl 2-thioxoimidazolidine-1-carbothioate No CAS available		
M222F011	70964	None	4,5-dihydro-1H-imidazole 504-75-6		

Code Numbers			Description	Compound found in	Structure
Substance/ Metabolite Code	Reg No.	Synonyms/ Old nomenclature	Chemical Name CAS-No.		
M222F012	Not assigned	None	2-Imidazolidinol 1628741-67-2		
M222F013	6014473	None	2-oxoimidazolidine-1-carbaldehyde 41731-11-7	Plant	
M222F014	Not assigned	None	No CAS available		
M222F015	6012392	None	1-1'-methanediyldiimidazolidin-2-one 13311-64-3		
M222F016	6014472	None	2-thioxoimidazolidine-1-carbaldehyde 954379-26-1		
M222F017	283749	None	1H-imidazole 288-32-4		
M222F018	Not assigned	None	No CAS available		
M222F019	Not assigned	None	2-hydroxyimidazolidine-1-carbaldehyde No CAS available		
M222F020	Not assigned	None	1-(4,5-dihydro-1H-imidazol-2-yl)imidazolidin-2-ol No CAS available		

Code Numbers			Description	Compound found in	Structure
Substance/ Metabolite Code	**Reg No.**	**Synonyms/ Old nomenclature**	**Chemical Name CAS-No.**		
M222F021	Not assigned	N-ac-EDA	N-acetyl-ethylenediamin 1001-53-2	Plant, Animal	
M222F022	6002546	Jaffe's base	1-(4,5-dihydro-1H-imidazol-2-yl)imidazolidine-2-thione 484-92-4	Plant, Animal	
M222F023	4183259	EDA Ethylenediamine	Ethane-1,2-diamine 107-15-3	Plant, Animal	
M222F024	Not assigned	None	1-methyl-5,6-dihydroimidazo[2,1-c][1,2,4]dithiazole-3-thione No CAS available	Rat	
M222F025	Not assigned	None	3,5-dihydro-2H-imidazo[1,5-b][1,2,5]thiadiazole-6-thione No CAS available	Rat	
M222F026	Not assigned	None	S-methyl 2-thioxoimidazolidine-1-carbothioate No CAS available	Rat	

CA 6.1 Storage stability of residues

The following information is copied from the Monograph prepared by RMS Italy in context of the Annex I inclusion of metiram.

Stability of residues (OECD data point numbers IIA 6.1 and IIIA 8.1)

Metiram is stable in plant matrix for at least 12 months and up to 18 months in grapes The stability of ETU depends on the matrix (stable up to 12 months in tomatoes and processed products, apple juice and sauce, wine; stable up to 3 months in grapes). Limited stability in potatoes –7 days-. Uncertain stability in apples, with recoveries of 0, 12 and 74% at 1 month in 3 different studies. Unknown stability in other crops. The stability of Metiram and ETU in animal matrix is 26 weeks.

Stability investigations for the determination of Metiram and ETU residues in food of plant and animal origin were evaluated in the context of the inclusion in Annex I under Directive 91/414/EEC. These studies evaluated previously are summarized in Table 6.1- 1 for the reviewer´s convenience.

Table 6.1- 1: Summary of peer-reviewed storage stability studies

Author.	Study	Crop/ Matrix	Analyte	Storage interval	Stable
Larese J. 1989	Storage stability of metiram and ethylenethiourea in frozen potatoes – Addendum: Twelve months ethylenethiourea and metiram stability Enviro-Bio-Tech Ltd., Bernville – USA BASF Aktiengesellschaft, Limburgerhof, Germany BASF DocID 1989/5086 GLP, Unpublished	Potato	Metiram ETU	12 months	yes no
Mamouni, A. 1994	Storage stability of metiram in white grapes RCC Umweltchemie AG, Itingen, Switzerland BASF Aktiengesellschaft, Limburgerhof, Germany BASF DocID 1994/11068 GLP, Unpublished	White grapes	Metiram	18 months	yes
Benz, A. et al 2002	Storage stability study of incurred ETU residues in potatoes. BASF AG, Agrarzentrum Limburgerhof, Limburgerhof, Germany BASF Aktiengesellschaft, Ludwigshafen, Germany BASF DocID 2002/1004096	potatos	ETU (incurred)	No residues found	-
Benz, A. et al 2002	Storage stability study of incurred ETU residues in grapes. BASF AG, Agrarzentrum Limburgerhof, Limburgerhof, Germany BASF Aktiengesellschaft, Ludwigshafen, Germany BASF DocID 2002/1012093	grapes	ETU (incurred)	3 months	yes
Christman, P.J. 1988	Determination of the Stability of Metiram and ETU residues in/on Animal Products Hazleton Laboratories America Inc., Madison USA BASF Aktiengesellschaft, Limburgerhof, Germany BASF DocID 1988/5127 Addendum: to BASF DocID 1988/5100 GLP, Unpublished.	food of animal origin	Metiram ETU	26 weeks	yes yes

Storage stability of food of animal origin

As no new feeding or any residue study of animal origin has been conducted, no new stability study in animal matrices has been executed.

Storage stability of food of plant origin

Multiple freezer storage stability investigations have been performed. The studies were performed applying two different techniques. Both of them are considered as equally suitable in the most recent OECD guideline.

- In the first type of studies, Metiram and its metabolites EU and EBIS were spiked to homogenised and coarsely ground plant material.

- In the second type of studies, the crops (mainly grapes) were treated with Polyram DF, the solo formulation of Metiram. The storage stability of incurred ETU residues was investigated over a period of time, but also depending on different homogenisation techniques. In parallel the Metiram residues were measured.

The entire information available summarised below. The results obtained confirmed the stability of Metiram under frozen conditions. The data indicate limited storage stability over a period of approximately 12 months when samples are stored as entire material. Homogenisation should occur immediately prior to residue analysis. The metabolites show a significant lower stability, depending on matrix type and processing methodology.

Report: CA 6.1/1
Meyer M., 2016
Storage stability Study of Metiram and its two Metiram metabolites (EU and EBIS) in plant matrices
2015/1260660
Guidelines: SANCO/825/00 rev. 8.1 (16 November 2010), EEC 7032/VI/95 rev. 5, OECD 506 (Oct. 2007), OECD-DOC ENV/MC/CHEM(98)17 Paris 1998
GLP: yes
(certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1. Test Material: Metiram (as EBDC and $CS_{2)}$, EU (M222F003), EBIS (M222F004)
Description: Metiram (as EBDC, $CS_{2)}$, EU and EBIS
Lot/Batch #: 93.6% / 92.7% (Metiram), 99.6% (EU), 95.5% (EBIS)
Purity: CP052744 / 300014 (Metiram), L83-48 (EU), L83-136 (EBIS)
CAS#: 9006-42-2 (Metiram), 75-15-0 (CS_2), 120-93-4 (EU), 33813-20-6 (EBIS)
Development code: Metiram: BAS 222 F
EU: M222F003
EBIS: M222F004
Spiking levels: 0.05 - 0.5 mg/kg (EBDC)
1.0 mg/kg (CS_2)
0.01 - 0.1 mg/kg (EU)
0.1 mg/kg (EBIS)

2. Test Commodity: Plant matrices
Crop: cucumber, onion, lettuce (CS_2 and EBDC)
rape seed, white bean, potato and grapes, lettuce (EU)
grapes, lettuces, potatoes (EBIS)
Type: not reported
Variety: not reported
Botanical name: *Brassica napus L., Phaseolus vulgaris L., Solanum tuberosum L., Vitis vinifera L., Lactuca sativa L., Allium cepa L., Cucumis sativus L.*
Crop parts(s) or processed commodity: not reported
Sample size: not reported

B. STUDY DESIGN AND METHODS

1. Test procedure

Metiram by EBDC

The storage stability test was carried out in 4 analytical assays, respectively in the time intervals of 0, 12, 18 and 24 months (+ 4 spare sets). The matrices to be tested for EBDC are cucumber, onion and lettuce. The specimens were sprayed with the test item Metiram at a mean concentration level of 3.2 mg/kg for onion, 0.9 mg/kg for lettuce and 0.3 mg/kg for cucumber. The specimens were stored at ≤ -18 °C and analyzed after different time intervals. In preparation of the storage stability the matrices were homogenized in the presence of dry ice.

Metiram by CS_2

The storage stability test was carried out in 4 analytical assays, respectively in the time intervals of 0, 12, 18 and 24 months (+ 4 spare sets). The matrices to be tested for Metiram via CS_2 are cucumber, onion and lettuce. The specimens were sprayed with the test item Metiram at a mean concentration level of 1.3 mg/kg for onion, 0.5 mg/kg for lettuce and 0.3 mg/kg for cucumber. The specimens were stored at ≤ -18 °C and analyzed after different time intervals. In preparation of the storage stability the matrices were homogenized in the presence of dry ice.

EU

The storage stability test was carried out in 7 analytical assays, respectively in the time intervals of 0, 1, 3, 6, 12, 18 and 24 months (+ 5 spare sets). The matrices to be tested for EU were lettuce (aqueous matrix), rape seed (oily matrix), white bean (protein containing matrix), potato (starch containing matrix) and grapes (acid matrix). The specimens were spiked with the test item EU at a concentration level of 0.1 mg/kg. The specimens were stored at ≤ -18 °C and analyzed after different time intervals. In preparation of the storage stability the matrices were homogenized in the presence of dry ice (with exception of the test matrix grapes).

. The matrices to be tested for EU were lettuce (aqueous matrix), rape seed (oily matrix), white bean (protein containing matrix), potato (starch containing matrix) and grapes (acid matrix). The specimens were spiked with the test item EU at a concentration level of 0.1 mg/kg. The specimens were stored at ≤ -18 °C and analyzed after different time intervals. In preparation of the storage stability the matrices were homogenized in the presence of dry ice (with exception of the test matrix grapes).

EBIS

Please note the following: At the start of the study no analytical method for EBIS was available, it was developed in study 389443 (IF-13/02308815) and the development turned out to be very complicated and time consuming. In order to meet the scheduled timelines of this study the storage specimens destined for the storage times 12, 18 and 24 months as well as the spare set 3 were prepared and stored deep frozen without having a valid method for EBIS.

During the development work and pretests hints were observed that EBIS might be unstable in the tested matrices. In order to test this, the spare set 3 was analyzed after a storage time of 72 days for the matrices for which a valid method was available at that point (grapes, lettuce and potato). The specimens were spiked with the test item EBIS at a concentration level of 0.1 mg/kg. The specimens were stored at ≤ -18 °C and analyzed after 72 days. In preparation of the storage stability the matrices were homogenized in the presence of dry ice (with exeption of the test matrix grapes).

2. Description of analytical procedures

The specimens were analysed for residues of Metiram according to BASF method No. L0089/01 and as carbondisulfide according to BASF method L0234/01. The residues of EU and EBIS were determined with method L0233/01.

Principle of BASF Method L0089/01:
The ethylene-bisdithiocarbamate (EBDC) moiety is formed out of BAS 222 F and extracted from the specimen with a buffer solution consisting of EDTA, cysteine, methanol and sodium hydroxide adjusted to pH 11.0. The formed ethylene-bisdithiocarbamate (EBDC) analyte is methylated with iodmethane prior to chromatography. Specimens are quantified by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The limit of quantitation (LOQ) of the method is 0.05 mg/kg, apart from rape seed, where the LOQ is 0.1 mg/kg.

Principle of method L0234/01:
Metiram is transformed to CS_2 by means of orthophosphoric acid. Subsequently, the CS_2 is transferred to isooctane with a flow of nitrogen.
The quantification was carried out using gas chromatography with mass spectrometric detection (GC-MS). The limit of quantitation (LOQ) of the method is 0.10 mg/kg (0.056 mg/kg expressed as CS_2). Two mass fragments were determined. One was used for evaluation, the other one for confirmation.

Principle of the Method L0233/01:
EU (Reg.No. 27270) is extracted from plant material with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol/water. After centrifugation, an aliquot is taken and the methanol is evaporated from the extract. The pH is adjusted to 8 before evaporating. The remaining water phase is cleaned by liquid/liquid partition (water/ethylacetate) on an Extrelut column. After concentration of the eluate, the residue is determined by LC-MS/MS. The limit of quantitation (LOQ) of the method is 0.01 mg/kg.

Principle of method L0233/01:
EBIS (Reg.No. 243959) is extracted from plant material with a mixture of acetonitril/formic acid (1000/1, v/v) in the presence of thiourea. After centrifugation, an aliquot is taken and cleaned by dispersive SPE against C18. The supernatant is used for the determination of EBIS by LC-MS/MS. The limit of quantitation (LOQ) of the method is 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Metiram (by EBDC)

Table 6.1- 2 shows the month zero results of Metiram (by EBDC), which were used as reference to calculate the residue recoveries [%] in Table 6.1- 3.

Table 6.1- 2: Month zero specimens for Metiram (by EBDC)

Matrix	Storage intervals [months]	EBDC residue level found				Month zero mean amount (mg/kg)
		Individual results (mg kg-1)				
Onion	0	3.08	3.71	3.33	2.83	3.24
Lettuce	0	0.997	0.508	1.12	1.15	0.944
Cucumber	0	0.365	0.337	0.345	0.299	0.336

The data used to assess the storage stability of Metiram (by EBDC) in onion, lettuce and cucumber are provided in Table 6.1- 3. The results are given in mg/kg and in % of month zero mean amount, and not corrected with procedural recoveries.

Table 6.1- 3: Storage stability of Metiram (by EBDC) in plant matrices

Matrix	Month	Residue Level found in Stored Sample					Recovery of freshly spiked specimens, (mean, %)
		Individual results (mg/kg)		Individual results (% of month zero mean amount)		Mean (% of month zero mean amount)	
Onion	12	2.8	3.3	88.1	102.4	**95.2**	87.9
	18	3.4	3.3	104.6	102.8	**103.7**	88.7
	24	3.2	3.3	98.0	102.9	**100.5**	84.5
Lettuce	12	0.111	0.092	11.7	9.7	**10.7**	86.7
	18	0.115	0.095	12.2	10.1	**11.1**	97.9
	24	0.065	0.069	6.9	7.3	**7.1**	87.5
Cucumber	12	0.132	0.150	39.1	44.5	**41.8**	85.3
	18	0.050	0.049	14.8	14.4	**14.6**	99.7
	24	0.032	0.037	9.5	11.1	**10.3**	97.4

The means of the procedural recoveries for Metiram (by EBDC) at 0.05 - 0.5 mg/kg are shown in Table 6.1- 4.

Table 6.1- 4: Means of procedural recoveries for Metiram (by EBDC)

Matrix	Storage intervals [months]	Recoveries EBDC [%]	
		Mean [%]	RSD [%]
Onion	12, 18, 24	87	2.5
Lettuce	12, 18, 24	91	6.6
Cucumber	12, 18, 24	94	8.0

RSD = Relative Standard Deviation

Metiram (by CS_2)

Table 6.1- 5 shows the month zero results of Metiram (by CS_2), which were used as reference to calculate the residue recoveries [%] in Table 6.1- 6.

Table 6.1- 5: Month zero specimens for Metiram (by CS_2)

Matrix	Storage intervals [months]	CS_2 residue level found				Month zero mean amount (mg/kg)
		Individual results (mg kg-1)				
Onion	0	1.21	1.29	1.24	1.33	1.26
Lettuce	0	0.659	0.525	0.448	0.424	0.514
Cucumber	0	0.376	0.386	0.309	0.303	0.343

The data used to assess the storage stability of Metiram (by CS_2) in onion, lettuce and cucumber are provided in Table 6.1- 6. The results are given in mg/kg and in % of month zero mean amount, and not corrected with procedural recoveries.

Table 6.1- 6: Storage stability of Metiram (by CS_2) in plant matrices

Matrix	Month	Residue Level found in Stored Sample					Recovery of freshly spiked specimens, (mean, %)
		Individual results (mg/kg)		Individual results (% of month zero mean amount)		Mean (% of month zero mean amount)	
Onion	12	1.0	1.0	79.9	82.1	**81.0**	87.2
	18	0.887	0.921	70.2	72.9	**71.5**	76.2
	24	0.840	0.801	66.5	63.4	**64.9**	79.5
Lettuce	12	0.570	0.587	110.9	114.3	**112.6**	97.9
	18	0.480	0.508	93.4	98.8	**96.1**	82.5
	24	0.425	0.491	82.8	95.6	**89.2**	86.5
Cucumber	12	0.108	0.094	31.5	27.5	**29.5**	78.0
	18	0.059	0.067	17.3	19.5	**18.4**	79.8
	24	0.048	0.049	13.9	14.3	**14.1**	82.3

The means of the procedural recoveries for Metiram (by CS_2) at 1.0 mg/kg are shown in Table 6.1- 7.

Table 6.1- 7: Means of procedural recoveries for Metiram (by CS_2)

Matrix	Storage intervals [months]	Recoveries CS_2 [%]	
		Mean [%]	RSD [%]
Onion	12, 18, 24	81	8.3
Lettuce	12, 18, 24	89	9.8
Cucumber	12, 18, 24	80	7.9

RSD = Relative Standard Deviation

EU

The data used to assess the storage stability of EU in rape seed, white bean, potato, grape and lettuce are provided in Table 6.1- 8.

Table 6.1- 8: Storage stability of EU in plant matrices

Matrix	Month	Residue Level found in Stored Sample					Recovery of freshly spiked specimens, (mean, %)
		Individual results (mg/kg)		Individual results (% of nominal)		Mean (% of nominal)	
Rape seed	0	0.078	0.081	77.6	80.8	**79.2**	83.3
	1	0.062	0.067	62.3	66.6	**64.5**	76.7
	3	0.040	0.053	40.3	52.8	**46.5**	84.3
	6	0.043	0.040	42.5	40.3	**41.4**	77.6
	12	0.053	0.051	52.9	51.2	**52.1**	109.3
	18	0.027	0.029	27.4	29.1	**28.3**	79.5
	24	0.039	0.040	39.0	40.3	**39.6**	75.2
White bean	0	0.069	0.064	69.3	63.6	**66.5**	74.5
	1	0.070	0.074	70.2	74.0	**72.1**	72.8
	3	0.094	0.064	93.7	63.6	**78.7**	70.6
	6	0.068	0.050	67.7	49.4	**58.6**	74.1
	12	0.078	0.077	78.2	77.0	**77.6**	98.2
	18	0.068	0.072	67.9	71.9	**69.9**	74.1
	24	0.080	0.067	80.1	66.9	**73.5**	70.9
Potato	0	0.082	0.077	82.2	77.4	**79.8**	85.2
	1	0.068	0.077	67.5	77.2	**72.3**	72.8
	3	0.081	0.082	80.4	81.5	**80.9**	86.3
	6	0.074	0.077	73.6	76.5	**75.1**	85.4
	12	0.076	0.081	75.9	80.7	**78.3**	91.1
	18	0.057	0.078	56.8	78.0	**67.4**	78.1
	24	0.083	0.084	83.0	84.0	**83.5**	95.5
Grapes	0	0.076	0.070	76.1	71.0	**73.5**	71.2
	1	0.049	0.061	48.8	60.7	**54.8**	68.7
	3	0.069	0.071	67.5	69.4	**68.5**	83.7
	6	0.064	0.053	63.4	52.7	**58.0**	85.7
	12	0.049	0.056	50.3	56.8	**53.6**	97.0
	18	0.048	0.034	47.8	33.2	**40.5**	96.5
	24	0.064	0.069	65.6	68.6	**67.1**	92.9
Lettuce	0	0.069	0.072	68.5	72.1	**70.3**	71.0
	1	0.075	0.078	74.9	77.5	**76.2**	81.3
	3	0.060	0.059	60.2	59.3	**59.8**	81.9
	6	0.055	0.049	54.8	49.1	**51.9**	94.7
	12	0.036	0.034	35.5	33.9	**34.7**	76.3
	18	0.035	0.032	34.4	31.8	**33.1**	101.5
	24	0.035	0.035	34.8	34.8	**34.8**	93.4

The means of the procedural recoveries for EU at 0.01 - 0.1 mg/kg are shown in Table 6.1- 9.

Table 6.1- 9: Means of procedural recoveries for EU

Matrix	Storage intervals [months]	Recoveries EU [%]	
		Mean [%]	RSD [%]
Rape seed	0, 1, 3, 6, 12, 18, 24	84	14
White bean	0, 1, 3, 6, 12, 18, 24	77	15
Potato	0, 1, 3, 6, 12, 18, 24	85	9
Grapes	0, 1, 3, 6, 12, 18, 24	85	14
Lettuce	0, 1, 3, 6, 12, 18, 24	86	13

RSD = Relative Standard Deviation

EBIS

The data used to assess the storage stability of EBIS in potato, grapes and lettuce are provided in Table 6.1- 10.

Table 6.1- 10: Storage stability of EBIS in plant matrices

Matrix	Days	Residue Level found in Stored Sample					Recovery of freshly spiked specimens, (mean, %)
		Individual results (mg/kg)		Individual results (% of nominal)		Mean (% of nominal)	
Potato	72	0.0060	0.0050	6.0	5.0	5.5	85.6
Grapes	72	0.0079	0.0099	8.3	9.7	9.0	104.4
Lettuce	72	0.0250	0.0240	24.9	24.3	24.6	91.8

The means of the procedural recoveries for EBIS at 0.1 mg/kg are shown in Table 6.1- 11.

Table 6.1- 11: Means of procedural recoveries for EBIS

Matrix	Storage intervals [days]	Recoveries EBIS [%]			
		Mean [%]	RSD [%]	Overall Mean [%]	Overall RSD [%]
Potato	72	86	-		
Grapes	72	104	-	94	9.2
Lettuce	72	92	-		

RSD = Relative Standard Deviation

III. CONCLUSION

The results obtained from this storage stability study indicate the following:
(based on non-corrected recoveries of the nominal content)

Metiram (measured via EBDC) is stable under deep frozen conditions (≤ -18 °C) in the tested matrix onion for the investigated time period of about 18 months, while Metiram (by EBDC) is not stable in the tested matrices lettuce and cucumber.
Metiram (by CS_2) is stable under deep frozen conditions (≤ -18 °C) in the tested matrices onion and lettuce for the investigated time period of about 18 months (lettuce 24 months), while Metiram (by CS_2) is not stable in the tested matrix cucumber.
The discrepancy for the stability of Metiram in lettuce is actually not explainable, because the principle of measurement should not have any influence on it. Taking into account the stable residue values for metriam within the stability study on incurred ETU residues (BASF DocID 2010/1169547), it can be assumed that Metiram is stable in lettuce at least for 12 months. Nevertheless the results of the EBDC-measurements have to be further clarified.

EU is stable under deep frozen conditions (≤ -18 °C) in the tested matrices white bean and potato for an investigated time period of about 12 months, 1 month in lettuce, but not stable in the tested matrices rape seed and grapes, not taking into account the procedural recoveries of freshly spiked specimens. If this is taken into account storage stability of 24 months for white bean, potato and grape, 3 months for lettuce as well as 1 month for rape seed may be provided.

EBIS is not stable under deep frozen conditions (≤ -18 °C) in the tested matrices potato, grapes and lettuce for the investigated time period of 72 days. As a results of these findings the investigation of the storage stability of EBIS in this study was cancelled and an investigation of the short term storage stability under deep frozen conditions (≤ -18 °C) was carried out in separate study (DocID 2014/1028661).

Report: CA 6.1/2
Schatz N., 2015a
Storage stability of the Metiram metabolite EBIS in plant matrices
2014/1028661
Guidelines: SANCO/825/00 rev. 8.1 (16 November 2010), OECD-DOC ENV/MC/CHEM(98)17 Paris 1998, EEC 7032/VI/95 rev. 5, OECD 506 (Oct. 2007)
GLP: yes
(certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1.
Test Material: EBIS (M222F004)
Description: EBIS
Lot/Batch #: L83-136
Purity: 96.7% / 95.5%
CAS#: 33813-20-6
Development code: EBIS: M222F004
Spiking levels: 0.1 mg/kg

2.
Test Commodity: Plant matrices
Crop: rape seed, white bean, potato, grapes, lettuce, onion and cucumber
Type: not reported
Variety: not reported
Botanical name: *Brassica napus L., Phaseolus vulgaris L., Solanum tuberosum L., Vitis vinifera L., Lactuca sativa L., Allium cepa L., Cucumis sativus L.*
Crop parts(s) or processed commodity: not reported
Sample size: not reported

B. STUDY DESIGN AND METHODS

1. Test procedure

The stability of EBIS in plant matrices (rape seed, white bean, potato, grapes, lettuce, onion and cucumber) under deep frozen conditions was investigated. The samples were spiked with the test item EBIS at a concentration level of 0.1 mg/kg. The samples were stored at ≤ -18 °C and analysed after different time intervals (0 to at least 60 days). In preparation of the storage stability, the matrices were homogenized in the presence of dry ice, with the exception of grapes, white beans and rape seeds. These matrices were not homogenized prior to the start of the storage stability as the BASF Method L0233/01 is performed with unhomogenized samples.

2. Description of analytical procedures

Samples were analysed with the BASF method L0233/01 (IF-13/02308815) which enables the quantification of residues of EBIS in different matrices.

Principle of the Method L0233/01:
EBIS is extracted with a mixture of acetonitrile/formic acid in combination with a thiourea solution. This step is followed by a clean-up step utilizing C18-EC. Samples are diluted with a solution of acetonitrile/H_2O/formic acid before being determined by LC-MS/MS.
The limit of quantitation (LOQ) of the method is 0.01 mg/kg.

II. RESULTS AND DISCUSSION

The data used to assess the storage stability of EBIS in rape seed, white bean, potato, grape, lettuce, onion, cucumber are provided in Table 6.1- 12.

Table 6.1- 12: Storage stability of EBIS in plant matrices

Matrix	Day	Residue Level found in Stored Sample					Recovery of freshly spiked samples, (mean, %)
		Individual results (mg/kg)		Individual results (% of nominal)		Mean (% of nominal)	
Rape seed	0	0.090	0.091	88.2	89.6	**88.9**	95.7
	3	0.023	0.024	22.9	23.2	**23.0**	91.8
	5	0.017	0.019	16.4	18.8	**17.6**	93.1
	7	0.015	0.015	14.9	15.3	**15.1**	98.4
	14	0.029	0.028	28.2	28.2	**28.2**	82.7
	31	0.020	0.017	20.3	16.8	**18.6**	88.2
	45	0.025	0.027	25.0	26.2	**25.6**	89.8
	60	0.017	0.016	16.5	15.4	**16.0**	110
White bean	0	0.089	0.092	88.0	90.3	**89.2**	95.5
	3	0.055	0.057	55.6	57.4	**56.5**	84.4
	5	0.058	0.075	58.6	74.0	**66.3**	97.6
	7	0.044	0.046	44.1	45.7	**44.9**	95.2
	14	0.047	0.043	47.4	42.9	**45.2**	84.7
	31	0.047	0.042	46.8	42.3	**44.5**	83.5
	45	0.057	0.057	57.1	57.0	**57.0**	98.6
	63	0.052	0.055	50.9	55.2	**53.0**	109
Potato	0	0.090	0.094	89.3	93.3	**91.3**	98.4
	3	0.032	0.029	31.4	29.3	**30.4**	98.3
	5	0.020	0.028	20.1	28.4	**24.3**	107
	7	0.020	0.020	20.1	19.7	**19.9**	83.9
	14	0.022	0.023	21.8	22.7	**22.3**	93.3
	31	0.016	0.023	16.4	23.1	**19.8**	105
	45	0.015	0.015	14.3	15.3	**14.8**	110
	67	0.0068	0.0077	6.7	7.7	**7.2**	96.5
Grapes	0	0.087	0.082	85.8	90.0	**87.9**	83.1
	3	0.063	0.068	62.2	70.5	**66.4**	93.8
	5	0.071	0.068	71.1	67.2	**69.1**	101
	7	0.055	0.055	54.5	56.5	**55.5**	78.7
	14	0.054	0.050	53.2	52.9	**53.0**	84.0
	31	0.036	0.032	36.4	31.8	**34.1**	87.3
	45	0.025	0.024	24.9	23.3	**24.1**	94.3
	67	0.016	0.016	17.0	16.8	**16.9**	104
Lettuce	0	0.099	0.093	97.6	91.9	**94.7**	83.1
	3	0.045	0.050	44.3	49.7	**47.0**	101
	5	0.045	0.039	44.4	38.4	**41.4**	98.0
	7	0.033	0.036	32.3	35.7	**34.0**	78.1
	14	0.038	0.050	37.3	48.9	**43.1**	95.1
	31	0.021	0.026	20.8	25.8	**23.3**	94.2
	45	0.041	0.043	40.6	42.1	**41.4**	110
	60	0.063	0.060	61.9	59.0	**60.5**	109

Matrix	Day	Residue Level found in Stored Sample					Recovery of freshly spiked samples, (mean, %)
		Individual results (mg/kg)		Individual results (% of nominal)		Mean (% of nominal)	
Onion	0	0.104	0.095	103	93.8	**98.2**	99.6
	3	0.053	0.059	52.2	59.1	**55.6**	101
	5	0.058	0.057	58.2	57.3	**57.8**	106
	7	0.040	0.043	39.8	42.2	**41.0**	87.4
	14	0.044	0.048	43.6	47.8	**45.7**	110
	31	0.034	0.037	33.9	37.1	**35.5**	103
	45	0.034	0.037	33.9	37.5	**35.7**	108
	60	0.049	0.044	48.9	43.6	**46.2**	102
Cucumber	0	0.099	0.101	97.6	101	**99.3**	97.1
	3	0.064	0.068	63.8	66.5	**65.1**	102
	5	0.057	0.048	56.8	47.7	**52.3**	103
	7	0.045	0.046	44.6	45.8	**45.2**	83.6
	14	0.050	0.055	49.6	55.0	**52.3**	93.1
	31	0.041	0.049	40.8	48.9	**44.8**	101
	45	0.041	0.041	40.8	40.0	**40.4**	102
	60	0.043	0.039	42.4	38.7	**40.6**	109

The results obtained from this storage stability study indicate that EBIS is not stable under deep frozen conditions (≤ -18 °C) in any of the tested matrices (rape seed, white bean, potato, grape, lettuce, onion, cucumber) for the investigated time period of about 60 days.
The decline in concentration of EBIS showed a similar progress in all matrices. A fast decrease in concentration of EBIS could be observed during the first 7 days of storage. After this time, the further decrease in concentration took place at a slower rate.

The means of the procedural recoveries at 0.1 mg/kg are shown in Table 6.1- 13.

Table 6.1- 13: Means of procedural recoveries

Matrix	Storage intervals [days]	Recoveries EBIS [%]	
		Mean [%]	RSD [%]
Rape seed	0, 3, 5, 7, 14, 31, 45, 60	94	8.7
White bean	0, 3, 5, 7, 14, 31, 45, 63	94	11.0
Potato	0, 3, 5, 7, 14, 31, 45, 67	99	8.5
Grapes	0, 3, 5, 7, 14, 30, 45, 67	91	10.0
Lettuce	0, 3, 5, 7, 14, 30, 45, 60	96	12.0
Onion	0, 3, 5, 7, 14, 31, 45, 60	102	7.7
Cucumber	0, 3, 5, 7, 14, 31, 45, 60	99	7.9

RSD = Relative Standard Deviation

III. CONCLUSION

The results obtained from this storage stability study indicate that EBIS is not stable under deep frozen conditions (≤ -18 °C) in any of the tested matrices (rape seed, white bean, potato, grape, lettuce, onion, cucumber) for the investigated time period of about 60 days. The decline in concentration of EBIS showed a similar progress in all matrices. A fast decrease in concentration of EBIS could be observed during the first 7 days of storage. After this time, the further decrease in concentration took place at a slower rate.

Report:	CA 6.1/3 Benz-Birck A. et al., 2011a Storage stability study of incurred ETU residues in lettuce 2010/1169547
Guidelines:	none
GLP:	yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1.

Test Material:	Metiram, ETU, BAS 222 28 F
Description:	Metiram (BAS 222 F), ETU, BAS 222 28 F (Metiram: 70% nominal, WG formulation)
Lot/Batch #:	2000-2
Purity:	not reported
CAS#:	9006-42-2, BAS 222 F
Development code:	Metiram: BAS 222 F ETU: M222F002
Spiking levels:	0.25 mg/kg (with exception of 0.5 mg/kg in sampling occasion 2, day 0 and 2.5 mg/kg in sampling occasion 4, day 1).

2.

Test Commodity:	Lettuce (Leaf vegetables, herbs and edible flowers)
Crop:	Lettuce
Type:	not reported
Variety:	not reported
Botanical name:	*Lactuca sativa L.*
Crop parts(s) or processed commodity:	head
Sample size:	12 heads (min. 4 kg)

B. STUDY DESIGN AND METHODS

1. Test procedure

During the 2001 growing season, one field trial was conducted in a representative lettuce growing area in Germany, in order to provide lettuce specimens with incurred residues of ethylenethiourea (ETU), a common metabolite of all ethylenebisdithiocarbamates, for assessing the storage stability in lettuce. In addition, this study also investigated whether or not the method of specimen preparation and the degree of homogenisation (size of surface) had any influence on the rate of degradation.
The aim was to generate sufficiently high (quantifiable) ETU residues in the lettuce specimens. Therefore application rates were significantly exaggerated compared to the usual agricultural practice (GAP) used and the sampling regime corresponded with a worst case scenario. The test item BAS 222 28 F (70% Metiram, WG) was applied four times to head lettuce at a rate of 2.24 kg as/ha (3.2 kg of formulated product/ha). The first application was carried out on 21.05.2001 followed by three further applications 7, 18 and 28 days later. The spray volume used was 400 L/ha.
Head lettuce specimens from the control plot were collected immediately before the 2nd application, at sampling occasion 1. Head lettuce specimens from the treated plot were collected at 3 and 8 days after the 2nd application at sampling occasions 2 and 3. Due to the low residue level in specimens collected at sampling occasion 3, a 3rd application and, after analysis of residue levels at sampling occasion 4, a 4th application was performed. Sampling 6 was performed 3 days after the fourth application. Sampling occasions 2 (3DAA2), 4 (3DAA3) and 6 (3DAA4) were used for investigations on specimen preparation and storage stability.

In order to compare three different methods of specimen preparation, the specimens were either stored unprocessed as entire field specimens and processed under frozen conditions with a wooden hammer on the day of analysis ("F") or were prepared on the day of sampling. Therefore, the lettuce heads of three specimens were segmented into three pieces with a ceramic knife. The thirds were allocated to three mixed samples, which were processed by the following three methods:
1. The sample material was cut into small pieces with a ceramic knife ("MA").
2. The sample material was homogenized with a commercial mill ("MB").
3. The sample material was homogenized with a Stephan mill after addition of dry ice ("MC").

The processed samples were aliquoted and stored frozen until analysis. In addition, control samples, which were prepared from untreated specimens with a ceramic knife on the day of sampling, were aliquoted, frozen and analyzed with each measurement series.
For the storage stability investigation, analysis of ETU was planned on 0, 1, 3 (±2), 7 (±2), 14 (±2), 28 (±2), 42 (±2), 56 (±2), 84 (±7), 112 (±7), 140 (±7), 168 (±7), 230 (±7), 365 (±14) days of storage. This report is the final report describing the result up to 358 days after sampling occasion 2 and up to 396 days after sampling occasion 6, respectively.

2. Description of analytical procedures

The samples were analysed for ETU using BASF method No. 373/1 with some adjustments. These adjustments are incorporated into the revised method 373/2. The validated LOQ of the revised method No. 373/2 was 0.01 mg/kg. In the current study, individual results were extrapolated to the LOQ of 0.01 mg/kg.
Principle of BASF Method no. 373/1: ETU was extracted from the plant material with a mixture of sodium ascorbate, ethyleneurea, ammonium chloride and methanol-water. After centrifugation an aliquot was taken and the methanol was evaporated from the extract. The pH was adjusted to 8 before evaporating. The remaining water phase was cleaned by liquid/liquid (water/dichloromethane) partition on an Extrelut/Al_2O_3 column. After concentration of the eluate, the residue was determined by HPLC using pulsed amperometric detection.

The mean procedural recovery was 76% at a fortification level of 0.25 mg/kg (with exception of 0.5 mg/kg in sampling occasion 2, day 0 and 2.5 mg/kg in sampling occasion 4, day 1).

Before storage, the processed samples were also analysed for Metiram in order to evaluate the initial residue level. The analysis was conducted using BASF method No. 135/4 which determines the active ingredient as CS_2. The limit of quantitation of the method is 0.05 mg/kg. The mean procedural recovery was approximately 81% at a fortification level of 0.5 or 5.0 mg/kg.
Principle of BASF Method no. 135/4: Carbon disulphide was released from Metiram and comparable substances by heating with hydrochloric acid and tin chloride. Reaction with the anion of methanol formed by KOH lead to the formation of a xanthogenate which was determined photometrically at 302 nm. The limit of quantitation is 0.05 mg/kg Metiram for all matrices.

II. RESULTS AND DISCUSSION

Sampling occasion 2 (3 days after the 2nd application)

The corrected initial mean ETU values of lettuce samples after processing with a ceramic knife ("MA") were 0.274 mg/kg, with a commercial mill 0.160 mg/kg and with dry ice in a Stephan mill ("MC") 0.120 mg/kg. The field specimen ("F") stored unprepared for one day and crushed in frozen state with a wooden hammer showed a corrected initial mean value of 0.115 mg/kg.

"MA": The individual results of the ETU concentration in samples stored after processing with a ceramic knife showed a considerable variation. The residue level decreased to values lower than 70% of the corrected initial mean values, but increased again to 75% on storage day 42 and to 69% on storage day 172.

"MB": The residue levels in samples stored after processing with a commercial mill showed a significant decrease and ranged between 21% and 59% of the corrected initial mean values.

"MC": The individual results in samples stored after processing with dry ice in a Stephan mill apparently showed increased residue levels at several storage intervals. The stability was demonstrated over the investigated time period of more than one year.

"F": The individual results in specimens stored unprepared and crushed in frozen state with a wooden hammer showed an apparent increase of the residue level at the majority of storage intervals. The stability was demonstrated for the investigated time interval of more than one year.

Procedural recoveries were recorded for every storage interval and ranged between 48.8% (storage day 5) and 117.95% (storage day 1) for sampling occasion 2. A degradation curve was simulated from the results of measurement series with procedural recoveries over 70% with corrected values. The most evident results are:

- The unprepared field samples ("F") and the samples processed with dry ice in a Stephan mill ("MC") showed the best storage stability over a year and a flat curve at a high residue level (calculated stabilities of "F": 2221 days and "MC": 1553 days, 70% of initial value).
- After homogenisation with a ceramic knife ("MA"), the residue levels started with the highest values, after storage a degradation to a residue level of approx. 0.13 mg/kg was observed
- For samples prepared with a commercial mill ("MB") a rapid decline to a low residue level of approx. 0.05 mg/kg was observed

The data used to assess the storage stability of ETU in lettuce treated with BAS 222 28 F at sampling occasion 2 are provided in Table 6.1- 14.

Table 6.1- 14: Residues of ETU in stored lettuce at sampling occasion 2

Processing Method	Day	ETU Residue level					Procedural recovery (mean, %)
		Individual results (mg/kg)		% of mean value day 0		Mean value of % of day 0	
Process MA (ceramic knife)	0[1]	0.272	0.276	99	101	**100**	101.6
	Mean value day 0: 0.274						
	1	0.165	0.228	60	83	**72**	114.9
	5	0.128	0.120	47	44	**45**	51.7
	7	0.174	0.179	64	66	**65**	75.5
	13	0.090	0.109	33	40	**36**	94.7
	28	0.118	0.145	43	53	**48**	81.1
	42	0.169	0.244	62	89	**75**	(95.5)[2]
	56	0.097	0.090	36	33	**34**	71.5
	85	0.132	0.123	48	45	**47**	81.0
	112[3]						
	138	0.078	0.105	28	38	**33**	64.3
	172	0.158	0.220	58	81	**69**	65.9
	230	0.131	0.123	48	45	**47**	66.6
	358	0.069	0.061	25	22	**24**	73.0
Process MB (commercial mill)	0[1]	0.181	0.139	113	87	**100**	101.6
	Mean value day 0: 0.160						
	1	0.034	0.032	21	20	**21**	114.9
	5	0.035	0.039	22	25	**23**	51.7
	7	0.063	0.072	40	45	**42**	75.5
	13	0.030	0.047	19	29	**24**	94.7
	28	0.030	0.051	19	32	**25**	81.1
	42	0.060	0.073	37	45	**41**	(95.5)[2]
	56	0.059	0.058	37	36	**37**	71.5
	85	0.058	0.055	36	34	**35**	81.0
	112[3]						
	138	0.048	0.040	30	25	**28**	64.3
	172	0.085	0.104	53	65	**59**	65.9
	230	0.074	0.059	46	37	**42**	66.6
	358	0.036	0.049	23	31	**27**	73.0
Process MC (Stephan mill/dry ice)	0[1]	0.109	0.131	91	109	**100**	101.6
	Mean value day 0: 0.120						
	1	0.203	0.167	169	139	**154**	114.9
	5	0.207	0.182	173	151	**162**	51.7
	7	0.218	0.192	181	160	**171**	75.5
	13	0.045	0.027	37	22	**30**	94.7
	20[4]	0.086	0.121	71	101	**86**	68.8
	28	0.209	0.141	174	117	**146**	81.1
	42	0.331	0.494	275	411	**343**	(95.5)[2]
	56	0.125	0.114	104	95	**99**	71.5
	85	0.157	0.144	131	120	**125**	79.9
	112[3]						
	138	0.068	0.061	57	51	**54**	77.7
	172	0.159	0.223	132	185	**159**	65.9
	230	0.115	0.222	96	185	**140**	80.0
	358	0.112	0.136	93	113	**103**	96.2

Processing Method	Day	ETU Residue level					Procedural recovery (mean, %)
		Individual results (mg/kg)		% of mean value day 0		Mean value of % of day 0	
Field (F) Specimen (unprepared)	0						
	1[1]	0.106	0.123	92	108	**100**	114.9
	Mean value day 1: 0.115						
	5	0.205	0.151	178	132	**155**	51.7
	7	0.145	0.185	127	161	**144**	75.5
	13	0.205	0.259	178	225	**202**	94.7
	28	0.165	0.128	144	112	**128**	81.1
	42	0.109	0.128	95	112	**103**	(95.5)[2]
	56	0.093	0.082	81	71	**76**	71.5
	85	0.116	0.274	101	239	**170**	81.0
	112[3]						
	138	0.046	0.101	40	88	**64**	64.3
	172	0.175	0.146	153	128	**140**	78.3
	230	0.117	0.115	102	100	**101**	66.6
	358	0.074	0.097	65	85	**75**	73.0

1 values of individual results corrected with procedural recovery
2 one procedural recovery determined only
3 analysis of sampling occasion 2, day 112 ± 7 was not reported due incorrect fortification
4 sampling occasion 2, storage day 20: samples prepared according to method "MC" measured only

Additionally, processed lettuce samples and the corresponding unprepared field specimens were analysed for Metiram after six storage intervals. Lettuce samples prepared according to method "MB" showed the lowest residue level of Metiram.

The initial BAS 222 F residues of lettuce from sampling occasion 2 are presented in Table 6.1-15.

Table 6.1- 15: Residues of Metiram and CS_2 in lettuce at sampling occasion 2

Day	Process MA		Process MB		Process MC		Field specimens F	
	Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]
0	15.14	8.47	13.86	7.75	14.82	8.29	15.14	8.47
	16.55	9.26	12.89	7.21	15.07	8.43	16.55	9.26
13	14.68	8.22	7.61	4.26	13.79	7.71	16.64	9.31
	14.53	8.13	9.84	5.50	13.22	7.40	18.11	10.13
42	10.24	5.73	11.03	6.17	15.07	8.43	16.15	9.03
	12.94	7.24	10.38	5.81	13.34	7.46	12.83	7.18
172	10.86	6.08	7.99	4.47	7.55	4.23	11.79	6.59
	9.79	5.48	7.51	4.20	9.97	5.58	12.38	6.93
230	14.11	7.86	12.13	6.74	13.01	7.26	13.38	7.48
	10.59	5.87	11.49	6.37	12.95	7.24	17.58	9.77
362	11.19	6.26	7.85	4.39	10.89	6.09	11.27	6.31
	11.98	6.71	7.76	4.34	10.74	6.01	12.48	6.98

1 calc. factor Metiram to CS_2: 0.5595
n.m. not measured

Sampling occasion 3 (8 days after the 2nd application)
The determination of the ETU concentration in samples processed according to method "MA" showed a considerably decreased residue level (< 0.05 mg/kg). These results indicate that a fast degradation or metabolism of ETU occurred on the field. Metiram was therefore applied for a third time.

Sampling occasion 4 (3 days after the 3rd application)
Five storage intervals were analysed after the third application. The residue levels were still shown to be low and a fourth application was carried out. The further investigation of the stored samples was cancelled.

The data used to assess the storage stability of ETU in lettuce treated with BAS 222 28 F at sampling occasion 4 are provided in Table 6.1- 16.

Table 6.1- 16: Residues of ETU in stored lettuce at sampling occasion 4

Processing Method	Day	ETU Residue level					Procedural recovery (mean, %)
		Individual results (mg/kg)		% of mean value day 0		Mean value of % of day 0	
Process MA (ceramic knife)	0[1]	0.105	0.097	104	96	**100**	94.7
	Mean value day 0: 0.101						
	1	0.071	0.060	70	60	**65**	110.6
	2	0.028	0.013	28	13	**20**	70.0
	7	0.052	0.071	52	70	**61**	(54.0)[2]
	14	0.028	< 0.01	28	n.a.	**28**	40.8
Process MB (commercial mill)	0[1]	0.105	0.101	102	98	**100**	94.7
	Mean value day 0: 0.103						
	1	0.057	0.052	55	50	**53**	110.6
	2	0.015	< 0.01	15	n.a.	**15**	70.0
	7	0.047	0.060	46	59	**52**	(54.0)[2]
	14	0.010	0.015	10	15	**12**	40.8
Process MC (Stephan mill/dry ice)	0[1]	0.040		100		**100**	94.7
	1	0.116	0.081	287	200	**243**	110.6
	2	0.024	< 0.01	60	n.a.	**60**	70.0
	7	0.203	0.030	503	73	**288**	(54.0)[2]
	14	0.047	< 0.01	116	n.a.	**116**	40.8
Field (F) Specimen (unprepared)	0						
	1[1]	0.115	0.106	104	96	**100**	110.6
	Mean value day 1: 0.111						
	2	0.089	0.078	81	71	**76**	70.0
	7	0.051	0.060	46	54	**50**	(54.0)[2]
	14	0.067	0.015	61	13	**37**	40.8

1 values of individual results corrected with procedural recovery
2 one procedural recovery determined only
n.a. not applicable

The initial BAS 222 F residues of lettuce from sampling occasion 4 are presented in Table 6.1-17.

Table 6.1- 17:Residues of Metiram and CS_2 in lettuce at sampling occasion 4

Day	Process MA		Process MB		Process MC		Field specimens F	
	Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]
0	16.26	9.10	8.57	4.80	12.96	7.25	n.m.	n.m.
	17.88	10.00	13.02	7.28	13.50	7.55	n.m.	n.m.

1 calc. factor Metiram to CS_2: 0.5595
n.m. not measured

Sampling occasion 6 (3 days after the 4th application)
Procedural recoveries for sampling occasion 6 ranged between 45.60% and 110.88%. Recoveries lower than 70% were obtained for several storage intervals and for the initial analysis on day 0. In addition, for a number of measurement series, only one procedural recovery was valid. For this reason, samples from sampling occasion 2 yielded the most valuable results and degradation curves were simulated only on the basis of these data. However, confirming the results obtained from sampling occasion 2, the lettuce samples after homogenisation with a commercial mill (method "MB") contained the lowest ETU levels.

The data used to assess the storage stability of ETU in lettuce treated with BAS 222 28 F at sampling occasion 6 are provided in Table 6.1- 18.

Table 6.1- 18: Residues of ETU in stored lettuce at sampling occasion 6

Processing Method	Day	ETU Residue level					Procedural recovery (mean, %)
		Individual results (mg/kg)		% of mean value day 0		Mean value of % of day 0	
Process MA (ceramic knife)	0[1]	0.371	0.309	109	91	**100**	(61.9)[2]
	Mean value day 0: 0.340						
	1	0.140	0.122	41	36	**39**	55.0
	4	0.182	0.090	54	26	**40**	55.0
	7	0.106	0.050	31	15	**23**	(103.5)[2]
	14	0.415	0.381	122	112	**117**	69.8
	33	0.204	0.091	60	27	**43**	72.0
	43	0.040	0.036	12	11	**11**	74.4
	56	0.042	0.069	12	20	**16**	69.8
	83	0.130	0.095	38	28	**33**	(81.9)[2]
	111	0.066	0.058	19	17	**18**	71.9
	144	0.185	0.163	55	48	**51**	(77.3)[2]
	173	0.143	0.141	42	42	**42**	70.5
	230	0.034	0.059	10	17	**14**	65.6
	396	0.184	0.140	54	41	**48**	(86.2)[2]

Processing Method	Day	ETU Residue level					Procedural recovery (mean, %)
		Individual results (mg/kg)		% of mean value day 0		Mean value of % of day 0	
Process MB (commercial mill)	0[1]	0.322	0.239	115	85	**100**	(61.9)[2]
	Mean value day 0: 0.281						
	1	0.036	n.m.[3]	13	n.a.	**13**	55.0
	4	0.024	0.044	9	16	**12**	55.0
	7	0.064	0.041	23	15	**19**	(103.5)[2]
	14	0.161	0.120	57	43	**50**	69.8
	33	0.039	0.055	14	20	**17**	72.0
	43	0.025	0.022	9	8	**8**	74.4
	56	< 0.01	0.023	n.a.	8	**8**	69.8
	83	0.055	0.063	20	22	**21**	(81.9)[2]
	111	0.057	0.039	20	14	**17**	71.9
	144	0.121	0.079	43	28	**36**	(77.3)[2]
	173	0.077	0.079	27	28	**28**	70.5
	230	0.043	0.044	15	16	**15**	65.6
	396	0.059	0.073	21	26	**24**	(86.2)[2]
Process MC (Stephan mill/dry ice)	0[1]	0.177	0.116	121	79	**100**	(61.9)[2]
	Mean value day 0: 0.147						
	1	0.239	0.175	163	119	**141**	55.0
	4	0.182	0.185	124	126	**125**	55.0
	7	0.347	0.109	237	74	**155**	(103.5)[2]
	14	0.509	0.595	347	406	**377**	69.8
	33	[3]	0.120	n.a.	82	**82**	48.8
	43	0.119	0.172	81	117	**99**	75.8
	56	0.163	0.148	111	101	**106**	88.5
	83	0.333	0.330	227	225	**226**	(81.9)[2]
	111	0.200	0.148	136	101	**118**	87.6
	144	0.210	0.262	143	179	**161**	75.9
	173	0.332	0.302	226	206	**216**	84.4
	230	0.235	0.204	160	139	**150**	105.2
	396	0.346	0.305	236	208	**222**	98.7
Field (F) Specimen (unprepared)	0			91	109	**100**	55.0
	1[1]	0.462	0.556				
	Mean value day 1: 0.509						
	4	[3]	0.190	n.a.	37	**37**	55.0
	7	0.134	0.176	26	34	**30**	(103.5)[2]
	14	0.394	0.466	77	92	**84**	69.8
	33	0.224	0.112	44	22	**33**	72.0
	43	0.144	0.089	28	18	**23**	74.4
	56	0.093	0.135	18	27	**22**	69.8
	83	0.136	0.188	27	37	**32**	(81.9)[2]
	111	0.107	0.087	21	17	**19**	71.9
	144	0.188	0.171	37	34	**35**	(77.3)[2]
	173	0.084	0.114	17	22	**19**	70.5
	230	0.076	0.143	15	28	**21**	65.6
	396	0.129	0.065	25	13	**19**	(86.2)[2]

n.m. not measured
n.a. not applicable
1 values of individual results corrected with procedural recovery
2 one procedural recovery determined only
3 measurement not evaluated

The initial BAS 222 F residues of lettuce from sampling occasion 6 are presented in Table 6.1-19.

Table 6.1- 19:Residues of Metiram and CS_2 in lettuce at sampling occasion 6

Day	Process MA		Process MB		Process MC		Field specimens F	
	Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]	Metiram	CS_2[1]
0	17.04	9.54	13.80	7.72	17.66	9.88	n.m.	n.m.
	15.15	8.48	11.59	6.48	16.84	9.42	n.m.	n.m.

1 calc. factor Metiram to CS_2: 0.5595
n.m. not measured

III. CONCLUSION

The results of the ETU analysis showed an influence of the homogenization method on the rate of degradation.

The residue level in samples after processing with a ceramic knife (method "MA") showed an apparent decrease. In samples processed with a commercial mill (method "MB"), a strong decrease of the residue level right after processing was observed. After processing with dry ice in a Stephan mill (method "MC"), a high residue level and storage stability were observed for the investigated period of more than one year.

After unprocessed storage of the entire lettuce head and crushing in frozen state with a wooden hammer ("F"), the residue levels were high and no degradation was observed for the investigated period of more than one year.

The results obtained after all processing methods showed a certain variability. This effect could be at least partly explained by the variability between the field specimens and by the inhomogeneity of the analyzed plant material.

The inaccuracy of the method of analysis was averaged by analyses in duplicate. Still, a certain variability of the individual results was observed.

CA 6.2 Metabolism, distribution and expression of residues

Annex II Dossier :
Regarding metabolism in plants, studies in apples and potatoes were previously evaluated during the Annex I inclusion process and considered as suitable.
Regarding metabolism in livestock, studies in chicken and goat were previously evaluated during the Annex I process and considered as suitable.

AIR3 Dossier :
A new metabolism study was conducted in lettuce.

Regarding metabolism in plants, the representative use of the present dossier (potato) is supported by the previously evaluated metabolism studies (covering crop category of root/tuber vegetables). In order to provide a general view on the metabolism of metiram in foliar applied crops, an additional metabolism study in lettuce, representing a third crop category, was conducted. Taken together the results obtained for three different crop categories (fruits/fruiting vegetables, root/tubers, leafy vegetables) show that metabolism pathways of metiram are comparable and consequently can be extrapolated to foliar applied crops in general. Noteworthy, the metiram metabolism is qualitatively not different from the metabolism elucidated for other dithiocarbamate fungicides.

Regarding metabolism in livestock, the previously evaluated studies in chicken and goat show metabolism pathways comparable to in rat (see section metiram AIR3 dossier MCA 5.1). Noteworthy, the metiram metabolism is qualitatively not different from the metabolism found for other dithiocarbamate fungicides.

In brief, in plants (apple, potato, lettuce) and livestock (goat, hen), metiram desintegrates rapidly into dynamic intermediates which after entering the metabolic carbon pool are incorporated into carbohydrates, protein and other natural products as the terminal residue.

In 2008 and in context of the re-evaluation of MRLs according to Reg. 396/2005, Art. 12, BASF SE has submitted an EU MRL compilation dossier to Italy acting as Rapporteur Member State (see also "*Italy, 2010: Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174 p*"). In this EU MRL compilation dossier (DocID 2008/1042839), the following tables are included.

Metabolism in plants (OECD data point numbers IIA 6.2.1, IIA 6.7, IIIA 8.2 and IIIA 8.7)

Plant groups covered	Apples (fruits), potatoes (root and tuber vegetables), Lettuce (leafy vegetables)
Rotational crops	Wheat, beet, kale
Plant residue definition for monitoring	Metiram (expressed as CS_2)
Plant residue definition for risk assessment	Metiram (expressed as CS_2) ETU (in processed commodities)
Conversion factor (monitoring to risk assessment)	Not applicable

Metabolism in livestock (OECD data point numbers IIA 6.2.2 to IIA 6.2.5, IIA 6.7, IIIA 8.4 and IIIA 8.7)

Animals covered	Goat and hens
Animal residue definition for monitoring	Metiram expressed as CS_2
Animal residue definition for risk assessment	Metiram expressed as CS_2
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No (not applicable)

CA 6.2.1 Metabolism, distribution and expression of residues in plants

Annex II Dossier :
Regarding metabolism in plants, studies in <u>apples</u> and <u>potatoes</u> were previously evaluated during the Annex I inclusion process and considered as suitable.

AIR3 Dossier :
A new metabolism study was conducted in <u>lettuce</u>.

Overall, plant metabolism studies were performed in three crops representing three different crop categories, namely apple (crop category: fruit/fruiting vegetable), potato (crop category: root/tuber), and lettuce (crop category: leafy vegetable). The metabolism pathways in all three crops were comparable and consequently can be extrapolated to foliar applied crops in general. In addition, the pathways were comparable to the pathways known for the other dithiocarabamate fungicides.
In brief, metiram - as are the other dithiocarbamate fungicides - is a non-systemic fungicide. Once deposited on the plant surface, the non-soluble metal ion complex is not translocated further into the plant. Rather, upon contact with a solvent system, the metal complex undergoes chemical desintegration (solvolysis) releasing dynamic intermediates which enter the general metabolic carbon pool and by this are incorporated into biological products (e.g. carbohydrates, amino acids, lipds).

Table 6.2.1- 1: Summary of available metabolism studies in plants

Crop group	Crops	Application	Sampling	Dossier reference
Fruits	apples	1st method of treatment: streaking pure, radiolabelled test material onto surface of apples and leaves as suspension using micropipette 2nd method of treatment: foliar spray application of test material as admixture of radiolabelled and non-radiolabelled BAS 222 F, 4x 3.36 - 4.85 kg a.s./ha (treatment 1: 4.85 kg a.s./ha, treatment 2-4: 3.36 kg a.s./ha)	0, 15, 27 DAT	CA 6.2.1/1
		foliar application, 5x 1.5 kg a.s./ha	83 DAT	CA 6.2.1/2
		foliar spraying to apple plants, 2x 0.240 g a.i/m^2	4 DAT	CA 6.2.1/3
Root / tuber vegetables	potatoes	foliar spraying to potato plants, 4x 1.794 - 3.587 kg a.s./ha (treatment 1-2: 1.794 kg a.s./ha, treatment 3-4: 3.587 kg a.s./ha)	21 DAT	CA 6.2.1/4
		foliar spraying to potato plants, 4x 2.0 kg a.s./ha	1 DAT	CA 6.2.1/5
		foliar spraying to potato plants, 2x 2.0 kg a.s./ha	21 DAT	CA 6.2.1/6
Leafy vegetables	lettuce	post emergence treatment, 3 x 0.2 kg as/ha	7 DAT	CA 6.2.1/7

DAT: days after last treatment

Metabolism in <u>apple</u> (crop category: fruits/fruiting vegetables)

Three metabolism studies in apple are available. They have been evaluated previously and considered valid (Italy, 2010: Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174 p)
In DocID 1990/10669 (report CA 6.2.1/1) foliar application of metiram was shown to result in much higher residues on the surface compared with the inside (pulp), predominantly parent metiram. Regarding transformation products, the predominant endproducts of metiram metabolism in apple were natural product fractions (i.e. sugar, lignin, cellulose, lipids, amino acids etc.). EBIS, EU and ETU were present at 2-4 % TRR. Similar to parent, metabolites were predominantly located at the surface. Notably, EBIS found in whole apple (3.8% TRR) is attributed to predominantly surface (3.2%TRR) and peel (0.41% TRR) and only traces in pulp (0.17% TRR). These results are confirmed by investigations after foliar application of metiram reported in two documents, DocID1986/0524 (report CA 6.2.1/2) and DocID 1986/0526 (report CA 6.2.1/3), regarding the <u>surface (peel)</u> as the predominant location of the residue as well as the <u>parent complex</u> as the predominant component of the residue.

Report:	*CA 6.2.1/1* *Hubert T.D., 1990a* *Metiram: Nature of the residue in apples* *1990/10669*
Guidelines:	*EPA 171-4(a)*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

Report:	*CA 6.2.1/2* *Bieber W.-D.,Kroehn R., 1986a* *Study on the metabolism of the Metiram complex (ethylene-14C-labelled) in apples* *1986/0524*
Guidelines:	*none*
GLP:	*yes*

Report:	*CA 6.2.1/3* *Bieber W.-D.,Kroehn R., 1986b* *Study on the metabolism of the Metiram complex (thiocarbonyl-14C-labelled) in apples* *1986/0526*
Guidelines:	*none*
GLP:	*yes*

Metabolism in potato (crop category: root/tuber)

Three metabolism studies in potato are available. They have been evaluated previously and considered valid (Italy, 2010: Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174 p)
In DocID 1990/10668 (report CA 6.2.1/4) foliar application of potato plants with metiram was shown to result in similar low levels in peel and pulp, both plant parts which were not directly exposed to the spray application. While immediate decomposition products, notably EBIS, EU, and ETU were present only in minor amounts, major metabolites were biomolecules such as glycine, creatinine, and allantoin. Their subsequent incorporation into natural plant product fractions is indicated by the presence of radioactivity in natural product fractions such as proteins and carbohydrates. These results are confirmed by investigations after foliar application of metiram reported in two documents, DocID1986/0523 (report CA 6.2.1/5) and DocID 1986/0523 (report CA 6.2.1/6), regarding the surface (tops of potato plant) as the predominant location of the residue.

Report:	*CA 6.2.1/4* *Wu J., 1990a* *Metabolism of 14C-Metiram complex in potatoes - Nature of the residue in potatoes: Analysis and quantitation of metabolites* *1990/10668*
Guidelines:	*EPA 171-4, EPA Subdivision O of the Pesticide Assessment Guidelines, EPA 40 CFR 158.125*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

Report:	*CA 6.2.1/5* *Bieber W.-D.,Kroehn R., 1986c* *Study on the metabolism of the Metiram complex (ethylene-14C-labelled) in potatoes* *1986/0523*
Guidelines:	*none*
GLP:	*yes*

Report:	*CA 6.2.1/6* *Bieber W.-D.,Kroehn R., 1986d* *Study on the metabolism of the Metiram complex (thiocarbonyl-14C-labelled) in potatoes* *1986/0525*
Guidelines:	*none*
GLP:	*yes*

Metabolism in <u>lettuce</u> (crop category: leafy vegetable)

One metabolism study in lettuce is available (DocID 2009/1049027, report CA 6.2.1/7). This study was conducted, in addition to the available studies in apple and potato, with the objective to provide metabolism data representative for a third crop category. Based on these new results in lettuce, showing metabolism of metiram comparable to the other two crop categories, a general definition of the residue can be proposed. A summary of the lettuce metabolism study is provided below.
In brief, foliar application is shown to result in high residues on the plant surface (predominantly the unchanged parent compound). The immediate decomposition products characteristic for dithiocarbamates were present in major proportions (sum of EU and ETU at 15% TRR) and minor proportion (EBIS at 2.3% TRR). In addition, M222F007 (TDIT) a compound previously reported as occasionally occuring soil metabolite was identified in this study, however only at very low proportion (1.4% TRR). The subsequent incorporation of the decomposition products into natural plant constituents is indicated by the presence of radioactivity in natural product fractions such as proteins and carbohydrates.

The metabolism study in lettuce is summarized below:

Report:	CA 6.2.1/7 Bross M.,Glaessgen W.E., 2010a Metabolism of 14C-Metiram (14C-BAS 222 F) in lettuce 2009/1049027
Guidelines:	EPA 860.1300: Nature of the Residue in Plants Livestock, EPA 860.1000, EEC 7028/VI/95 rev. 3 Appendix A (EU): Metabolism and distribution in plants (draft of 22 July 1997)
GLP:	yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany)

Executive Summary

I. MATERIAL AND METHODS (2009/1049027)

A. MATERIALS

1.	**Test Material:**	^{14}C-BAS 222 F
	Description:	^{14}C-BAS 222 F (Metiram), labelled in the ethylene bridge (Specific radioactivity: 4.68 MBq/mg)
	Lot/Batch #:	153-3003 (^{14}C-BAS 222 F)
	Purity:	> 98% (by Iodometry)
	CAS#:	9006-42-2
	Stability of test Compound:	The residues in lettuce, treated with BAS 222 F were stable under the chosen experimental conditions (-18°C, 15 months)

2. Test Commodity: Leaf vegetables & fresh herbs
Crop: Lettuce
Type: not reported
Variety: Nadine
Botanical name: *Lactuca sativa* L.
Crop parts(s) or processed commodity: head
Sample size: lettuce head: 4412 g

3. Soil: Loamy sand soil (USDA scheme loamy sand; German scheme DIN 4220: soil type loamy sand)
The soil physicochemical properties are described below (see Table 6.2.1- 2).

Table 6.2.1- 2: Soil physicochemical properties

Soil Type	pH	Organic Carbon [%]	Sand [%]	Silt [%]	Clay [%]	Maximal water holding capacity [g water/100 g dry soil]	CEC[1] [meq Ba/100 g dry soil]
Loamy sand soil* Loamy sand**	6.5*** 7.0$^{\Delta}$	0.9	82*	12*	6*	29	8

* USDA scheme ** German scheme DIN 4220 *** ($CaCl_2$) Δ (H_2O) 1 cation exchange capacity

B. STUDY DESIGN AND METHODS

1. Test procedure

Metiram (BAS 222 F) belongs to the class of ethylenebis (dithiocarbamate) (EBDC) fungicides. These non-systemic foliar applied compounds with mainly protective activity are widely used to control fungal diseases in many fruit and vegetable crops. The metabolism of ^{14}C-BAS 222 F (Metiram) was investigated in leaf lettuce following post emergence treatment at a nominal application rate of 3 x 0.2 kg as/ha (approximately 1.786 lb/A). The spray applications were performed using radioactive material labelled in the ethylene bridge after mixing with the blank WG formulation BAS 222 28 F. Three applications were carried out in intervals of seven days, and the lettuce heads were harvested seven days after the final treatment to investigate the nature and the level of radioactive residues. All samples were stored in a freezer at ≤ -18°C.

2. Description of analytical procedures

TRR combusted:
For the determination of the TRR combusted, aliquots of homogenized solid plant samples were weighed and combusted by means of an automatic sample. The $^{14}CO_2$ evolved during combustion was trapped by an absorption liquid, and the collected radioactivity was measured by liquid scintillation counting (LSC).

Extraction:
Aliquots of homogenized plant material were extracted three times with methanol. The methanol extracts of the three steps were combined and measured by LSC. The residue was further extracted with water (twice). The aqueous extracts were also combined and analyzed by means of LSC.

The results of the methanol extraction and the water extraction were summarized and referred to as extractable radioactive residues (ERR).

The residue after solvent extraction of each sample was dried and homogenized. Aliquots were combusted for the determination of the residual radioactive residue (RRR).

Partition of extractable radioactive residues on Extrelut columns:
The methanol and water extracts were characterized by partition experiments on Extrelut columns. The partition step was also used for removing the most likely suspended metal complexes from the extracts, since they accumulate during HPLC.

The column was eluted with dichloromethane, followed in some cases by a second elution step with water. The eluates were mixed prior to determination of the radioactivity by LSC measurement of aliquots. The same partition procedure was also carried out for 20 ml aliquots of the NH_40H solubilizate of the residual radioactive residue (RRR, second work up).

Characterization of the RRR:
In order to characterize the residual radioactive residue, an aliquot of the dried residue after solvent extraction (second work up) was homogenized with 1 % NH_40H. A subsample of the NH_40H solubilizate was applied on an Extrelut column and the solubilized metabolites were eluted with dichloromethane. An aliquot of the eluate was concentrated, diluted with water and investigated with HPLC.

The rest of the eluate was adjusted to pH 3.8 and the proteins were precipitated by the addition of acetone, stirring with a glass rod and standing over night at 4 °C. Since no visible sediment had been observed after the first step and no precipitate was to be seen after the second step, the sample was filtered and analyzed by HPLC. Aliquots of the individual liquid samples were analyzed by LSC measurement.

Two further subsamples of the NH_40H solubilizate were partitioned on two parallel Extrelut columns as described above, and the radioactive residues in the dichloromethane eluates were quantitated by LSC.

Determination of Metiram in solid samples as (unlabeled) CS_2 by application of BASF method No. 135/4:
In order to determine the amounts of the parent compound metiram (and / or other metabolites or degradates with the ability to liberate CS_2) in the solid phases of Extrelut columns and in the residues after solvent extraction or solubilization with aqueous ammonia, respectively, the residue analytical method No. 135/4 was applied. This method is based on the decomposition of bis-dithiocarbamates by reductive cleavage with stanneous hydrochloric acid. The carbon disulfide formed is distilled with a stream of nitrogen, washed by passage through adsorption tubes with zinc acetate and sulfuric acid, and adsorbed in a methanolic solution of potassium hydroxide. Quantitation of CS_2 is achieved by photometric measurement of the absorbance at 302 nm of the resulting xanthogenate.

The solid phases of the Extrelut columns or subsamples of the dried residues (RRR or NH_4OH residue) were completely transferred to Erlenmeyer flasks and subjected to the decomposition procedure.

As a deviation to BASF method No. 135/4, an automated HPLC system without a stationary phase (2 ml loop instead of a column) equipped with a flow-through UV detector was used instead of an UV photometer for the quantitation of the xanthogenate.

3. Identification of metabolites

The identification of the metabolites is based on HPLC-MS and HPLC-NMR analyses. All the quantitation of the metabolites is based on the HPLC analysis of the concentrated dichloromethane eluates obtained after Extrelut partition of the methanol extract and the aqueous extract or, in one case, also of the eluate after partition of the NH_4OH solubilizate from the residual radioactive residue, using HPLC system 1 with a Prevail C18 column. The second HPLC system was used for confirmatory purposes.

II. RESULTS AND DISCUSSION

A. TOTAL RADIOACTIVE RESIDUES (TRRs)

Due to the inhomogeneity of the samples, the total radioactive residue (TRR) was calculated by adding the extractable and the residual radioactive residues (ERR + RRR). The total radioactive residue in lettuce head collected seven days after the final treatment accounted for 43.491 to 108.445 mg/kg in three different work ups. The calculated TRR in the second work up which was used for all further quantitative evaluations amounted to 108.445 mg/kg.

The TRRs are summarised in Table 6.2.1- 3.

Table 6.2.1- 3: Total Radioactive Residue (TRR) in lettuce samples after treatment with ^{14}C-BAS 222 F

Matrix	DAT[1)]	TRR determined [2)] [mg/kg]	TRR calculated [3)] [mg/kg]
Lettuce head	7	78.502	43.491
Lettuce head	7	n.d.	108.445
Lettuce head	7	124.164	105.376

1) DAT = Days After Last Treatment; 2) determined by direct combustion; 3) calculated as the sum of ERR + RRR
n.d. not determined

B. EXTRACTION, CHARACTERIZATION AND IDENTIFICATION OF RESIDUES

1. Extraction of residues

Although it is known that the parent molecule is not soluble without any degradation, the samples were extracted with methanol followed by water. Clear purpose of the work up procedures selected was to identify as many metabolites / hydrolytic degradation products as possible for deriving a metabolic degradation pathway. Due to the chemical nature of the parent compound, any differentiation between hydrolytic degradation products formed during the analytical procedures and "real" plant metabolites is not possible.

The extractability of the radioactive residues in lettuce head with methanol and water was relatively low with portions of 22.5 to 33.8% TRR extracted in the three different work ups.

The major part of the radioactive residues detected was not extractable with methanol and water but remained in the residual radioactive residue (RRR, 66.2 to 77.5% TRR in three different work ups).

The results of the extraction of ^{14}C-BAS 222 F derived radioactivity from lettuce samples are shown in Table 6.2.1- 4.

Table 6.2.1- 4: Extractability of radioactive residues in lettuce head after post emergence treatment with ^{14}C-BAS 222 F

Matrix	DAT [1]	TRR calculated [2]	Methanol		Water		ERR [3]		RRR [4]	
		[mg/kg]	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
Lettuce head Work up 1[5]	7	43.491	8.757	20.1	5.943	13.7	14.700	33.8	28.791	66.2
Lettuce head Work up 2[6]	7	108.445	16.821	15.5	7.596	7.0	24.417	22.5	84.028	77.5
Lettuce head Work up 3[7]	7	105.376	16.558	15.7	7.895	7.5	24.453	23.2	80.923	76.8

1) DAT = Days After Treatment; 2) TRR was calculated as the sum of ERR + RRR; 3) ERR = Extractable Radioactive Residues; RRR = Residual Radioactive Residue (after solvent extraction); 5) storage time = 5 days; 6) storage time = 278 days; 7) storage time = 460 days

2. Identification, characterization and quantitation of extractable residues

The metabolites in both the methanol extracts and the aqueous extracts were classified by their behaviour during partition on Extrelut columns: about one third to half of the radioactive residues detected in the crude extracts were eluted with dichloromethane while more than half of the radioactive residues remained on the stationary phases, most likely due to their poor solubility. When the residual radioactive residue after solvent extraction was subsequently treated with an aqueous ammonia solution, the major part of the radioactive residues (73.6 % TRR) was solubilized.

The investigations performed indicate that the parent compound metiram is only partially metabolized / degraded. Nearly half of the total radioactive residue was determined to be present in the residual radioactive residue after solvent extraction as unchanged active substance (49.840 mg/kg or 46.0% TRR) by application of the residue analytical method No. 135/4 (decomposition and detection of unlabelled CS_2). Due to its chemical nature as metal ion complex, the parent compound could not be detected in any extract and in the NH_4OH solubilizate from the residual radioactive residue after partition on Extrelut.

As known for most of the metabolites of EBDCs, the identified metabolites may at least in part have been formed also by abiotic processes like solvolysis or hydrolysis during / after extraction. Thus, it remains uncertain whether or to which extent the observed metabolites have been formed by true plant metabolism.

Four metabolites of BAS 222 F were identified by HPLC-MS and HPLC-NMR analysis of the methanol extract after partition on Extrelut. The metabolites detected in higher amounts in leaf lettuce were ETU and EU which occurred mainly in the NH_4OH solubilizate and are already known as degradates or intermediates from other plant metabolism studies. Two further degradation products were identified as EBIS and the metabolite TDIT which has recently been reported to occur also in soil and in water / sediment systems. The hydrolytic degradation product ETU can be generated directly from metiram and / or from EBIS and / or from TDIT, and is further metabolized to EU.

The total concentration of the scarcely resolved metabolites ETU and EU in the extracts and the NH_4OH solubilizate accounted for 15.950 mg/kg corresponding to 14.7% TRR. EBIS was detected in a total concentration of 2.441 mg/kg or 2.3% TRR, and TDIT was detected only in the extractable radioactive residues in an amount of 1.545 mg/kg or 1.4% TRR.

The major part of the radioactive residues detected was not extractable with methanol and water but remained in the residual radioactive residue (RRR). When the RRR after solvent extraction in the second work up (84.028 mg/kg or 77.5% TRR) was treated with an aqueous ammonia solution, most of the residual radioactive residue (79.787 mg/kg or 73.6% TRR) was solubilized, and 12.146 mg/kg or 11.2% TRR were recovered in the NH_4OH residue.

The solubilization step with aqueous ammonia quantitatively released the parent compound metiram from the residues after solvent extraction indicating that the chemical nature as metal ion complex was the reason for the poor solvent extractability of the parent compound.

In addition; the NH_4OH solubilizate contained a portion of soluble radioactive residues (31.910 mg/kg or 29.4% TRR) which was recovered in the dichloromethane eluate after Extrelut partition and subsequently analyzed by HPLC. The major component in this eluted portion was identified as ETU (and / or EU) accompanied by minor amounts of the metabolite EBIS. No evidence was found indicating that the ammonia solubilizate contained considerable amounts of radioactive residues incorporated into the protein pool of lettuce head.

The final non-extractable residues after ammonia solubilization contained only very low amounts of metiram and / or other metabolites or degradate containing a CS_2 substructure (two sulfur atoms bound to the same carbon atom). The major portion of radioactive residues consisted of further degradation products of BAS 222 F without any CS_2 moiety. Most likely, these degradation products were physically associated with or incorporated in insoluble natural products like starch or cell wall polymers.

The results are shown in Table 6.2.1- 5.

Table 6.2.1- 5: Summary of identified and characterized radioactive residues extracted from lettuce head after post emergence treatment with ^{14}C-BAS 222 F (harvested 7 DAT; second work up)

Designation	Extracts				Solubilizate with aqueous ammonia Lab0034		Sum	
	Methanol Extract Lab0025		Aqueous Extract Lab0026					
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Total Radioactive Residues (TRR)							**108.445**	**100.0**
Extractable radioactive residues (ERR)	16.821	15.5	7.596	7.0	79.787	73.6	24.417	22.5
Identified in ERR								
EU and / or ETU	1.366	1.2	0.444	0.4	see below		1.810	1.7
EBIS	0.525	0.5	1.152	1.1	see below		1.677	1.6
TDIT	1.307	1.2	0.238	0.2	see below		1.545	1.4
Total Identified in ERR							**5.032**	**4.6**
Characterized in ERR								
Formamide derivative	0.392	0.4	n.d.	n.d.	see below		0.392	0.4
Further HPLC peaks (each below 0.4 mg/kg or 0.4% TRR)	1.449	1.3	0.417	0.4	see below		1.866	1.7
Extrelut solid phase[1]	10.177	9.4	4.041	3.7	see below		14.218	13.1
Total Characterized in ERR							**16.476**	**15.2**
Total Identified and / or Characterized in ERR							**21.508**	**19.8**
Residual radioactive residue (RRR, Lab0027)							84.028	77.5
Identified in RRR (residual radioactive residue)[2]								
ETU and / or EU in supernatant after treatment with aqueous ammonia (Lab0034)					14.141	13.0	14.141	13.0
EBIS in supernatant after treatment with aqueous ammonia (Lab0034)					0.764	0.7	0.764	0.7
TDIT in supernatant after treatment with aqueous ammonia (Lab0034)					n.d.	n.d.	0.000	0.0
Total Identified in RRR[2]							**14.905**	**13.7**
Characterized in RRR[2,3]								
Formamide derivative in supernatant after treatment with aqueous ammonia (Lab0034)					n.d.	n.d.	0.000	0.0
Further HPLC peaks in supernatant after treatment with aqueous ammonia (Lab0034; each below 8.0 mg/kg or 7% TRR)					17.005	15.7	17.005	15.7
Extrelut solid phase of the NH4OH solubilizate (Lab0034)[1,4]					57.698	53.2	57.698	53.2
Total Characterized in RRR[2]							**74.703**	**68.9**
Total Identified and / or Characterized in RRR[2]							**89.608**	**82.6**
Total Identified and Characterized (ERR and RRR)							**111.116**	**102.4**
Final Residue (Lab0035)[3]							**12.146**	**11.2**
Total Identified and Characterized (ERR and RRR) + Final Residue							**123.262**	**113.6**

n. d. = not detected / identified

1) Determination of the non-eluted radioactive residues adsorbed on Extrelut columns by LSC of the decomposition solutions (method No. 135/4) of partition experiments carried out in parallel
2) Treatment with aqueous ammonia was applied for solubilization, or metiram (and / or other metabolites or degradates with the ability to liberate CS_2) was determined as CS_2 applying method No. 135/4 to a parallel subsample
3) Metiram (and / or other metabolites or degradates containing a substructure of two sulfur atoms bound to the same carbon atom, see discussion in the text) was determined as CS2 applying method No. 135/4 (see Table 6.2.1-6)
4) Since the elution with dichloromethane was less effective in the parallel partition experiments in the case of the NH_4OH solubilizate, the value for the Extrelut solid phases may be over-estimated for Lab0034

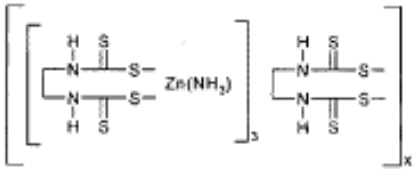
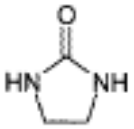
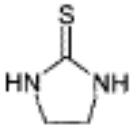
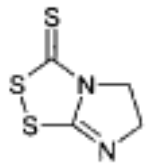
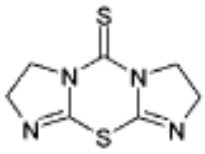
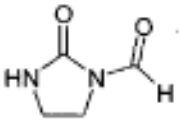
Table 6.2.1-6: Summary of the results of the determination of Metiram as CS_2 in solid remainders (after extraction) of lettuce head after post emergence treatment with ^{14}C-BAS 222 F (harvest 7 DAT; second work up) using BASF method No. 135/4

Sample description	[mg/kg][1]	[% TRR][1]
RRR	49.840	46.0
NH_4OH residue	0.416	0.4

1) Mean values of two parallel determinations

A summary of all identified components in lettuce head after post emergence treatment with ^{14}C-BAS 222 F is given in Table 6.2.1-7. The total radioactive residues (TRR) were calculated as the sum of ERR and RRR. In contrast, the amounts given in mg/kg are calculated from the TRR values not taking the change of specific radioactivity into account. Therefore, in order to obtain more precise data, metabolite specific correction factors have to be applied (see Conclusion, Table 6.2.1-8).

Table 6.2.1- 7: Summary of identified and characterized components in lettuce head samples post emergence treatment with ^{14}C-BAS 222 F (harvested 7 DAT)

Designation Metabolite Code (Reg. No.)		Structure	Lettuce head (7 DAT)[1] (second work up)	
			mg/kg	% TRR
Metiram BAS 222 F (250284)[2]			49.840	46.0
Imidazolidine-2-one (ethyleneurea) BF 222-EU / EU[3] (27270)			15.950	14.7
Imidazolidine-2-thione (ethylenethiourea) ETU[3] (146099)				
"Ethylene-bis- (isothiocyanate)sulfide" BF 222-EBIS / DIDT (243959)			2.441	2.3
TDIT (M = 212)			1.545	1.4
Formamide derivative[4] (M = 114)			0.392	0.4
Further HPLC peaks (unknown)			18.871	17.4
Extrelut solid phases[5]			14.218	13.1
Final residue			12.146	11.2
Sum			**115.404**	**106.4**

1) Including radioactive residues released from RRR
2) Metiram (and / or other metabolites or degradates with the ability to liberate CS_2) was quantitated in the residual radioactive residues (RRR) as CS_2 applying the residue analytical method No. 135/4
3) EU and ETU were not separated by HPLC in system 1; values have to be read as mg/kg,(or % TRR, respectively) of EU and / or ETU
4) Probably an artifact formed of EU
5) Due to its chemical properties, it is likely that the radioactive residues retained on the Extrelut column mainly consist of the parent compound metiram

3. Metabolic pathway

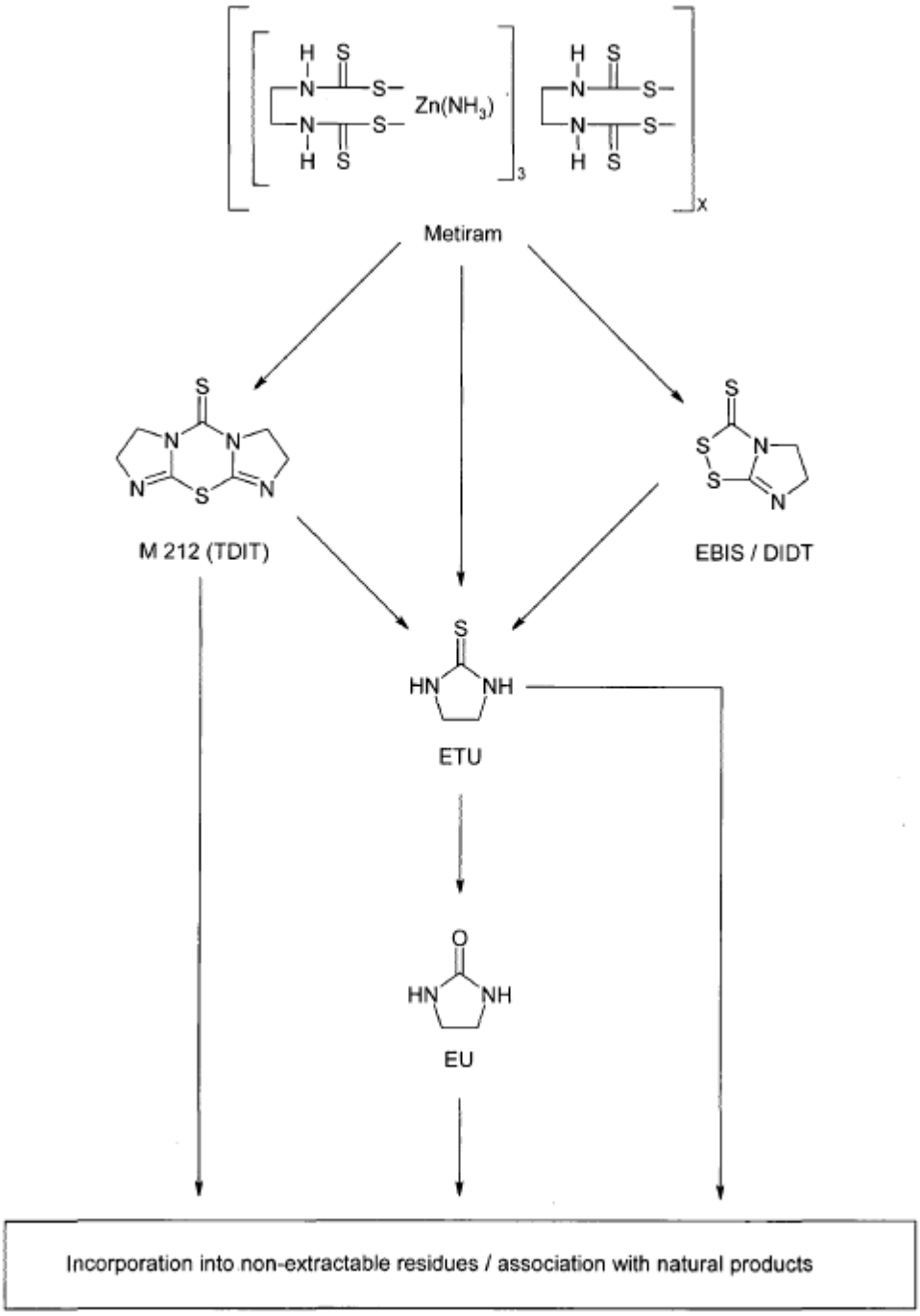
In leaf lettuce, metiram (BAS 222 F) is only partially metabolized within seven days after the last application. At least half of the total radioactive residues were still present as unchanged active substance which was only poorly extractable with methanol and water, but detected in association with the residues after solvent extraction (RRR) and solubilized with aqueous ammonia. The metabolic pathway for the degradation is shown in Figure 6.2.1-1.

Hydrolysis (or generally solvolysis) is known to play an important role in the decomposition of metiram, and dissolution or extraction can only be achieved under decomposition. Since the solvolytic degradation leads to the formation of essentially the same decomposition products, it can hardly be determined whether the identified metabolites arise from true plant metabolism, from transformation reactions on the plant surface after application, or from artificial degradation upon solvent extraction.

The metabolites detected in higher amounts in lettuce are the known derivatives ETU and EU which occurred particularly in the NH_4OH solubilizate but also constituted major components in the methanol extracts (total concentration of both barely resolved metabolites in extracts and NH_4OH solubilizate: 15.950 mg/kg or 14.7% TRR, compare Table 6.2.1- 7). Two further metabolites were observed in considerable amounts predominantly in the extractable radioactive residues and identified by HPLC-MS as EBIS and TDIT. Several minor unknown degradation products were characterized by their chromatographic properties as medium-polar derivatives eluting between EU / ETU and EBIS in reversed-phase HPLC.

The portion of the residual radioactive residue which was not solubilized by treatment with aqueous ammonia (NH_4OH residue) is composed of metabolites of metiram not containing any CS_2 substructure. These non-extractable residues may have been formed either by physical incorporation of degradation products into insoluble starch / cell wall polymers or via complete metabolization of primarily embedded active substance. Incorporation into proteins (which were precipitated with cold acetone from the NH_4OH solubilizate after Extrelut partition) was not observed in considerable amounts.

Figure 6.2.1-1: Metabolic pathway of ^{14}C-BAS 222 F in lettuce



4. Storage stability

All samples were stored at approximately -18°C during the course of the study. A comparison of the metabolite patterns obtained by HPLC analysis and of the extractability of the stored sample material at the beginning and at the end of the investigation period showed that there was no major change in the nature of the radioactive residues during sample storage over a period of about 15 months.

III. CONCLUSION

The nature of the residues of metiram was investigated in lettuce growing in plastic containers under laboratory conditions. Lettuce heads were applied three foliar spray applications of 2 kg as/ha.The TRR level in lettuce head harvested 7 days after the last application amouted to 108.4 mg/kg. The extractability was relatively low (below 35%). The high RRR is indicative of effective incorporation of the radiocarbon into natural plant constituents (e.g. starch, cell wall polymers). Identification and characterization of the total radioactive residue did show the predominant proportion of the residue is the unchanged parent compound metiram (46% TRR). Importantly, metiram is a metal ion complex which desintegrates upon contact with water. Due to its chemical properties its extraction is only achievable upon desintegration of the complex (solvolysis) which results in formation of dynamic intermediates, e.g. EBIS, ETU, and EU. Within the context of plant metabolism studies it is not possible to determine whether such dynamic intermediates are abiotically formed desintegration products or in fact, metabolites generated by plant metabolism.
Using radio-HPLC, the transformation products ETU (M222F002) and EU (M222F003) were not quantifiable separately. Together, they were present at major amounts (14.7% TRR). Two further degradation products were identified at low amounts as EBIS (M222F004, 2.3% TRR) and as TDIT (M222F007, 1.4% TRR). In addition, a minor portion of radioactive residues was observed after solvent extraction and subsequent treatment with aqueous ammonia: These non-extractable residues are most likely formed by physical association or incorporation of metiram transformation into insoluble natural products such as starch or cell wall polymers. Note, the levels of transformation products reported are 16.0 mg/kg (EU and/or ETU), 2.4 mg/kg (EBIS), 1.5 mg/kg (TDIT) when expressed as metiram parent equivalents. To obtain absolute residue levels a correction factor accounting for the molecular mass difference has to be applied. The following table provides the calculated molecular weight correction factors. It was copied from document BASF DocID2015/1087922 (see section MCA 6.10).

Table 6.2.1- 8: Metiram metabolites: molecular weight correction factors

Metabolite	Units[1)]	Total molecular weight[2)]	Molecular weight correction factor[3)]
M222F004 (EBIS)	4	705.2	0.65
M222F003 (EU)	4	344.4	0.32
M222F002 (ETU)	n.a.[4)]	n.a.	n.a.
M222F023 (EDA)	4	240.4	0.22
M222F021 (N-AcEDA)	4	408.4	0.38
M222F022 (Jaffe`s Base)	2	340.4	0.31
M222F007 (TDIT)	2	426.6	0.39
M222F001	2	460.4	0.42
Glycine	n.a.	n.a.	n.a.
M222F008 (Hydantoin)	4	400.4	0.37
M222F013 (Formamide derivative)	4	456.4	0.42

1) number of molecules that may potentially be formed from one molecule metiram (= n)
2) n x molecular weight [g/mol]
3) calculated as (n x molecular weight)/1088.7 g/mol)
4) n.a. not applicable

Conclusion on section 6.2.1: metabolism in crops

Plant metabolism studies were performed in three crops, namely apple (crop category: fruits/fruiting vegetables), potato (crop category: root/tuber), and lettuce (crop category: leafy vegetable). The metabolism pathways in all three crops were comparable. Noteworthy, the metabolism of metiram in plants is comparable to the well known pathways for dithiocarbamates fungicides.
In brief, metiram, as are the other dithiocarbamate fungicides, is a non-systemic fungicide. Once deposited on the plant surface the non-soluble metal ion complex is not translocated further into the plant. Rather, upon contact with a solvent system, the metal complex undergoes chemical desintegration (solvolysis) releasing dynamic intermediates which enter the general metabolic carbon pool and thereby are incorporated into biological products (e.g. carbohydrates, amino acids, lipds).
In conclusion, the metabolism of metiram can be considered sufficiently elucidated in fruits, roots/tuber and leafy vegetables. Considering this conclusion is based on crops representing three different crop categories (including also rotational crops, see section MCA 6.6) this metabolism data can be extrapolated to plant crops in general thereby allowing a general definition of the relevant residue in commodities of plant origin (foliar spray application, see section MCA 6.7).
Following application of metiram to the target plant, the compound remains on the plant surface. In raw agricultural commodities (RAC) metiram is generally the predominant component of the residue, and as such an appropriate marker compound for enforcement (see section MCA 6.7).
Dynamic intermediates formed upon desintegration of the metiram complex as well as naturally occurring plant constituents are further components of the residue. While naturally occuring plant constituents are not relevant for the definition of the residue, a potential relevance of these dynamic intermediates has been evaluated (see section MCA 6.7 and 6.10 for a detailed relevance assessment).

CA 6.2.2 Poultry

Annex II Dossier :
Regarding metabolism of metiram in poultry, studies in hen were previously evaluated during the Annex I inclusion process and were considered as suitable.

AIR3 Dossier :
No new metabolism study was conducted.

Regarding metiram, the previously evaluated studies support the representative use (potato) of the present dossier: DocID1990/5080 (see MCA 6.2.2/1), DocID 1990/5131 (see MCA 6.2.2/2), DocID 1989/5049 (see MCA 6.2.2/3), DocID1988/5016 (see MCA 6.2.2/4). In brief, chicken were dosed with seven consecutive daily doses of metiram (14C-BAS 222F in capsules, 4 mg/kg bw/day). Analysis of egg and tissues did reveal incorporation of radiocarbon into naturally occuring cell constituents in significant amounts (e.g. lipids and proteins as predominant terminal residue) indicating extensive metabolism of metiram. In addition, several small molecular weight transformation products of metiram were identified (EBIS, ETU, EU, Jaffes Base, EDA/NAcetyl-EDA).
In the framework of a metabolism study, cell constituents such as lipids and proteins are extractable only to a limited extent with the consequence that in certain cases, a high proportion of the radioactivity remains non-identified. This is also the case for the metiram poultry metabolism study: the proportion of non-identified residue reported does reflect the rapid conversion of the dynamic intermediates into natural cell constituents rather than being a deficiency of the study.

In conclusion, the metabolic pathway of metiram in poultry is well elucidated. Noteworthy, it is comparable to the metabolic pathways found in other animals, both ruminants (see section MCA 6.2.3) and rat (see section MCA 5.1.1). In brief, upon contact with water the metal ion complex desintegrates (solvolysis) and releases dynamic intermediates such as EBIS, Jaffes Base, ETU, EU and EDA. These degradation products are stepwise further metabolized to glycine and thereby the radiocarbon is channelled into the metabolic carbon pool. In consequence, the radiocarbon is incorporated into naturally occurring cell constituents such as lipids and proteins as the predominant terminal residue.

Regarding the degradation product ETU potentially occurring in feed items (processed plant commodities), data on metabolism in poultry is not required (the rationale is described in detail in BASF DocID 2002/1006209, *Metiram: Metabolism of ETU in livestock, Statement of the Notifer to ECCO 120, May 22, 2002*) [see KCA 6.2/1 2002/1006209]. In brief, the rationale is : concerning the metiram residue intake of poultry, the contribution of ETU from processed feed items is very low (worst case assumptions result in an estimation of 0.003 mg/animal/d). Furthermore, poultry metabolism studies with metiram show that the ETU is formed in the animal itself and is rapidly eliminated (either by excretion or by further transformation into natural cell constituents). Both facts considered together, ETU levels in commodities of animal origin are insignificant (and thus do not need to be included in a definition of the residue, see section MCA 6.7).

In conclusion, additional poultry studies with ETU as test item are not required nor justified, considering both limited knowledge gain as well as animal welfare perspective.

Report:	*CA 6.2.2/1* *[redacted]1990b* *Metabolism of 14C-Metiram complex in laying hens. Analysis and quantitation of metabolites and/or the corresponding natural products in eggs and tissues* *1990/5080*
Guidelines:	*EPA 171-4, EPA Subdivision O of the Pesticide Assessment Guidelines, EPA 40 CFR 158.125*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

Report:	*CA 6.2.2/2* *Marco G.J.,Novak R.A., 1990a* *Executive summary of Metiram hen metabolism studies conducted by the Metiram Task Force* *1990/5131*
Guidelines:	*EPA 171-4, EPA Subdivision O of the Pesticide Assessment Guidelines, EPA 40 CFR 158.125*
GLP:	*no*

Report:	*CA 6.2.2/3* *[redacted] 1989a* *Metiram and Ethylenethiourea residue analysis: Analysis of tissues and eggs from laying hens dosed with 14C-Metiram* *1989/5049*
Guidelines:	*EPA 171-4*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

Report:	*CA 6.2.2/4* *[redacted] 1989a* *Metabolism feeding study in laying hens using 14C-Metiram* *1988/5016*
Guidelines:	*EPA 171-4*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

CA 6.2.3 Lactating ruminants

Annex II Dossier :
Regarding metabolism of metiram in ruminants, studies in goat were previously evaluated during the Annex I inclusion process and were considered as suitable.

AIR3 Dossier :
No new metabolism study was conducted.

Regarding metiram, the previously evaluated studies support the representative use (potato) of the present dossier: DocID1988/7002665 (see CA 6.2.3/1), and DocID1989/10487 (see CA 6.2.3/2).
In brief, goats were dosed with five consecutive daily doses of metiram (14C-BAS 222 F in capsules, 77 mg/day). Noteably, all relevant matrices were analysed, with identification/characterization of metabolite as well as bound residues meeting guideline requirements. Analysis of milk and tissues did reveal significant incorporation of radiocarbon into naturally occurring cell constituents (e.g. with carbohydrates, lipids, proteins as predominant terminal residue) indicating extensive metabolism of metiram : subsequent to decomposition of the metal ion complex, the short lived dynamic intermediates such as EBIS, ETU and EU as well as EDA are further metabolized to glycine thereby channelling radiocarbon into the metabolic cycleIn addition, several small molecular weight transformation of metiram were identified (EBIS, ETU, EU, Jaffes Base, and EDA/NAcetyl-EDA).

In conclusion, the metabolic pathway of metiram in ruminant is well elucidated. Noteworthy, it is comparable to the metabolic pathways found in other animals, both poultry (see section MCA 6.2.2) and rat (see section MCA 5.1.1). In brief, upon contact with water the metal ion complex desintegrates (solvolysis) and releases dynamic intermediates such as EBIS, Jaffes Base, ETU, EU and EDA. These degradation products are stepwise further metabolized to glycine and thereby the radiocarbon is channelled into the metabolic carbon pool. In consequence, the radiocarbon is incorporated into naturally occurring cell constituents such as lipids and proteins as the predominant terminal residue.

Regarding the degradation product ETU potentially occurring in feed items (processed plant commodities), data on metabolism in ruminant is not required (the rationale is described in detail in BASF DocID 2002/1006209, *Metiram: Metabolism of ETU in livestock, Statement of the Notifer to ECCO 120, May 22, 2002*) [see KCA 6.2/1 2002/1006209]. In brief, the rationale is : concerning the metiram residue intake of ruminant, the contribution of ETU from processed feed items is very low (worst case assumptions result in an estimation of 0.17 mg/animal/d for beef cattle and 0.07 mg/animal/d for dairy cow). Furthermore, goat metabolism studies with metiram show that the ETU is formed in the animal itself and is rapidly eliminated (either by excretion or by further transformation into natural cell constituents). Both facts considered together, ETU levels in commodities of animal origin are insignificant (and thus do not need to be included in a definition of the residue, see section MCA 6.7).
In conclusion, additional poultry studies with ETU as test item are not required nor justified, considering both limited knowledge gain as well as animal welfare perspective.

Report:	*CA 6.2.3/1* [redacted] *1989a* *Metabolism of 14C-Metiram complex in lactating goats - Analysis and quantification of metabolites and/or the corresponding natural products in milk and tissues* *1989/10487*
Guidelines:	*EPA 171-4*
GLP:	*yes* *(certified by United States Environmental Protection Agency)*

Report:	*CA 6.2.3/2* [redacted]*1986a* *The biokinetics and metabolism of Metiram complex in lactating goats* *1986/10190*
Guidelines:	*none*
GLP:	*yes*

CA 6.2.4 Pigs

A metiram metabolism study in pigs is not required. Metabolism in ruminants (goat, see MCA 6.2.2) and rat (see MCA 5.1.1) are comparable and can be extrapolated to pigs as well.

CA 6.2.5 Fish

A metiram metabolism study in fish is not required. The representative use supported in the present dossier, potato, is not considered to serve as feed item for fish.

More specifically, according to Commission regulation 283/2013, metabolism studies in fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications. The conditions under which such a study should be performed are further described in the Working document of the EU Commission SANCO/11187/2013, rev. 3 on the nature of pesticide residues in fish. The document specifies that the accumulation of compounds with low lipophilicity via the diet is known to be negligible and that fish metabolism studies are therefore required for active substances with a log P_{ow} equal or greater than 3 and an expected feed burden above 0.1 mg/kg DM. In the case of metiram representative uses, both criteria do not apply (logP_{ow}<3, expected feed burden <0.1 mg/kg DM) .

Conclusion on section 6.2: metabolism in livestock animals

Livestock metabolism studies were performed in hen (laying poultry) and goat (lactating ruminant). The metabolism pathways in poultry and goat were comparable to rat. Therefore, the findings can be extrapolated to pig and a metabolism study in pig is not required. A metabolism study in fish is not required ($\log P_{ow} < 3$, expected feed burden <0.1 mg/kg DM). Noteworthy, the metabolism of metiram in livestock is comparable to the well known pathways for dithiocarbamate fungicides.

The metabolic pathway of metiram in livestock animals, including poultry, ruminants, and pig can be considered sufficiently elucidated. In brief, the parent compound metiram is not resorbed in the gastrointestinal tract. Rather, upon contact with water, the metal ion complex desintegrates (solvolysis) and releases dynamic intermediates such as EBIS, Jaffes Base, ETU, EU and EDA. These degradation products are stepwise further metabolized to glycine and thereby the radiocarbon is channeled into the metabolic carbon pool. In consequence, the radiocarbon is incorporated into naturally occurring cell constituents such as lipids and proteins as the predominant terminal residue.

In conclusion, the terminal residue in livestock commodities is predominantly naturally occurring cell constituents, such as lipids in proteins. Such compound fractions are not relevant for the definition of the residue. In addition, several dynamic intermediates were identified, some of which are CS_2-releasing molecules and therefore are detected by the multi-residue method analysing residues of dithiocarbamates measured as CS_2. A potential relevance of these metabolic intermediates for the residue definition is evaluated in detail in section MCA 6.7.

CA 6.3 Magnitude of residues trials in plants

The present dossier supports the representative formulation WG BAS 222 28 F used in the representative use, potatoes. In this section, the residue data for potatoes are summarized.

CA 6.3.1 Potatoes

In support of the representative use in potatoes, a total of 23 cGAP compliant new field trials on potatoes were conducted. The cGAP is given in Table 6.3.1- 1. The residue trials were performed in various European Member States in N-EU and S-EU during the growing seasons 2012, 2013 and 2014 and thereby fulfill the requirements of seasonal and geographical distribution (see Table 6.3.1- 2).

Table 6.3.1- 1: Summary of the critical GAP for the proposed use in potatoes for BAS 222 28 F

Crop	Outdoor/ Protected	Growth stage (BBCH)	Maximum number of applications	Minimum application interval (days)	Maximum		Minimum PHI (days)
					Rate (kg as/ha)	Water (L/ha)	
Potatoes	Outdoor	21 - 89	3	7	1.26	100 - 1000	14

Table 6.3.1- 2: Number of residue trials conducted per geographical region and vegetation period - BAS 222 28 F

Crop	Vegetation Period	Number of Trials					Reference
		EU North	Country	EU South	Country	Total	
Potato	2014	4	DE, NL, UK	4	ES, IT, GR	8	6.3.2/1
Potato	2013	4	DE, FR, UK	4	ES, IT, FR, GR	8	6.3.2/2
Potato	2012	4	DE, UK	4	ES, GR	8	6.3.2/3
Total number of trials per Region		**12**		**12**	**Total number of trials**	**24**	

Table 6.3.1- 3: Overall summary of residue data for metiram from potato residue trials

Crop	Region	RAC	n	Residue level (mg/kg)								
				CS_2			Metiram, determined as CS_2			Metiram, determined as EBDC		
				Min.	HR	STMR	Min.	HR	STMR	Min.	HR	STMR
Potato	N-EU	tuber	11	<0.056	0.056	0.056	<0.1	<0.1	<0.1	<0.05	<0.05	<0.05
	S-EU	tuber	12	<0.056	0.056	0.056	<0.1	<0.1	<0.1	<0.05	<0.05	<0.05

Table 6.3.1- 4: Overall summary of residue data for ETU, EU and EBIS from potato residue trials

Crop	Region	RAC	n	Residue level (mg/kg)								
				ETU			EU			EBIS		
				Min.	HR	STMR	Min.	HR	STMR	Min.	HR	STMR
Potato	N-EU	tuber	11	<0.01	0.038	0.01	<0.01	0.03	0.01	<0.01	<0.01	<0.01
	S-EU	tuber	12	<0.01	0.023	0.01	<0.01	0.01	0.01	<0.01	<0.01	<0.01

The study reports are summarized below.

Table 6.3.1- 5: Potato residue data: summary of maximum storage interval and storage stability

Crop	DocID	Study No.	Maximum storage interval (days)*					Storage stability (days)				
			Metiram by CS_2	Metiram by EBDC	ETU	EU	EBIS	Metiram by CS_2	Metiram by EBDC	ETU	EU	EBIS
Potatoes	2015/1000321	731171	135	83	48 Δ (17 for PHI specimens) Δ	48 (17 for PHI specimens)	48 Δ (17 for PHI specimens) Δ	373	373	0	365	0
	2014/1000222	389461	350	431 Δ	263 Δ	263	263 Δ					
	2012/1272625	389454	318	428 Δ	310 Δ	448 Δ	452 Δ					

* of deep frozen samples from harvest until extraction

Δ freezer storage stability not confirmed (see section MCA 6.1)

Table 6.3.1- 6: Potato residue data: summary of storage intervals of PHI samples

DocID	Study No.	PHI Specimen No.*	Storage interval of PHI specimens* (days)				
			Metiram by CS_2	Metiram by EBDC	ETU	EU	EBIS
2015/1000321	731171	L1403820007	92	66	16 Δ	16	16 Δ
		L1403830007	28	23	16 Δ	16	16 Δ
		L1403840007	43	38	9 Δ	9	9 Δ
		L1403850007	33	62	13 Δ	13	13 Δ
		L1403860007	121	39	10 Δ	10	10 Δ
		L1403870007	113	31		17	17 Δ
		L1403870008			11 Δ		
		L1403880007	13	48	13 Δ	13	13 Δ
		L1403890007	43	18	11 Δ	11	11 Δ
2014/1000222	389461	L1301180007	259	238	189 Δ		190 Δ
		L1301180008				186	
		L1301190007	257	215	166 Δ		
		L1301190008				163	164 Δ
		L1301200007	249	225	176 Δ	176	177 Δ
		L1301210007	239	215	166 Δ	166	167 Δ
		L1301220007	211	182	135 Δ	135	134 Δ
		L1301230007	284	263	216 Δ	216	215 Δ
		L1301240007	243	221	174 Δ	174	173 Δ
		L1301250007	324	295	248 Δ	248	247 Δ
2012/1272625	389454	L1205240007	364	457Δ	357 Δ	350	504 Δ
		L1205250007	273	366	266 Δ	259	413 Δ
		L1205260007	223	335	216 Δ	209	364 Δ
		L1205270007	207	319	200 Δ	193	348 Δ
		L1205280007	302	414Δ	295 Δ	288	443 Δ
		L1205290007	270	382Δ	263 Δ	256	411 Δ
		L1205300007	239	349	230 Δ	223	378 Δ
		L1205310007	232	342	223 Δ	216	371 Δ

* PHI samples (when higher residues were detected in specimens sampled at a later sampling event then these residue values were taken)

Δ freezer storage stability not confirmed (see section MCA 6.1)

Report: CA 6.3.1/1
Meyer M.,Gabriel E.J., 2015a
Study on the residue behaviour of Metiram (BAS 222 F) in potato after treatment with BAS 222 28 F under field conditions in Germany, the Netherlands, the United Kingdom, Italy, Spain and Greece, 2014
2015/1000321

Guidelines: EC 1107/2009 of the European Parliament and of the Council of 21 Oct 2009, EU Regulation Regulation 544/2011 (10 June 2011) implementing Regulation No 1107/2009, EEC 7029/VI/95 rev. 5, EEC 7525/VI/95 rev. 9 (March 2011), SANCO/825/00 rev. 8.1 (16 November 2010), SANCO/3029/99 rev. 4 (11 July 2000)

GLP: yes
(certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1.

Test Material:	BAS 222 28 F	
Description:	BAS 222 28 F: 700 g/kg of BAS 222 F (metiram), WG formulation	
Lot/Batch #:	FRE-000977	
Purity:	Not relevant	
CAS#:	Metiram (BAS 222 F): 9006-42-2	
Development code:	Metiram: BAS 222 F ETU: M222F002 EU: M222F003 EBIS: M222F004	
Spiking levels:	BAS 222 F (by EBDC): BAS 222 F (by CS_2): ETU, EU, EBIS:	0.05, 0.5 mg/kg 0.1, 1.0 mg/kg 0.01, 0.1 mg/kg

2.

Test Commodity:	root and tuber vegetables
Crop:	potato
Type:	*Solanum tuberosum* L.
Variety:	Musica, Toscana, Home guard, Lady Claire, Carlita, Jaerla, Kennebeck
Crop parts(s) or processed Commodity:	potato / tuber
Sample size:	2.0 kg (24 tubers)

B. STUDY DESIGN AND METHODS

1. Test procedure

During the growing season of 2014, eight field trials with potatoes were conducted in Germany, the United Kingdom, the Netherlands, Greece, Italy and Spain, in order to determine the magnitude of the residues of metiram (BAS 222 F) after application of BAS 222 28 F.
The WG formulation BAS 222 28 F was applied three times at single rates of 1.4 kg as/ha for BAS 222 F in a spray volume of 200 L/ha in order to determine the magnitude of the residues of the active ingredient on Raw Agricultural Commodities (RAC). The first application took place 26 - 29 DBH (days before harvest), the second application 20 - 22 DBH and the third application 13 - 15 DBH, except for trial L140385, where only two applications at 21 and 14 DBH were performed. Specimens were collected at 0, 6 - 8, 13 - 15 and 20 - 22 days after the last application (DALA).

Table 6.3.1- 7 Application and sampling details for trials conducted in 2014

Region	No. of trials	No. of Appl.	F, G, I[2]	Method	Test Item	Active Substance	Application		Target Timing	
							Rate (kg a.s./ha)	Water vol. (L/ha)	Appl. (DBH)[3]	Sampl. (DALA)[1]
EU North & South	8	3	F	-	BAS 222 28 F (WG)	Metiram BAS 222 F	1.4	200	1st appl.: 26 - 29 2nd appl.: 20 - 22 3rd appl.: 13 - 15	0 6 - 8 13 - 15 20 - 22

1) Days after last application,
2) Field, Glasshouse or Indoor,
3) Days before harvest

2. Description of analytical procedures

The specimens were analyzed for residues of metiram according to BASF method No. L0089/01 and as carbondisulfide according to BASF method L0234/01. The residues of ETU were determined according to the BASF method No. L0176/01. The residues of EU and EBIS were determined with BASF method L0233/01.
The limit of quantitation (LOQ) of the method L0089/01 was 0.05 mg/kg and for metiram as carbondisulfide it was 0.10 mg/kg. The LOQ of the method L0176/01 was 0.01 mg/kg. The LOQ for EU and EBIS were 0.01 mg/kg with the applied method.
The results of procedural recovery experiments averaged at about 100% for BAS 222 F (by EBDC) at fortification levels between 0.05 and 0.5 mg/kg, at 80.2% for BAS 222 F (by CS_2) at fortification levels between 0.1 and 1.0 mg/kg, at 87.4% for ETU, at 83.0% for EU and at 92.4% for EBIS at fortification levels between 0.01 and 0.1 mg/kg.

BASF method L0089/01was used to determine Metiram as EBDC:
The ethylene-bisdithiocarbamate (EBDC) moiety was formed out of BAS 222 F and extracted from the specimen with a buffer solution consisting of EDTA, cysteine, methanol and sodium hydroxide adjusted to pH 11.0. The formed ethylene-bisdithiocarbamate (EBDC) analyte was methylated with iodmethane prior to C18 SPE clean up. Specimens were quantified by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The limit of quantitation (LOQ) was 0.05 mg/kg.

BASF method L0234/01 was used to determine Metiram as CS_2
Metiram was transformed to CS_2 by means of orthophosphoric acid. Subsequently, the CS_2 was transferred to isooctane with a flow of nitrogen. The quantification was carried out using GC-MS. The limit of quantitation (LOQ) was 0.10 mg/kg.

BASF method L0176/01 was used to determine ETU:
ETU was extracted from the specimen material with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water. After centrifugation an aliquot was taken and the methanol was evaporated from the extract. The pH was adjusted to 8 before evaporating (in some cases after evaporation). The remaining water phase was cleaned by liquid/liquid (water/dichloromethane) partition on an Extrelut column. After concentration of the eluate, the residue was determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EU was determined according to BASF method L0233/01:
The extraction from EU was performed with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water and was followed by a clean-up by liquid-liquid partition on an Extrelut column where ethyl acetate was used for the elution.
Water was added prior the evaporation of the specimen extract. For the final reconstitution of the specimen extract a solution of H_2O/MeOH was used. The determination was performed by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EBIS was determined according to BASF method L0233/01:
The extraction from EBIS was performed with a mixture of acetonitrile/formic acid in combination with a thiourea solution and was followed by a clean-up step utilizing C18-EC. Specimens were diluted with a solution of acetonitrile/H_2O/formic acid before being determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

The results of procedural recovery experiments are summarized in Table 6.3.1- 8.

Table 6.3.1- 8 Summary of recoveries

Matrix	Fortification Level (mg/kg)	Summary Recoveries			
		n	Mean (%)	SD (+/-)	RSD (%)
Method No. L0089/01		**Metiram (by EBDC)**			
Potato/Tuber	0.05, 0.5	8	100	7.3	7.3
Method No. L0234/01		**Metiram (by CS_2)**			
Potato/Tuber	0.1, 1.0	12	80.2	8.6	11
Method No. L0176/01		**ETU**			
Potato/Tuber	0.01, 0.1	16	87.4	9.6	11
Method No. L0233/01		**EU**			
Potato/Tuber	0.01, 0.1	15	83.0	11	13
Method No. L0233/01		**EBIS**			
Potato/Tuber	0.01, 0.1	16	92.4	10	11

II. RESULTS AND DISCUSSION

Residue data of the field trials is summarized in Table 6.3.1- 9 and Table 6.3.1- 10. Detailed information is shown in Table 6.3.1- 13 to Table 6.3.1- 16.

Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ. The maximum storage interval of deep frozen samples from harvest until extraction was 83 days for metiram (by EBDC), 135 days for metiram (by CS_2) and 48 days for ETU (17 days for PHI specimens), 48 days for EU (17 days for PHI specimens) and 48 days for EBIS (17 days for PHI specimens). The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

Table 6.3.1- 9 Summary of metiram level in BAS 222 28 F treated potato (Trials L140382 – L140384 and L140386 – L140389)

Region	Matrix	DALA [1)]	BBCH	Range of CS_2 Residues [2)] [mg/kg]	Range of metiram Residues (by CS_2) [mg/kg]	Range of metiram Residues (by EBDC) [mg/kg]
EU North & South	Potato (tuber)	0	45 – 48	< 0.056	< 0.1	< 0.05 - 0.064
		6 – 8	46 – 48	< 0.056	< 0.1	< 0.05
		13 – 15	48 – 49	< 0.056	< 0.1	< 0.05
		20 – 22	48 - 49	< 0.056	< 0.1	< 0.05

[1)] DALA = Days after Last Application

[2)] the conversion factor from CS_2 to metiram is 1.79

Table 6.3.1- 10 Summary of ETU, EU, and EBIS level in BAS 222 28 F treated potato (Trials L140382 – L140384 and L140386 – L140389)

Portion analysed	No. of specimens	DALA [1)]	BBCH	Range of ETU Residues [mg/kg]	Range of EU Residues [mg/kg]	Range of EBIS Residues [mg/kg]
EU North & South	Potato (tuber)	0	45 – 48	< 0.01	< 0.01	< 0.01
		6 – 8	46 – 48	< 0.01	< 0.01	< 0.01
		13 – 15	48 – 49	< 0.01 – 0.01	< 0.01	< 0.01
		20 – 22	48 - 49	< 0.01 – 0.01	< 0.01	< 0.01

[1)] DALA = Days after Last Application

Table 6.3.1- 11 Summary of metiram level in BAS 222 28 F treated potato (Trial L140385)

Region	Matrix	DALA [1)]	BBCH	Range of CS_2 Residues [2)] [mg/kg]	Range of metiram Residues (by CS_2) [mg/kg]	Range of metiram Residues (by EBDC) [mg/kg]
EU North	Potato (tuber)	7	48	< 0.056	< 0.1	< 0.05
		14	48	< 0.056	< 0.1	< 0.05
		20	49	< 0.056	< 0.1	< 0.05

[1)] DALA = Days after Last Application

[2)] the conversion factor from CS_2 to metiram is 1.79

Table 6.3.1- 12 Summary of ETU, EU, and EBIS level in BAS 222 28 F treated potato (Trial L140385)

Portion analysed	No. of specimens	DALA [1)]	BBCH	Range of ETU Residues [mg/kg]	Range of EU Residues [mg/kg]	Range of EBIS Residues [mg/kg]
EU North	Potato (tuber)	7	48	< 0.01	< 0.01	< 0.01
		14	48	< 0.01	< 0.01	< 0.01
		20	49	< 0.01	< 0.01	< 0.01

[1)] DALA = Days after Last Application

Table 6.3.1- 13 Level of metiram in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DA LA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140382 yes 2014	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	46	0 8 14 22	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140383 yes 2014	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 6 13 20	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140384 yes 2014	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0 8 13 22	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140385 yes 2014	Potato	The Netherlands	**Note: trial underdosed** BAS 222 28 F: 2x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	7 14 20	tuber tuber tuber	<0.056 <0.056 <0.056	<0.1 <0.1 <0.1	<0.05 <0.05 <0.05

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 14 Level of metiram in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DA LA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code:	731171	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2015/1000321					7	tuber	<0.056	<0.1	<0.05
Trial No.	L140386					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2014									
Study code:	731171	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45/47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2015/1000321					6	tuber	<0.056	<0.1	<0.05
Trial No.	L140387					15	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2014									
Study code:	731171	Potato	Italy	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0	tuber	<0.056	<0.1	0.064
Doc ID:	2015/1000321					7	tuber	<0.056	<0.1	<0.05
Trial No.	L140388					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2014									
Study code:	731171	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2015/1000321					7	tuber	<0.056	<0.1	<0.05
Trial No.	L140389					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2014									

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 15 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DA LA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code:	731171	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	46	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2015/1000321					8	tuber	<0.01	<0.01	<0.01
Trial No.	L140382					14	tuber	<0.01	<0.01	<0.01
GLP:	yes					22	tuber	<0.01	<0.01	<0.01
Year:	2014									
Study code:	731171	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2015/1000321					6	tuber	<0.01	<0.01	<0.01
Trial No.	L140383					13	tuber	0.01	<0.01	<0.01
GLP:	yes					20	tuber	<0.01	<0.01	<0.01
Year:	2014									
Study code:	731171	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2015/1000321					8	tuber	<0.01	<0.01	<0.01
Trial No.	L140384					13	tuber	<0.01	<0.01	<0.01
GLP:	yes					22	tuber	<0.01	<0.01	<0.01
Year:	2014									
Study code:	731171	Potato	The Netherlands	**Note: trial underdosed** BAS 222 28 F: 2x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	7	tuber	<0.01	<0.01	<0.01
Doc ID:	2015/1000321					14	tuber	<0.01	<0.01	<0.01
Trial No.	L140385					20	tuber	<0.01	<0.01	<0.01
GLP:	yes									
Year:	2014									

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 16 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DA LA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140386 yes 2014	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 7 14 21	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140387 yes 2014	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45/47	0 6 15 21	tuber tuber tuber tuber	<0.01 <0.01 <0.01 0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140388 yes 2014	Potato	Italy	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0 7 14 21	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	731171 2015/1000321 L140389 yes 2014	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 7 14 21	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Trials L140382 – L140384 and L140386 – L140389

No residues of metiram (by EBDC) above the limit of quantitation (< 0.05 mg/kg) were found in any of the analysed treated specimens, except for the 0 DALA specimen of trial L140388, where 0.064 mg/kg were found.
No residues of metiram were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of CS_2 above the limit of quantitation (< 0.056 mg/kg (< 0.1 mg/kg expressed as metiram)) were found in any of the analysed treated specimens.
No residues of CS_2 were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of ETU above the limit of quantitation (< 0.01 mg/kg) were found in any of the analysed treated specimens, except for the specimens L1403830007 (13 DALA) and L1403870008 (21 DALA), where 0.010 mg/kg were found each.
No residues of metiram were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of EU above the limit of quantitation (< 0.01 mg/kg) were found in any of the analysed treated specimens.
No residues of EU were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of EBIS were found above the limit of quantitation (< 0.01 mg/kg) in any of the analysed treated specimens.
No residues of EBIS were found above the limit of quantitation in any of the analysed untreated specimens.

Trial L140385

Trial L140385 will be reported separately as due to an infection with phythophtora infestans only two applications could be made and not all samplings were available. For trial L140385 plot 2 was treated two times at 21 and 14 DBH with 2.0 kg/ha of BAS 222 28 F (1.4 kg/ha of metiram (BAS 222 F), WG formulation, with a spray volume of 200 L/ha. 3 samplings were carried out (no 0 DALA sampling).

No residues of metiram (by EBDC) above the limit of quantitation (< 0.05 mg/kg) were found in any of the analysed treated specimens of trial L140385.
No residues of metiram were found above the limit of quantitation in any of the analysed untreated specimens of trial L140385.

No residues of CS_2 above the limit of quantitation (< 0.056 mg/kg (< 0.1 mg/kg expressed as metiram)) were found in any of the analysed treated specimens of trial L140385.
No residues of CS_2 were found above the limit of quantitation in any of the analysed untreated specimens of trial L140385.

No residues of ETU above the limit of quantitation (< 0.01 mg/kg) were found in any of the analysed treated specimens of trial L140385.
No residues of ETU were found above the limit of quantitation in any of the analysed untreated specimens of trial L140385.

No residues of EU above the limit of quantitation (< 0.01 mg/kg) were found in any of the analysed treated specimens of trial L140385.
No residues of EU were found above the limit of quantitation in any of the analysed untreated specimens of trial L140385.

No residues of EBIS above the limit of quantitation (< 0.01 mg/kg) were found in any of the analysed treated specimens of trial L140385.
No residues of EBIS were found above the limit of quantitation in any of the analysed untreated specimens of trial L140385.

III. CONCLUSION

Eight field trials with potatoes were conducted in Europe (North and South) in season 2014. BAS 222 28 F was applied three times at single rates of 1.4 kg/ha BAS 222 F (2.0 kg/ha of WG formulation BAS 222 28 F) in a spray volume of 200 L/ha. (Note, seven field trials are considered further, omitting one trial L140385 due to deviations from the GAP). Residue analysis of samples taken at different time intervals after the last application (0, 6 - 8, 13 - 15 and 20 - 22 DALA) showed a decline of residue levels.

At the recommended PHI of 14 days, residues of metiram (determination as CS_2 and EBDC), CS_2, EU and EBIS were below the limit of quantitation (LOQ <0.056, <0.05 mg/kg, <0.10. <0.01 mg/kg). Residues of ETU were between <0.01 - 0.01 mg/kg.

Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ. The maximum storage interval of deep frozen samples from harvest until extraction was 83 days for metiram (by EBDC), 135 days for metiram (by CS_2) and 48 days for ETU (17 days for PHI specimens), 48 days for EU (17 days for PHI specimens) and 48 days for EBIS (17 days for PHI specimens). The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

Report: CA 6.3.2/2
Meyer M., 2014d
Study on the residue behaviour of Metiram (BAS 222 F) in potato after treatment with BAS 222 28 F under field conditions in Germany, Northern France, the United Kingdom, Southern France, Greece, Italy and Spain, 2013
2014/1000222

Guidelines: EC 1107/2009 of the European Parliament and of the Council of 21 Oct 2009, EEC 79/117, EEC 91/414, EU Regulation 1107/2009 with Regulation 554/2011, EEC 7029/VI/95 rev. 5 Appendix B (July 22 1997), EEC 7525/VI/95 rev. 9 (March 2011), SANCO/825/00 rev. 8.1 (16 November 2010)

GLP: yes
(certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1.

Test Material:	BAS 222 28 F	
Description:	BAS 222 28 F: 700 g/kg of BAS 222 F (metiram), WG formulation	
Lot/Batch #:	FRE-000825	
Purity:	Not relevant	
CAS#:	Metiram (BAS 222 F): 9006-42-2	
Development code:	Metiram: BAS 222 F	
	ETU: M222F002	
	EU: M222F003	
	EBIS: M222F004	
Spiking levels:	BAS 222 F (by EBDC):	0.05, 0.5, 5.0 mg/kg
	BAS 222 F (by CS_2):	0.1, 1.0 mg/kg
	ETU and EU:	0.01, 0.1 mg/kg
	EBIS:	0.01, 0.1 mg/kg

2.

Test Commodity:	root and tuber vegetables
Crop:	potato
Type:	*Solanum tuberosum* L.
Variety:	Marabell, Allians, Spunta, Harmony, Jaerla, Primura, Condor
Crop parts(s) or processed Commodity:	potato / tuber
Sample size:	2.0 kg (12 tubers)

B. STUDY DESIGN AND METHODS

1. Test procedure

During the growing season of 2013, eight field trials with potatoes (field conditions) were conducted in Germany, Northern France, the United Kingdom, Southern France, Greece, Italy and Spain, in order to determine the magnitude of the residues of metiram (BAS 222 F) after application of BAS 222 28 F.

The WG formulation BAS 222 28 F was applied three times (27 - 29, 20 - 22 and 13 - 14 days before harvest) at single rates of 1.4 kg as/ha for BAS 222 F in a spray volume of 200 L/ha in order to determine the magnitude of the residues of the active ingredient on Raw Agricultural Commodities (RAC).

Specimens were collected at 0, 6 - 8, 13 - 14 and 20 - 22 days after the last application (DALA).

Table 6.3.1- 17 Application and sampling details for trials conducted in 2013

Region	No. of trials	No. of Appl.	F, G, I[2]	Method	Test Item	Active Substance	Application		Target Timing	
							Rate (kg a.s./ha)	Water vol. (L/ha)	Appl. (DBH)[3]	Sampl. (DALA)[1]
EU North & South	8	3	F	-	BAS 222 28 F (WG)	Metiram BAS 222 F	1.4	200	1st appl.: 27 - 29 2nd appl.: 20 - 22 3rd appl.: 13 - 14	0 6 - 8 13 - 14 20 - 22

1) Days after last application,
2) Field, Glasshouse or Indoor,
3) Days before harvest

2. Description of analytical procedures

The specimens were analyzed for residues of metiram according to BASF method No. L0089/01 and as carbondisulfide according to BASF method L0234/01. The residues of ETU were determined according to the BASF method No. L0176/01. The residues of EU and EBIS were determined with BASF method L0233/01.
The limit of quantitation (LOQ) of the method L0089/01 was 0.05 mg/kg and for metiram as carbondisulfide it was 0.10 mg/kg. The LOQ of the method L0176/01 was 0.01 mg/kg. The LOQ for EU and EBIS were 0.01 mg/kg with the applied method.
The results of procedural recovery experiments averaged at about 79.8% for BAS 222 F (by EBDC) at fortification levels between 0.05 and 5.0 mg/kg, at 73.9% for BAS 222 F (by CS_2) at fortification levels between 0.1 and 1.0 mg/kg, at 90.3% for ETU, at 80.3% for EU and at 88.9% for EBIS at fortification levels between 0.01 and 0.1 mg/kg.

BASF method L0089/01was used to determine Metiram as EBDC:
The ethylene-bisdithiocarbamate (EBDC) moiety was formed out of BAS 222 F and extracted from the specimen with a buffer solution consisting of EDTA, cysteine, methanol and sodium hydroxide adjusted to pH 11.0. The formed ethylene-bisdithiocarbamate (EBDC) analyte was methylated with iodmethane prior to C18 SPE clean up. Specimens were quantified by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The limit of quantitation (LOQ) was 0.05 mg/kg.

BASF method L0234/01 was used to determine Metiram as CS_2
Metiram was transformed to CS_2 by means of orthophosphoric acid. Subsequently, the CS_2 was transferred to isooctane with a flow of nitrogen. The quantification was carried out using GC-MS. The limit of quantitation (LOQ) was 0.10 mg/kg.

BASF method L0176/01 was used to determine ETU:
ETU was extracted from the specimen material with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water. After centrifugation an aliquot was taken and the methanol was evaporated from the extract. The pH was adjusted to 8 before evaporating (in some cases after evaporation). The remaining water phase was cleaned by liquid/liquid (water/dichloromethane) partition on an Extrelut column. After concentration of the eluate, the residue was determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EU was determined according to BASF method L0233/01:
The extraction from EU was performed with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water and was followed by a clean-up by liquid-liquid partition on an Extrelut column where ethyl acetate was used for the elution.
Water was added prior the evaporation of the specimen extract. For the final reconstitution of the specimen extract a solution of H_2O/MeOH was used. The determination was performed by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EBIS was determined according to BASF method L0233/01:
The extraction from EBIS was performed with a mixture of acetonitrile/formic acid in combination with a thiourea solution and was followed by a clean-up step utilizing C18-EC. Specimens were diluted with a solution of acetonitrile/H_2O/formic acid before being determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

The results of procedural recovery experiments are summarized in Table 6.3.1- 18.

Table 6.3.1- 18 Summary of recoveries

Matrix	Fortification Level (mg/kg)	Summary Recoveries			
		n	Mean (%)	SD (+/-)	RSD (%)
Method No. L0089/01		**Metiram (by EBDC)**			
Potato/Tuber	0.05, 0.5, 5.0	6	79.8	9.4	11.8
Method No. L0234/01		**Metiram (by CS_2)**			
Potato/Tuber	0.1, 1.0	12	73.9	13	17
Method No. L0176/01		**ETU**			
Potato/Tuber	0.01, 0.1	12	90.3	6.3	6.9
Method No. L0233/01		**EU**			
Potato/Tuber	0.01, 0.1	12	80.3	8.1	10.1
Method No. L0233/01		**EBIS**			
Potato/Tuber	0.01, 0.1	12	88.9	7.8	8.7

II. RESULTS AND DISCUSSION

Residue data of the field trials is summarized in Table 6.3.1- 19 and Table 6.3.1- 20. Detailed information is shown in Table 6.3.1- 21 to Table 6.3.1- 24.

Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ. The maximum storage interval of deep frozen samples from harvest until extraction was 431 days for metiram (by EBDC), 350 days for metiram (by CS_2) and 263 days for ETU, EU and EBIS. The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

Table 6.3.1- 19 Summary of metiram level in BAS 222 28 F treated potato

Region	Matrix	DALA [1)]	BBCH	Range of CS_2 Residues [2)] [mg/kg]	Range of metiram Residues (by CS_2) [mg/kg]	Range of metiram Residues (by EBDC) [mg/kg]
EU North & South	Potato (tuber)	0	42 – 48	< 0.056	< 0.1	< 0.05 - 0.07
		6 – 8	45 – 48	< 0.056	< 0.1	< 0.05
		13 – 14	45 – 49	< 0.056	< 0.1	< 0.05
		20 – 22	49	< 0.056	< 0.1	< 0.05

[1)] DALA = Days after Last Application

[2)] the conversion factor from CS_2 to metiram is 1.79

Table 6.3.1- 20 Summary of ETU, EU, and EBIS level in BAS 222 28 F treated potato

Portion analysed	No. of specimens	DALA [1)]	BBCH	Range of ETU Residues [mg/kg]	Range of EU Residues [mg/kg]	Range of EBIS Residues [mg/kg]
EU North & South	Potato (tuber)	0	42 – 48	< 0.01 – 0.037	< 0.01	< 0.01
		6 – 8	45 – 48	< 0.01 – 0.028	< 0.01	< 0.01
		13 – 14	45 – 49	< 0.01 – 0.038	< 0.01 - 0.01	< 0.01
		20 – 22	49	< 0.01 – 0.031	< 0.01 - 0.01	< 0.01

[1)] DALA = Days after Last Application

Table 6.3.1- 21 Level of metiram in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DA LA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130118 yes 2013	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 8 14 21	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130119 yes 2013	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0 7 14 21	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130120 yes 2013	Potato	France (N)	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0 7 14 22	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130121 yes 2013	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 6 13 20	tuber tuber tuber tuber	<0.056 <0.056 <0.056 <0.056	<0.1 <0.1 <0.1 <0.1	<0.05 <0.05 <0.05 <0.05

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 22 Level of metiram in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DA LA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code:	389461	Potato	France (S)	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	44	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2014/1000222					8	tuber	<0.056	<0.1	<0.05
Trial No.	L130122					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2013									
Study code:	389461	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	42-45	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2014/1000222					7	tuber	<0.056	<0.1	<0.05
Trial No.	L130123					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2013									
Study code:	389461	Potato	Italy	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47-48	0	tuber	<0.056	<0.1	0.07
Doc ID:	2014/1000222					7	tuber	<0.056	<0.1	<0.05
Trial No.	L130124					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2013									
Study code:	389461	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2014/1000222					6	tuber	<0.056	<0.1	<0.05
Trial No.	L130125					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2013									

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 23 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DA LA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130118 yes 2013	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 8 14 21	tuber tuber tuber tuber	0.037 0.028 0.038 0.031	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130119 yes 2013	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0 7 14 21	tuber tuber tuber tuber	0.011 0.020 0.017 0.013	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130120 yes 2013	Potato	France (N)	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0 7 14 22	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389461 2014/1000222 L130121 yes 2013	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0 6 13 20	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 24 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DA LA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code:	389461	Potato	France (S)	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	44	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2014/1000222					8	tuber	<0.01	<0.01	<0.01
Trial No.	L130122					14	tuber	0.011	<0.01	<0.01
GLP:	yes					21	tuber	0.013	<0.01	<0.01
Year:	2013									
Study code:	389461	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	42-45	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2014/1000222					7	tuber	<0.01	<0.01	<0.01
Trial No.	L130123					14	tuber	<0.01	<0.01	<0.01
GLP:	yes					21	tuber	<0.01	<0.01	<0.01
Year:	2013									
Study code:	389461	Potato	Italy	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47-48	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2014/1000222					7	tuber	<0.01	<0.01	<0.01
Trial No.	L130124					14	tuber	<0.01	<0.01	<0.01
GLP:	yes					21	tuber	<0.01	<0.01	<0.01
Year:	2013									
Study code:	389461	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	45	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2014/1000222					6	tuber	0.018	<0.01	<0.01
Trial No.	L130125					14	tuber	0.023	0.010	<0.01
GLP:	yes					21	tuber	0.023	0.010	<0.01
Year:	2013									

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

No residues of Metiram (by EBDC) were found above the limit of quantitation (< 0.05 mg/kg), except for trial no. L130124 with 0.070 mg/kg for 0 DALA sampling.
No residues of metiram were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of CS_2 (Metiram by CS_2) were found above the limit of quantitation (< 0.056 mg/kg (< 0.1 mg/kg expressed as metiram) in any of the analysed treated specimens.
No residues of CS_2 were found above the limit of quantitation in any of the analysed untreated specimens.

In specimens taken at 0 DALA residues of ETU ranged from < 0.01 – 0.037 mg/kg. They remained at this level in the specimens taken 6 - 8 DALA (< 0.01 – 0.028 mg/kg), 13 - 14 DALA (< 0.01 – 0.038 mg/kg) as well as 20 - 22 DALA (< 0.01 – 0.031) mg/kg.
No residues of ETU were found above the limit of quantitation in any of the analysed untreated specimens, apart from the specimens taken in trial L130118. The following residue concentrations were found: 0.018 mg/kg (L1301180001), 0.019 mg/kg (L1301180002), 0.016 mg/kg (L1301180003) and 0.017 mg/kg (L1301180004).

No residues of EU were found above the limit of quantitation (< 0.01 mg/kg) in any of the analysed treated specimens, apart from the specimens taken 14 and 21 DALA in trial L130125 (L1301250007 and L1301250008) where 0.010 mg/kg were determined.
No residues of EU were found above the limit of quantitation in any of the analysed untreated specimens.

No residues of EBIS were found above the limit of quantitation (< 0.01 mg/kg) in any of the analysed treated specimens.
No residues of EBIS were found above the limit of quantitation in any of the analysed untreated specimens.

III. CONCLUSION

Eight field trials with potatoes were conducted in Europe (North and South) in season 2013. BAS 222 28 F was applied three times at single rates of 1.4 kg/ha BAS 222 F (2.0 kg/ha of WG formulation BAS 222 28 F) in a spray volume of 200 L/ha. Residue analysis of samples taken at different time intervals after the last application (0, 6 - 8, 13 - 14 and 20 - 22 DALA) showed a decline of residue levels.
At the recommended PHI of 14 days, residues of metiram (determination as CS_2 and EBDC) and CS_2 were below the limit of quantitation (LOQ <0.056, <0.05 mg/kg, <0.10 mg/kg). Residues of ETU were between <0.01 - 0.038 mg/kg and for EU between <0.01 - 0.01 mg/kg. Residues of EBIS were below the limit of quantitation (LOQ <0.01 mg/kg). Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ (except for trial L130118, residues of ETU of 0.016 mg/kg and 0.017 mg/kg were found at DALA 13 - 22). The maximum storage interval of deep frozen samples from harvest until extraction was 431 days for metiram (by EBDC), 350 days for metiram (by CS_2) and 263 days for ETU, EU and EBIS. The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

Report: CA 6.3.2/3
Meyer M., 2014c
Study on the residue behaviour of Metiram (BAS 222 F) in potato after treatment with BAS 222 28 F under field conditions in Germany, the United Kingdom, Greece and Spain, 2012
2012/1272625

Guidelines: EC 1107/2009 of the European Parliament and of the Council of 21 Oct 2009, EEC 79/117, EEC 91/414, EU Regulation Regulation 544/2011 (10 June 2011) implementing Regulation No 1107/2009, EEC 7029/VI/95 rev. 5 Appendix B (July 22 1997), EEC 7525/VI/95 rev. 9 (March 2011), SANCO/825/00 rev. 8.1 (16 November 2010), SANCO/3029/99 rev. 4 (11 July 2000)

GLP: yes
(certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1. Test Material: BAS 222 28 F
Description: BAS 222 28 F: 700 g/kg of BAS 222 F (metiram), WG formulation
Lot/Batch #: 80449975L0
Purity: Not relevant
CAS#: Metiram (BAS 222 F): 9006-42-2
Development code: Metiram: BAS 222 F
ETU: M222F002
EU: M222F003
EBIS: M222F004

Spiking levels:		
	BAS 222 F (by EBDC):	0.05, 0.5, 1.0 mg/kg
	BAS 222 F (by CS_2):	0.1, 1.0 mg/kg
	ETU and EU:	0.01, 0.1 mg/kg
	EBIS:	0.01, 0.05, 0.1 mg/kg

2. Test Commodity: root and tuber vegetables
Crop: potato
Type: *Solanum tuberosum* L.
Variety: Marabell, Quarta, Markies, Agria, Kennebec
Crop parts(s) or processed Commodity: potato / tuber
Sample size: 2.0 kg (12 tubers)

B. STUDY DESIGN AND METHODS

1. Test procedure

During the growing season of 2012, eight field trials with potatoes (field conditions) were conducted in Germany, the United Kingdom and Spain, in order to determine the magnitude of the residues of metiram (BAS 222 F) after application of BAS 222 28 F.
The WG formulation BAS 222 28 F was applied three times (27 - 30, 20 - 22 and 13 - 15 days before harvest) at single rates of 1.4 kg as/ha for BAS 222 F in a spray volume of 200 - 400 L/ha in order to determine the magnitude of the residues of the active ingredient on Raw Agricultural Commodities (RAC).
Specimens were collected at 0, 6 - 8, 13 - 15 and 20 - 22 days after the last application (DALA).

Table 6.3.1- 25 Application and sampling details for trials conducted in 2012

Region	No. of trials	No. of Appl.	F, G, I[2]	Method	Test Item	Active Substance	Application		Target Timing	
							Rate (kg a.s./ha)	Water vol. (L/ha)	Appl. (DBH)[3]	Sampl. (DALA)[1]
EU North & South	8	3	F	-	BAS 222 28 F (WG)	Metiram BAS 222 F	1.4	200-400	1st appl.: 27 -30 2nd appl.: 20 - 22 3rd appl.: 13 - 15	0 6 - 8 13 - 15 20 - 22

1) Days after last application,
2) Field, Glasshouse or Indoor,
3) Days before harvest

2. Description of analytical procedures

The specimens were analyzed for residues of metiram according to BASF method No. L0089/01 and as carbondisulfide according to BASF method L0234/01. The residues of ETU were determined according to the BASF method No. L0176/01. The residues of EU and EBIS were determined with BASF method L0233/01.
The limit of quantitation (LOQ) of the method L0089/01 was 0.05 mg/kg and for metiram as carbondisulfide it was 0.10 mg/kg. The LOQ of the method L0176/01 was 0.01 mg/kg. The LOQ for EU and EBIS were 0.01 mg/kg with the applied method.
The results of procedural recovery experiments averaged at about 92% for BAS 222 F (by EBDC) at fortification levels between 0.05 and 1.0 mg/kg, at 84% for BAS 222 F (by CS_2) at fortification levels between 0.1 and 1.0 mg/kg, at 87% for ETU, at 74% for EU and at 89% for EBIS at fortification levels between 0.01 and 0.1 mg/kg.

BASF method L0089/01was used to determine Metiram as EBDC:
The ethylene-bisdithiocarbamate (EBDC) moiety was formed out of BAS 222 F and extracted from the specimen with a buffer solution consisting of EDTA, cysteine, methanol and sodium hydroxide adjusted to pH 11.0. The formed ethylene-bisdithiocarbamate (EBDC) analyte was methylated with iodmethane prior to C18 SPE clean up. Specimens were quantified by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The limit of quantitation (LOQ) was 0.05 mg/kg.

BASF method L0234/01 was used to determine Metiram as CS_2
Metiram was transformed to CS_2 by means of orthophosphoric acid. Subsequently, the CS_2 was transferred to isooctane with a flow of nitrogen. The quantification was carried out using GC-MS. The limit of quantitation (LOQ) was 0.10 mg/kg.

BASF method L0176/01 was used to determine ETU:
ETU was extracted from the specimen material with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water. After centrifugation an aliquot was taken and the methanol was evaporated from the extract. The pH was adjusted to 8 before evaporating (in some cases after evaporation). The remaining water phase was cleaned by liquid/liquid (water/dichloromethane) partition on an Extrelut column. After concentration of the eluate, the residue was determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EU was determined according to BASF method L0233/01:
The extraction from EU was performed with a mixture of sodium ascorbate, thiourea, ammonium chloride and methanol-water and was followed by a clean-up by liquid-liquid partition on an Extrelut column where ethyl acetate was used for the elution.
Water was added prior the evaporation of the specimen extract. For the final reconstitution of the specimen extract a solution of H_2O/MeOH was used. The determination was performed by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

EBIS was determined according to BASF method L0233/01:
The extraction from EBIS was performed with a mixture of acetonitrile/formic acid in combination with a thiourea solution and was followed by a clean-up step utilizing C18-EC. Specimens were diluted with a solution of acetonitrile/H_2O/formic acid before being determined by LC-MS/MS. The limit of quantitation (LOQ) was 0.01 mg/kg.

The results of procedural recovery experiments are summarized in Table 6.3.1- 26.

Table 6.3.1- 26 Summary of recoveries

Matrix	Fortification Level (mg/kg)	Summary Recoveries			
		n	Mean (%)	SD (+/-)	RSD (%)
Method No. L0089/01		**Metiram (by EBDC)**			
Potato/Tuber	0.05, 0.5, 1.0	9	92	7.9	8.5
Method No. L0234/01		**Metiram (by CS_2)**			
Potato/Tuber	0.1, 1.0	14	84	10.9	13.0
Method No. L0176/01		**ETU**			
Potato/Tuber	0.01, 0.1	8	87	5.0	5.8
Method No. L0233/01		**EU**			
Potato/Tuber	0.01, 0.1	8	74	4.1	5.6
Method No. L0233/01		**EBIS**			
Potato/Tuber	0.01, 0.05, 0.1	12	89	13.9	15.6

II. RESULTS AND DISCUSSION

Residue data of the field trials is summarized in Table 6.3.1- 27 and Table 6.3.1- 28. Detailed information is shown in Table 6.3.1- 29 to Table 6.3.1- 32.

Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ. The maximum storage interval of deep frozen samples from harvest until extraction was 428 days for metiram (by EBDC), 318 days for metiram (by CS_2) and 310 days for ETU, 448 days for EU and 452 days for EBIS.
The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

Table 6.3.1- 27 Summary of metiram level in BAS 222 28 F treated potato

Region	Matrix	DALA [1)]	BBCH	Range of CS_2 Residues [2)] [mg/kg]	Range of metiram Residues (by CS_2) [mg/kg]	Range of metiram Residues (by EBDC) [mg/kg]
EU North & South	Potato (tuber)	0	45 – 48	< 0.056	< 0.1	< 0.05
		6 – 8	47 – 49	< 0.056	< 0.1	< 0.05
		13 – 15	48 – 49	< 0.056	< 0.1	< 0.05
		20 – 22	49	< 0.056	< 0.1	< 0.05

[1)] DALA = Days after Last Application
[2)] the conversion factor from CS_2 to metiram is 1.79

Table 6.3.1- 28 Summary of ETU, EU, and EBIS level in BAS 222 28 F treated potato

Portion analysed	No. of specimens	DALA [1)]	BBCH	Range of ETU Residues [mg/kg]	Range of EU Residues [mg/kg]	Range of EBIS Residues [mg/kg]
EU North & South	Potato (tuber)	0	45 – 48	< 0.01 – 0.019	< 0.01	< 0.01
		6 – 8	47 – 49	< 0.01 – 0.022	< 0.01	< 0.01
		13 – 15	48 – 49	< 0.01 – 0.026	< 0.01	< 0.01
		20 – 22	49	< 0.01 – 0.022	< 0.01	< 0.01

[1)] DALA = Days after Last Application

Table 6.3.1- 29 Level of metiram in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DALA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code:	389454	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					7	tuber	<0.056	<0.1	<0.05
Trial No.	L120524					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					22	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					8	tuber	<0.056	<0.1	<0.05
Trial No.	L120525					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	45	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					7	tuber	<0.056	<0.1	<0.05
Trial No.	L120526					13	tuber	<0.056	<0.1	<0.05
GLP:	yes					20	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					8	tuber	<0.056	<0.1	<0.05
Trial No.	L120527					15	tuber	<0.056	<0.1	<0.05
GLP:	yes					22	tuber	<0.056	<0.1	<0.05
Year:	2012									

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 30 Level of metiram in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[3] at last appl. (BBCH)	DALA[2]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	CS_2[1]	Metiram (by CS_2)	Metiram (by EBDC)
Study code:	389454	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 300 L/ha	45-47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					7	tuber	<0.056	<0.1	<0.05
Trial No.	L120528					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					22	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 400 L/ha	45-47	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					7	tuber	<0.056	<0.1	<0.05
Trial No.	L120529					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					20	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	46	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					6	tuber	<0.056	<0.1	<0.05
Trial No.	L120530					14	tuber	<0.056	<0.1	<0.05
GLP:	yes					20	tuber	<0.056	<0.1	<0.05
Year:	2012									
Study code:	389454	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	46	0	tuber	<0.056	<0.1	<0.05
Doc ID:	2012/1272625					8	tuber	<0.056	<0.1	<0.05
Trial No.	L120531					13	tuber	<0.056	<0.1	<0.05
GLP:	yes					21	tuber	<0.056	<0.1	<0.05
Year:	2012									

1) the conversion factor from metiram to CS_2 is 1.79
2) Days after last application
3) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 31 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (N-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DA LA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code:	389454	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	47	0	tuber	0.019	<0.01	<0.01
Doc ID:	2012/1272625					7	tuber	0.022	<0.01	<0.01
Trial No.	L120524					14	tuber	0.026	<0.01	<0.01
GLP:	yes					22	tuber	0.021	<0.01	<0.01
Year:	2012									
Study code:	389454	Potato	Germany	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 200 L/ha	48	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2012/1272625					8	tuber	<0.01	<0.01	<0.01
Trial No.	L120525					14	tuber	<0.01	<0.01	<0.01
GLP:	yes					21	tuber	<0.01	<0.01	<0.01
Year:	2012									
Study code:	389454	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	45	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2012/1272625					7	tuber	<0.01	<0.01	<0.01
Trial No.	L120526					13	tuber	<0.01	<0.01	<0.01
GLP:	yes					20	tuber	<0.01	<0.01	<0.01
Year:	2012									
Study code:	389454	Potato	United Kingdom	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	47	0	tuber	<0.01	<0.01	<0.01
Doc ID:	2012/1272625					8	tuber	<0.01	<0.01	<0.01
Trial No.	L120527					15	tuber	<0.01	<0.01	<0.01
GLP:	yes					22	tuber	<0.01	<0.01	<0.01
Year:	2012									

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

Table 6.3.1- 32 Level of ETU, EU, EBIS in BAS 222 28 F treated potato (S-EU)

Study details		Crop	Country	Formulation Application rate	GS[2] at last appl. (BBCH)	DALA[1]	Residues found[3] (mg/kg parent equiv.)			
							Matrix	ETU	EU	EBIS
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389454 2012/1272625 L120528 yes 2012	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 300 L/ha	45-47	0 7 14 22	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389454 2012/1272625 L120529 yes 2012	Potato	Greece	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 400 L/ha	45-47	0 7 14 20	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389454 2012/1272625 L120530 yes 2012	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	46	0 6 14 20	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01
Study code: **Doc ID:** **Trial No.** **GLP:** **Year:**	389454 2012/1272625 L120531 yes 2012	Potato	Spain	BAS 222 28 F: 3x 1.4 kg metiram/ha Spray volume: 250 L/ha	46	0 8 13 21	tuber tuber tuber tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01

1) Days after last application
2) Growth stage
For calculation purposes for example < 0.01 was set to 0.01

No residues of Metiram (by EBDC) above the limit of quantitation (0.05 mg/kg) were found in any of the analyzed treated and untreated specimens.

No residues of CS_2 (Metiram by CS_2) above the limit of quantitation (0.056 mg/kg) (0.1 mg/kg expressed as metiram) were found in any of the analyzed treated specimens.
In the untreated specimens L1205260001 and L1205260004 the residue concentrations were determined as 0.067 mg/kg and 0.073 mg/kg (0.12 mg/kg and 0.13 mg/kg expressed as metiram), respectively and hence were above the LOQ of 0.056 mg/kg (0.1 mg/kg expressed as metiram).
In all the other untreated specimens, no residues above the limit of quantitation were found at any sampling occasion.

In the treated specimens taken from trial L120524 residues of ETU remained relatively stable (0.02 – 0.03 mg/kg) over the sampling occasions. In all the other treated specimens, residues of ETU were below the limit of quantitation (< 0.01 mg/kg).
No residues of ETU above the limit of quantitation were found in any of the analyzed untreated specimens.

No residues of EU above the limit of quantitation were found in any of the analyzed treated and untreated specimens.

No residues of EBIS above the limit of quantitation were found in any of the analyzed treated and untreated specimens.

III. CONCLUSION

Eight field trials with potatoes were conducted in Europe (North and South) in season 2012. BAS 222 28 F was applied three times at single rates of 1.4 kg/ha BAS 222 F (2.0 kg/ha of WG formulation BAS 222 28 F) in a spray volume of 200-400 L/ha. Residue analysis of samples taken at different time intervals after the last application (0, 6 - 8, 13 - 15 and 20 - 22 DALA) showed a decline of residue levels.
At the recommended PHI of 14 days, residues of metiram (determination as CS_2 and EBDC), CS_2, EU and EBIS were below the limit of quantitation (<0.056, <0.05 mg/kg, <0.10. <0.01 mg/kg). Residues of ETU were between <0.01 - 0.026 mg/kg.
Samples from untreated control plots did not contain apparent residues of CS_2, EBDC, ETU, EU and EBIS, i.e. residues were below the corresponding LOQ (except for trial L120526 residues of CS_2 of 0.073 mg/kg (0.13 mg/kg for metiram determination as CS_2) were found at DALA 20 - 22). The maximum storage interval of deep frozen samples from harvest until extraction was 428 days for metiram (by EBDC), 318 days for metiram (by CS_2) and 310 days for ETU, 448 days for EU and 452 days for EBIS. The mean of the concurrent recoveries was within the acceptable range of 70 – 110% for CS_2, EBDC, ETU, EU and EBIS.

CA 6.4 Feeding studies

Annex II Dossier:
Livestock feeding studies with metiram (poultry and lactating ruminants) have previously been reviewed during the Annex I inclusion process. They were considered to be acceptable.

AIR3 Dossier:
No new studies were conducted.

In support of the representative use (potato) supported in the present dossier, the dietary exposure of livestock to metiram residues resulting from the use in potato needs to be considered. In particular, potential intake of the parent compound metiram and the metabolite ETU has to be addressed.

Regarding metiram intake, the available livestock feeding studies with metiram, allow to conclude that the estimated the residues in commodities of animal origin are below the LOQ for both metiram and ETU. For potato, field residue trials show that residue level of metiram and ETU are below the LOQ. In conclusion, the contribution to the livestock feed burden is insignificant. Therefore, the use supported in the present dossier is covered by previous estimations covering a broader range of metiram uses. A new estimation in the context of the present dossier is therefore not required. These previous estimations conclude that if the intake is <0.1 mg/kg/day, no residues in animal commodities are expected (i.e. metiram and ETU below the corresponding LOQ, see below).

Regarding ETU intake, the available residue data allows to conclude that livestock feeding studies with metabolite ETU are not required (see DocID 2002/1006209). In brief, the contribution of ETU to the intake is very low. Taking ETU residue in processed feed items into account, assuming worst case scenarios the following estimations are obtained:

Dairy cow	0.07 mg/animal/d
Beef cattle	0.17 mg/animal/d
Pigs	0.08 mg/animal/d
Chicken	0.003 mg/animal/d

Moreover, livestock metabolism studies with metiram show that the ETU formed in animal is rapidly eliminated either by excretion or by further transformation to natural products. In consequence, ETU levels in commodities of animal origin are insignificant and thus do not need to be included in a definition of the residue (see section 6.7). In conclusion, for ETU additional livestock studies (nature of residue, magnitude of residue) are not appropriate, considering both limited knowledge gain as well as animal welfare perspective).

For information, result from previous evaluations is provided below.

Information from Annex I inclusion process

The following table is copied from the Monograph prepared by Italy: based on an estimated feed burden below 0.1 mg/kg/day, the residues of metiram and ETU in animal commodities are expected to be below the corresponding LOQ:

Residues from livestock feeding studies

Estimated intakes by livestock ≤ 0.1 mg/kg/day:	Ruminant: yes/no	Poultry: yes/no	Pig: yes/no
Muscle	<0.05*/<0.02**		
Liver	<0.05*/<0.02**		
Kidney	<0.05*/<0.02**		
Fat	<0.05*/<0.02**		
Milk	<0.05*/<0.02**		
Eggs	<0.05*/<0.02**		

*LOD for metiram; **LOD for ETU
After normalization to a 1x dose level

Information from EU MRL compilation dossier (BASF DocID 2008/1042839)

Furthermore, in 2008 and in context of the re-evaluation of MRLs according to Reg. 396/2005, Art. 12, BASF SE provided an EU MRL compilation dossier (BASF DocID 2008/1042839) to Italy as the evaluating Member State (Italy, 2010: Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174p.). The following table is copied from this dossier. It confirms the previous conclusion that based on an estimated feed burden below 0.1 mg/kg/day, the residues of metiram and ETU in animal commodities are expected to be below the corresponding LOQ.

Residues from livestock feeding studies (OECD data point number IIA 6.4 and IIIA 8.4)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: Yes/no	Poultry: Yes/no	Pig: Not assessed
Muscle	<0.05*	<0.05*	no pig feeding study conducted; metabolism in rat and ruminant similar
Liver	<0.05*	<0.05*	
Kidney	<0.05*	<0.05*	
Fat	<0.05*	<0.05*	
Milk	<0.05*		
Eggs		<0.05*	

*LOQ for metiram (mg/kg)

CA 6.4.1 Poultry

Data/information on poultry feeding studies for metiram were reviewed during the Annex I inclusion process and was considered to be acceptable (see section MCA 6.4). No further data has been generated.

In summary, a residue transfer study was conducted in chicken. The dose levels tested were highly exaggerated compared to the dietary feed burden expected after feeding metiram-treated plant commodities (the animals were dosed with 0.3, 1.5, 3.0 and 150 mg/animal/d).
Egg samples and tissue samples were analysed for both metiram and ETU. In eggs, no residues were detected in samples from the three lower dose groups (0.3, 1.5, 3.0 mg/animal/d). In tissues, residue levels were below the LOQ of 0.05 mg/kg.
Residues of metiram and of ETU residues are expected to be below the respective LOQ (see see section MCA 6.4) after normalization to the estimated feed burden (1X dose level), both if the uses supported in the present dossier are considered as well as if all EU registered uses of metiram are considered.

Report:	CA 6.4.1/1 [redacted] 1987a The determination of residues of Metiram in the eggs and tissues of the laying hen following oral gavage of Metiram complex 1987/10156
Guidelines:	none
GLP:	yes (certified by Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)

Report:	CA 6.4.1/2 [redacted]1987b The determination of Ethylenethiourea (ETU) residues in the eggs and tissues of the laying hen following oral administration of Metiram complex 1987/10157
Guidelines:	none
GLP:	yes (certified by Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)

CA 6.4.2 Ruminants

Data/information on cow/goat feeding studies for metiram was reviewed as part of the Annex I inclusion process and was considered to be acceptable (see section MCA 6.4). No further data has been generated.

In summary, a residue transfer study was conducted in goat. The dose levels tested were highly exaggerated compared to the dietary feed burden expected after feeding metiram-treated plant commodities (the animals were dosed with 40, 200, 400 and 20 000 mg/animal/d).
Milk samples and tissue samples were analysed for both metiram and ETU. In milk, no residues were detected in samples from the three lower dose groups (0.3, 1.5, 3.0 mg/animal/d). In goat tissues, residue levels were below the LOQ of 0.05 mg/kg except for liver and fat (one subsample).
Residues of metiram and of ETU residues are expected to be below the respective LOQ (see section MCA 6.4) after normalization to the estimated feed burden (1X dose level), both if the uses supported in the present dossier are considered as well as if all EU registered uses of metiram are considered.

Report:	CA 6.4.2/1 [redacted] 1986a Residues of Metiram in milk and tissues of dairy cows 1986/10206
Guidelines:	none
GLP:	yes (certified by Department of Health and Social Security, London, United Kingdom)

Report:	CA 6.4.2/2 [redacted] 1986a Residues of Metiram in milk and tissues of dairy cows 1986/10205
Guidelines:	none
GLP:	yes (certified by Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)

Report:	CA 6.4.2/3 [redacted] 1986a Residues of ETU (Ethylene thiourea) in milk and tissues of dairy cows following oral adminstration of Metiram 1986/10184
Guidelines:	none
GLP:	yes (certified by Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)

CA 6.4.3 Pigs

A feeding study in pig is not required since the metabolism of metiram has been shown to be similar in rats and in ruminants.

CA 6.4.4 Fish

A feeding study in fish is not required considering the properties of metiram both the low logPow as well as the chemical properties as a "solvolytic" metal complex (see section 6.2).

In addition, currently no test method or guidance document is available. As a consequence waiving of this particular data requirement is considered acceptable according to the "guidance document for applicants on preparing dossiers for the approval of a chemical new active substance and the renewal of approval of the chemical active substance according to regulation (EU) No. 283/2013 and regulation (EU) No. 284/2013" (SANCO/10181/2013-rev.2 of 2-May-2013).

CA 6.5 Effects of Processing

CA 6.5.1 Nature of the residue

Annex II Dossier :
A high temperature hydrolysis study for metiram (14C-BAS 222 F) was reviewed during the Annex I inclusion process and was considered acceptable.

AIR3 Dossier :
No further studies have been performed.

In support of the representative use (potato) supported in the present dossier, the stability of the parent compound metiram under standard test conditions has to be taken into account. This study shows that metiram is effectively transformed to ETU when suspended and heated under the standard conditions simulating processing, notably representative for pasteurisation (pH 4, 90°C, 20 min), for baking/boiling/brewing (pH 5, 100°C, 60 min) and for sterilisation (pH 6, 120°C, 20 min).

In conclusion, the nature of the metiram residue in processed commodities is considered sufficiently elucidated. For processed commodities the residue definition for risk assessment is ETU (see section MCA 6.7).

Report:	*CA 6.5.1/1* *Hassink J., 2002a* *Hydrolysis of BAS 222 F at 90 C, 100 C, and 120 C* *2002/1005307*
Guidelines:	*EEC 94/37, EEC Method C7, FAO Revised Guidelines on Environmental Criteria for the Registration of Pesticides Revision 3 (28 August 1993), EPA 161-1*
GLP:	*yes* *(certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)*

CA 6.5.2 Distribution of the residue in inedible peel and pulp

Data on the distribution of residues between peel and pulp is not required for the representative use supported in the present dossier (potato).

CA 6.5.3 Magnitude of residues in processed commodities

In support of the representative use supported in the present dossier, no studies addressing potato processed commodities have to be taken into account. For potato residue levels in the RAC are below the LOQ, therefore a processing study is not required.

CA 6.6 Residues in Rotational Crops

Annex II Dossier:

Metabolism in rotational crop study (wheat, beet and kale) with metiram has previously been reviewed in the Annex I inclusion process.
The total radioactive residues in the edible parts of succeeding crops destined for human consumption were <0.2 mg/kg in kale, <0.5 mg/kg in beet (tuber) and <1.5 mg/kg in wheat (grain). As already observed in the plant metabolism studies, the metabolites of BAS 222 F were extensively incorporated into the carbon pool and hence, into the natural products of the plants. It was concluded that the exposure of the consumers to residues in rotational crops grown on plots treated with metiram is negligible. The following table was copied from the Monograph prepared by Italy.

Residues in succeeding crops

Based on the results on rotational crops and on the fast degradation of the a.i. it can be concluded that the application of Metiram will not lead to uptake of any residue of concern from soil by succeeding crops

AIR3 Dossier:

In addition, a new metabolism in rotational crop study (wheat, radish, lettuce) with metiram was conducted in 2009. The findings confirm the previous conclusion that application of metiram does not result in significant uptake of residue of concern into the succeeding crop. In contrast, metiram degradation products taken up from soil are effectively entering primary metabolism followed by incorporation into naturally occurring plant constituents. In conclusion, exposure of the consumers to metiram and its transformation products from rotational crops grown on soil treated with metiram is negligible. A magnitude of the residue study in rotational crop study is not required.

CA 6.6.1 Metabolism in rotational crops

Report: CA 6.6.1/1
Bross M. et al., 2010a
Confined rotational crop study with 14C-BAS 222 F
2009/1017248

Guidelines: EPA 860.1000: Background - PMRA Section 97.13 (Canada): Residue Chemistry Guidelines Confined Accumulation in Rotational Crops (June 1997), EPA 860.1000: EPA Residue Chemistry Test Guidelines, EPA 860.1850: Confined Accumulation in Rotational Crops, EEC 7524/VI/95 rev. 2 (July 22 1997)

GLP: yes
(certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany)

Executive Summary

I. MATERIAL AND METHODS

A. MATERIALS

1. Test Material: ^{14}C-BAS 222 F (Metiram)
Description: ^{14}C- BAS 222 F (radiolabeled in the ethylene bridge) (Specific radioactivity: 4.76 MBq/mg)
Lot/Batch #: 153-3101
Purity: 88.2% (chemical purity; Jodometry, Non-GLP)
CAS#: 9006-42-2
Stability of test Compound: The residues in lettuce, treated with BAS 222 F were stable under the chosen experimental conditions (-18°C, 30 months)

2. Test Commodity:
Crop: lettuce, white radish, spring wheat
Type: not reported
Variety: lettuce: Matilda, Estelle; white radish: April Cross; spring wheat: Thassos
Botanical name: *Lactuca sativa L., Rhaphanus sativus, Triticum L.*
Crop parts(s) or processed commodity: lettuce (unripe leaf and ripe head)
white radish (immature plant, mature top and root)
spring wheat (forage, straw, chaff and grain)

Sample size: Lettuce leaf: > 0.49 kg, Lettuce head: < 14.74 kg, White radish top: < 0.34 kg, White radish root:< 25.07 kg, Spring wheat forage: < 0.69 kg, Spring wheat straw: < 0.48 kg, Spring wheat chaff: < 0.85 kg, Spring wheat grain: > 0.154 kg.

3. Soil: Loamy sand soil was used. The soil physicochemical properties are described below (see Table 6.6.1- 1).

Table 6.6.1- 1 Soil physicochemical properties

USDA classification	
clay	5.5
silt	15.2
sand	79.3
soil class	loamy sand
DIN classification	
clay	5.5
silt	16.7
sand	77.7
soil class	loamy sand (DIN 4220)
Other soil parameters	
total nitrogen	0.07 %
total organic carbon	0.55 %
total carbon	0.55 %
pH ($CaCl_2$)	6.4
pH (H_2O)	7.1
effective cation exchange capacity	7.0 cmol/kg
max. water holding capacity	22.3 g/100 g dry soil
microbial biomass	9.9 mg C/100 g dry soil
microbial C / organic C	1.8 %
bulk density	1614 g/L
dry matter	88.3 %

B. STUDY DESIGN AND METHODS

1. Test procedure

A confined rotational crop study was conducted with ^{14}C-BAS 222 F (Metiram, Reg. No. 250284) radiolabeled in the ethylene bridge and blended with unlabelled test item. The active substance was suspended in acetone and applied to bare loamy sand soil in plastic containers at an application rate of 1 x 12.500 kg as/ha (approximately 11.16 lb/A). The nature and the level of radioactive residues were investigated in lettuce (unripe leaf and ripe head), white radish (immature plant, mature top and root) and spring wheat (forage, straw, chaff and grain) after plant back intervals of 30, 121 and 365 days. Plant samples were harvested at maturity, and additional immature lettuce leaf samples as well as immature white radish plant (plant back interval of 365 days only) and spring wheat forage samples were taken 29 to 41 days after planting, 13 days after sowing and 49 to 67 days after sowing, respectively. Soil samples were taken after plowing and after harvest of the mature crops for each plant back interval. The harvested material was stored in a freezer.

2. Description of analytical procedures

All plant samples and soil samples were homogenized and combusted to $^{14}C0_2$ which was trapped by an absorption and scintillation liquid and analyzed by LSC for the determination of the total radioactive residues.

Aliquots of homogenized plant material were extracted three times with methanol and two times with water. The methanol and water extracts were measured by LSC.

The results of the methanol extraction and the water extraction were summarized and referred to as extractable radioactive residues (ERR). The residue after solvent extraction of each sample was dried and homogenized. Aliquots were combusted for the determination of the residual radioactive residue (RRR).

In order to characterize the methanol extractable radioactive residues as organosoluble or water soluble fractions, liquid / liquid partition was carried out using isohexane, dichloromethane and ethyl acetate as organic solvents. Aliquots of the liquid phases were analyzed by LSC measurement.

Solubilization treatments of the Residual Radioactive Residues comprised treatments with aqueous ammonia, enzymes and sodium hydroxide.

After the extraction and partition procedures and the various solubilization treatments of the Residual Radioactive Residues after solvent extraction (RRR), HPLC analyses were carried out for the extracts, partition phases and solubilizates with a sufficient level of radioactivity.

For quantitation, HPLC method LC02, LC12 or LC08 with a Phenomenex Gemini C18 column was used. Confirmatory HPLC analyses were carried out using HPLC method LC05 with a YMC Polyamine II column.

HPLC method LC02/LC12
The eluent system consisted of 2 mobile phases (Eluent A: Water / cone. NH_4OH (1000 + 2.5, v/v), Eluent B: Acetonitrile) which were used applying gradient elution.

HPLC method LC08:
The eluent system consisted of 2 mobile phases (Eluent A: Water / cone. NH_4OH (1000 + 2.5, v/v), Eluent B: Acetonitrile + THF (550 + 450, v/v)) which were used applying gradient elution.

HPLC method LC05:
The eluent system consisted of 2 mobile phases (Eluent A: Water + 25 mM $NH_4H_2P0_4$ + 25 mM $(NH_4)_2HP0_4$, Eluent B: Acetonitrile) which were used applying gradient elution.

3. Identification of metabolites

Identification of the metabolites was based on analyses of purified fractions (seven fractions) isolated from methanol extracts of spring wheat straw (30 DAT) by HPLC-MS and co-chromatography experiments with reference items. Peak assignment in the other samples was done by comparison of the HPLC retention times and the elution profiles / metabolite patterns with those of the fractions investigated by HPLC-MS or co-chromatography experiments and with the reference items.

II. RESULTS AND DISCUSSION

A. TOTAL RADIOACTIVE RESIDUES (TRRs)

The calculated TRR (ERR +RRR) for unripe lettuce leaf accounted for 0.766 mg/kg after the plant back interval of 30 days. Lower levels of 0.180 and 0.112 mg/kg were found after the longer periods of soil aging (121 Days after Treatment and 365 DAT).

The total residues in ripe lettuce head reached comparable values of 0.656, 0.221 and 0.091 mg/kg after plant back intervals of 30, 121 and 365 days, respectively.

The total radioactive residues in unripe white radish plant (365 DAT) amounted to 0.094 mg/kg. The residue concentrations in mature white radish top also showed decreasing levels of 0.906, 0.283 and 0.093 mg/kg after increasing soil aging periods of 30, 121 and 365 days, respectively. In mature white radish root, lower TRR levels of 0.393 mg/kg (30 DAT), 0.136 mg/kg (121 DAT) and 0.059 mg/kg (365 DAT) were detected.

In spring wheat, the highest residue levels were measured in straw at all plant back intervals (4.245 mg/kg at 30 DAT, 1.739 mg/kg at 121 DAT and 1.424 mg/kg at 365 DAT, respectively). The TRR levels in wheat chaff accounted for 3.775 mg/kg, 1.023 mg/kg and 1.396 mg/kg after the soil aging periods of 30, 121 and 365 days. Somewhat lower residue levels of 2.752 mg/kg (30 DAT), 0.530 mg/kg (121 DAT) and 1.181 mg/kg (365 DAT) were observed in wheat grain. In spring wheat forage, residue levels of 1.690 mg/kg (30 DAT), 0.416 mg/kg (121 DAT) and 0.200 mg/kg (365 DAT) were detected.

After soil aging and plowing, the total radioactive residues in soil accounted for 2.510 mg/kg at 30 DAT, 1.402 mg/kg at 121 DAT and 1.599 mg/kg after a plant back interval of 356 days.

After harvest of individual mature crops, soil residue levels of 2.004 to 2.681 mg/kg (30 DAT), 1.744 to 1.769 mg/kg (121 DAT) and 1.367 to 1.473 mg/kg (365 DAT) were observed.

The results of the Total Radioactive Residues (TRR) after ^{14}C-BAS 222 F treatment in lettuce, white radish and spring wheat are provided in Table 6.6.1- 2, the results of the soil samples are shown in Table 6.6.1- 3.

Table 6.6.1- 2: Total Radioactive Residues in Rotational Crops Samples after Treatment with ^{14}C-BAS 222 F

Matrix	Days After Sowing / Planting DAP	TRR measured[1)] [mg/kg]	TRR calculated[2)] [mg/kg]
Plant back interval: 30 DAT			
Lettuce leaf	38	0.839	0.766
Lettuce head	59	0.785	0.656
White radish top	88	1.091	0.906
White radish root	88	0.377	0.393
Spring wheat forage	54	1.905	1.690
Spring wheat straw	131	5.096	4.245
Spring wheat chaff	131	3.890	3.775
Spring wheat grain	131	2.819	2.752
Plant back interval: 121 DAT			
Lettuce leaf	41	0.216	0.180
Lettuce head	55	0.225	0.221
White radish top	109	0.384	0.283
White radish root	109	0.159	0.136
Spring wheat forage	67	0.467	0.416
Spring wheat straw	146	1.856	1.739
Spring wheat chaff	146	1.007	1.023
Spring wheat grain	146	0.458	0.530
Plant back interval: 365 DAT			
Lettuce leaf	29	0.147	0.112
Lettuce head	56	0.100	0.091
White radish plant	13	0.087	0.094
White radish top	77	0.123	0.093
White radish root	77	0.081	0.059
Spring wheat forage	49	0.207	0.200
Spring wheat straw	109	1.370	1.424
Spring wheat chaff	109	1.426	1.396
Spring wheat grain	109	1.216	1.181

1) TRR was determined by direct combustion
2) TRR was calculated as the sum of ERR (extraction with methanol and water) + RRR
DAT = Days After Treatment

Table 6.6.1- 3: Total Radioactive Residues in Soil Samples after Treatment with ^{14}C-BAS 222 F

Soil samples **(Days After Treatment DAT)**	**Days After Sowing** DAP	**TRR measured[1)]** [mg/kg]
Plant back interval: 30 DAT		
After ploughing		
30 DAT	6	2.510
After harvest of mature crops		
Lettuce (89 DAT)	59	2.004
White radish (118 DAT)	88	2.681
Spring wheat (161 DAT)	131	2.137
Plant back interval: 121 DAT		
After ploughing		
121 DAT	0	1.402
After harvest of mature crops		
White radish (232 DAT)	111	1.744
Spring wheat (267 DAT)	146	1.769
Plant back interval: 365 DAT		
After ploughing		
365 DAT	0	1.599
After harvest of mature crops		
Lettuce (421 DAT)	56	1.380
White radish (442 DAT)	77	1.367
Spring wheat (474 DAT)	109	1.473

1) TRR was determined by direct combustion

B. EXTRACTION, CHARACTERIZATION AND IDENTIFICATION OF RESIDUES

1. Extraction of residues

The extractability of radioactive residues with methanol and water was above 50 % of the TRR for most of the lettuce samples (54.4 % to 65.2 % TRR; 46.1 % TRR for unripe lettuce leaf after 365 days) and around 50 % for mature white radish top and root (48.8 % to 61.0 % TRR; 39.4 % TRR for unripe white radish plant, 365 DAT). For spring wheat forage (37.0 % to 49.4 % TRR), straw (38.0 % to 50.8 % TRR) and chaff (25.6 % to 45.0 % TRR), the extraction efficiency was around or below 50 %. In the case of spring wheat grain, the extractability was lower with 13.6% to 19.0% TRR. The main part of the radioactive residues was generally extracted with methanol, except for wheat grain where water was more effective as extracting solvent.

The extractabilities with methanol and water are summarised in Table 6.6.1- 4.

Table 6.6.1- 4: Extractability of Radioactive Residues in Rotational Crops Samples after Treatment with ^{14}C-BAS 222 F T

Matrix	DAP	TRR calculated[1)]	Methanol Extract		Water Extract		ERR[2)]		RRR[3)]	
		[mg/kg]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Plant back interval: 30 DAT										
Lettuce leaf	38	0.766	0.438	57.2	0.061	8.0	0.499	65.2	0.267	34.8
Lettuce head	59	0.656	0.349	53.2	0.070	10.7	0.419	63.9	0.237	36.1
White radish top	88	0.906	0.359	39.6	0.140	15.5	0.499	55.0	0.407	45.0
White radish root	88	0.393	0.188	48.0	0.015	3.7	0.203	51.7	0.190	48.3
Spring wheat forage	54	1.690	0.699	41.4	0.135	8.0	0.834	49.4	0.856	50.6
Spring wheat straw	131	4.245	1.151	27.1	0.463	10.9	1.614	38.0	2.631	62.0
Spring wheat chaff	131	3.775	0.666	17.6	0.302	8.0	0.967	25.6	2.808	74.4
Spring wheat grain	131	2.752	0.175	6.4	0.278	10.1	0.453	16.5	2.299	83.5
Plant back interval: 121 DAT										
Lettuce leaf	41	0.180	0.087	48.2	0.011	6.2	0.098	54.4	0.082	45.6
Lettuce head	55	0.221	0.114	51.5	0.020	9.0	0.134	60.5	0.087	39.5
White radish top	109	0.283	0.097	34.2	0.044	15.6	0.141	49.8	0.142	50.2
White radish root	109	0.136	0.061	44.5	0.006	4.3	0.066	48.8	0.070	51.2
Spring wheat forage	67	0.416	0.132	31.8	0.022	5.2	0.154	37.0	0.262	63.0
Spring wheat straw	146	1.739	0.511	29.4	0.208	12.0	0.720	41.4	1.019	58.6
Spring wheat chaff	146	1.023	0.271	26.5	0.093	9.0	0.364	35.5	0.659	64.5
Spring wheat grain	146	0.530	0.037	7.0	0.064	12.0	0.101	19.0	0.429	81.0

Matrix	DAP	TRR calculated[1)]	Methanol Extract		Water Extract		ERR[2)]		RRR[3)]	
		[mg/kg]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Plant back interval: 365 DAT										
Lettuce leaf	29	0.112	0.043	38.0	0.009	8.1	0.052	46.1	0.060	53.9
Lettuce head	56	0.091	0.050	54.5	0.008	9.0	0.058	63.5	0.033	36.5
White radish plant	13	0.094	0.031	32.9	0.006	6.5	0.037	39.4	0.057	60.6
White radish top	77	0.093	0.042	44.7	0.008	8.0	0.049	52.8	0.044	47.2
White radish root	77	0.059	0.034	56.7	0.003	4.2	0.036	61.0	0.023	39.0
Spring wheat forage	49	0.200	0.064	31.8	0.011	5.5	0.075	37.3	0.126	62.7
Spring wheat straw	109	1.424	0.482	33.9	0.242	17.0	0.724	50.8	0.700	49.2
Spring wheat chaff	109	1.396	0.371	26.6	0.258	18.5	0.629	45.0	0.768	55.0
Spring wheat grain	109	1.181	0.059	5.0	0.101	8.6	0.160	13.6	1.021	86.4

1) TRR was calculated as the sum of ERR (extraction with methanol and water) + RRR
2) ERR = Extractable Radioactive Residue
3) RRR = Residual Radioactive Residue (after solvent extraction)
DAP = Days After Planting (or sowing, respectively)
DAT = Days After Treatment

The residual radioactive residues of metiram after solvent extraction ranged from a minimum of 34.8 % TRR (0.267 mg/kg, lettuce leaf 30 DAT) to a maximum of 86.4 % TRR (1.021 mg/kg, spring wheat grain 365 DAT).

2. Partition behaviour

In most cases, the major portions of the radioactive residues extracted with methanol were water soluble, and only lower portions were found in the organic fractions. In the cases of spring wheat chaff (30 DAT and 121 DAT) and grain (all plant back intervals), comparable portions were found in the organic phases (sum) and in the water phase. Results are summarised in Table 6.6.1-5.

Table 6.6.1- 5: Partition Characteristics of Radioactive Residues extracted with Methanol from Rotational Crop Samples

Matrix	DAP	Methanol extract		Organosoluble						Sum organosoluble		Water phase		Recovery[1)]
				Isohexane phase		Dichloromethane phase		Ethyl acetate phase						
		[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[%]
Plant back interval: 30 DAT														
Lettuce leaf	38	0.438	57.2	0.017	2.3	0.011	1.5	0.012	1.5	0.041	5.3	0.368	48.0	93.1
Lettuce head	59	0.349	53.2	0.020	3.0	0.006	0.9	0.009	1.3	0.034	5.2	0.285	43.5	91.6
White radish top	88	0.359	39.6	0.009	1.0	0.022	2.5	0.027	3.0	0.059	6.5	0.279	30.8	94.1
White radish root	88	0.188	48.0	0.007	1.7	0.004	1.0	0.005	1.2	0.015	3.9	0.168	42.7	97.2
Spring wheat forage	54	0.699	41.4	0.017	1.0	0.030	1.8	0.054	3.2	0.101	6.0	0.514	30.4	88.0
Spring wheat straw	131	1.151	27.1	0.052	1.2	0.145	3.4	0.129	3.0	0.326	7.7	0.599	14.1	80.3
Spring wheat chaff	131	0.666	17.6	0.106	2.8	0.143	3.8	0.080	2.1	0.329	8.7	0.300	8.0	94.5
Spring wheat grain	131	0.175	6.4	0.074	2.7	0.002	0.1	0.003	0.1	0.078	2.8	0.082	3.0	91.9
Plant back interval: 121 DAT														
Lettuce leaf	41	0.087	48.2	0.008	4.3	0.002	1.1	0.003	1.4	0.012	6.8	0.064	35.2	67.2
Lettuce head	55	0.114	51.5	0.007	3.1	0.002	1.0	0.003	1.5	0.013	5.7	0.094	42.4	93.4
White radish top	109	0.097	34.2	0.004	1.5	0.008	2.7	0.009	3.1	0.021	7.3	0.070	24.6	93.1
White radish root	109	0.061	44.5	0.003	2.0	0.001	0.9	0.001	1.0	0.005	3.9	0.052	38.3	94.7
Spring wheat forage	67	0.132	31.8	0.004	1.0	0.010	2.4	0.014	3.3	0.028	6.6	0.096	23.2	93.7
Spring wheat straw	146	0.511	29.4	0.031	1.8	0.104	6.0	0.060	3.5	0.194	11.2	0.283	16.3	93.3
Spring wheat chaff	146	0.271	26.5	0.018	1.7	0.094	9.2	0.031	3.0	0.143	14.0	0.155	15.2	110.1
Spring wheat grain	146	0.037	7.0	0.012	2.3	0.013	2.4	0.002	0.3	0.027	5.0	0.021	3.9	128.3

Matrix	DAP	Methanol extract		Organosoluble						Sum organosoluble		Water phase		Recovery[1)]
				Isohexane phase		Dichloromethane phase		Ethyl acetate phase						
		[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[%]
Plant back interval: 365 DAT														
Lettuce leaf	29	0.043	38.0	0.002	1.9	0.002	1.6	0.002	1.4	0.005	4.8	0.031	27.4	84.9
Lettuce head	56	0.050	54.5	0.003	2.9	0.002	2.0	0.001	1.4	0.006	6.3	0.042	45.8	95.6
White radish plant	13	0.031	32.9	0.001	1.2	0.003	3.2	0.002	2.1	0.006	6.5	0.022	23.4	90.9
White radish top	77	0.042	44.7	0.001	1.2	0.003	2.8	0.003	3.0	0.007	7.0	0.030	31.8	86.7
White radish root	77	0.034	56.7	0.001	1.2	0.001	2.2	0.001	1.3	0.003	4.7	0.029	48.9	94.5
Spring wheat forage	49	0.064	31.8	0.000	0.2	0.003	1.3	0.004	2.0	0.007	3.5	0.061	30.5	107.1
Spring wheat straw	109	0.482	33.9	0.031	2.2	0.033	2.3	0.031	2.2	0.096	6.7	0.349	24.5	92.2
Spring wheat chaff	109	0.371	26.6	0.024	1.7	0.020	1.4	0.024	1.7	0.067	4.8	0.268	19.2	90.4
Spring wheat grain	109	0.059	5.0	0.036	3.0	0.003	0.3	0.003	0.3	0.042	3.6	0.044	3.7	145.2

DAP = Days After Planting (or sowing, respectively)
DAT = Days After Treatment
1) Recovery calculated as (Isohexane phase + Dichloromethane phase + Ethyl acetate phase + Water phase) [mg/kg] o 100 / Methanol extract [mg/kg]

2. Identification, characterization and quantitation of extractable residues

The identification of metabolites was mainly based on fractionation of a wheat straw methanol extract (30 DAT) and analysis of the purified fractions (seven fractions) by HPLC-MS and / or co-chromatography experiments with reference items. In fraction 1 a group of three sugars (glucose, fructose and sucrose) was identified. In other samples the sugars (glucose, fructose and sucrose) were always collectively assigned, because they were not consistently separated upon quantitative HPLC analysis. The metabolite M222F001 of metiram was identified in fraction 5 by HPLC-MS. In the remaining fractions no further components were identified. No evidence was obtained for the occurrence of ETU (imidazolidine-2-thione) in the rotational crop samples.

In lettuce leaf the carbohydrates (glucose, fructose, sucrose) represented the main components in the extractable radioactive residues (0.295 mg/kg or 38.5 % TRR at 30 DAT, 0.060 mg/kg or 33.1 % TRR at 121 DAT and 0.011 mg/kg or 10.0 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component at 30 DAT and 121 DAT (0.123 mg/kg or 16.0% TRR and 0.011 mg/kg or 6.1 % TRR) and was also detected at 365 DAT (0.002 mg/kg or 2.2 % TRR). The carbohydrates (glucose, fructose, sucrose) and the metabolite M222F001 were also identified in the ammonia solubilizate after solvent extraction of 30 DAT (0.012 mg/kg or 1.6% TRR and 0.014 mg/kg or 1.9% TRR, respectively).

In lettuce head the carbohydrates (glucose, fructose, sucrose) were the main constituents in the extractable radioactive residues (0.273 mg/kg or 41.7 % TRR at 30 DAT, 0.085 mg/kg or 38.3% TRR at 121 DAT and 0.044 mg/kg or 47.9 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component at 30 DAT and 121 DAT (0.101 mg/kg or 15.3% TRR and 0.022 mg/kg or 9.8% TRR) and was also detected at 365 DAT (0.002 mg/kg and 2.0 mg/kg). The carbohydrates (glucose, fructose, sucrose) and the metabolite M222F001 were also identified in the solubilizates after solvent extraction of 30 DAT (0.055 mg/kg or 8.4 % TRR and 0.023 mg/kg or 3.7 % TRR, respectively).

In white radish plant (365 DAT) the carbohydrates (glucose, fructose, sucrose) were identified as the main components in the extractable radioactive residues (0.008 mg/kg or 8.7 % TRR) and metabolite M222F001 was also present (0.001 mg/kg or 0.8 % TRR).

The carbohydrates (glucose, fructose, sucrose) were the most abundant components in the extractable radioactive residues of white radish top (0.187 mg/kg or 20.6 % TRR at 30 DAT, 0.046 mg/kg or 16.4 % TRR at 121 DAT and 0.011 mg/kg or 12.1 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component at 30 DAT and 121 DAT (0.040 mg/kg or 4.4 % TRR and 0.008 mg/kg or 2.8 % TRR) and was also identified at 365 DAT (0.002 mg/kg or 2.3 % TRR). In the solubilizates after solvent extraction of 30 DAT the carbohydrates (glucose, fructose, sucrose) were the main constituents (0.099 mg/kg or 11.0% TRR) and metabolite M222F001 was the second most abundant component and (0.042 mg/kg or 4.6 % TRR).

In white radish root the carbohydrates (glucose, fructose, sucrose) represented the main constituents in the extractable radioactive residues (0.168 mg/kg or 42.8 % TRR at 30 DAT, 0.052 mg/kg or 38.4 % TRR at 121 DAT and 0.020 mg/kg or 33.5 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component at 30 DAT and 121 DAT (0.011 mg/kg or 2.9% TRR and 0.004 mg/kg or 2.7 % TRR) and was also detected at 365 DAT (0.002 mg/kg or 3.0 % TRR). The carbohydrates (glucose, fructose, sucrose) were also the main constituents in the solubilizates after solvent extract of 30 DAT (0.068 mg/kg or 17.3% TRR) and metabolite M222F001 was also the second most abundant component (0.011 mg/kg or 2.8% TRR).

In spring wheat forage the carbohydrates (glucose, fructose, sucrose) were the main constituents in the extractable radioactive residues (0.450 mg/kg or 26.6 % TRR at 30 DAT, 0.091 mg/kg or 21.9 % TRR at 121 DAT and 0.045 mg/kg or 22.3 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component at 30 DAT and 121 DAT (0.062 mg/kg or 3.6% TRR and 0.014 mg/kg or 3.3 % TRR) and was also identified at 365 DAT (0.002 mg/kg or 1.0 % TRR). In the solubilizates after solvent extraction of 30 DAT the carbohydrates (glucose, fructose, sucrose) were also the main constituents (0.101 mg/kg or 5.9 % TRR) and metabolite M222F001 was the second most abundant component (0.076 mg/kg or 4.5 % TRR).

The carbohydrates (glucose, fructose, sucrose) were the main components in the extractable radioactive residues of spring wheat straw (0.847 mg/kg or 20.0 % TRR at 30 DAT, 0.279 mg/kg or 16.1 % TRR at 121 DAT and 0.373 mg/kg or 26.2 % TRR at 365 DAT). The metabolite M222F001 was identified as the second most abundant component (0.298 mg/kg or 7.0% TRR at 30 DAT, 0.075 mg/kg or 4.3% TRR at 121 DAT and 0.054 mg/kg or 3.8 % TRR at 365 DAT). In the solubilizates after solvent extraction of 30 DAT and 121 DAT the carbohydrates (glucose, fructose, sucrose) were also the main constituents (0.204 mg/kg or 4.8 % TRR and 0.099 mg/kg or 5.7 % TRR) and metabolite M222F001 was the second most abundant component at 30 DAT and (0.119 mg/kg or 2.8 % TRR).

In spring wheat chaff the carbohydrates (glucose, fructose, sucrose) were the main constituents in the extractable radioactive residues (0.488 mg/kg or 12.9 % TRR at 30 DAT, 0.208 mg/kg or 20.4 % TRR at 121 DAT and 0.360 mg/kg or 25.8 % TRR at 365 DAT). The metabolite M222F001 was the second most abundant component (0.088 mg/kg or 2.3 % TRR at 30 DAT, 0.019 mg/kg or 1.8% TRR at 121 DAT and 0.039 mg/kg or 2.8 % TRR at 365 DAT). In the solubilizates after solvent extraction of 30 DAT the carbohydrates (glucose, fructose, sucrose) were also the main constituents (0.513 mg/kg or 13.6% TRR) and metabolite M222F001 was the second most abundant component (0.130 mg/kg or 3.4 % TRR).

In spring wheat grain the carbohydrates (glucose, fructose, sucrose) were the main constituents in the extractable radioactive residues and the solubilizates after solvent extraction (1.726 mg/kg or 62.7 % TRR at 30 DAT, 0.328 mg/kg or 61.9 % TRR at 121 DAT and 0.586 mg/kg or 49.6 % TRR at 365 DAT). The metabolite M222F001 was also identified (0.123 mg/kg or 4.5 % TRR at 30 DAT, 0.007 mg/kg or 1.3% TRR at 121 DAT and 0.046 mg/kg or 3.9 % TRR at 365 DAT).

The results of the carbohydrates (glucose, fructose, sucrose) and the metabolite M222F001 identified in the ammonia solubilizate after solvent extraction and in the extractable radioactive residues of 30 DAT are summarized in Table 6.6.1- 6.

Table 6.6.1- 6: Summary of identified components and portions characterized in rotational crop matrices after treatment with ^{14}C-BAS 222 F (^{14}C-Metiram; 1x12.500 kg as/ha) and plant back intervals of 30, 121 and 365 days

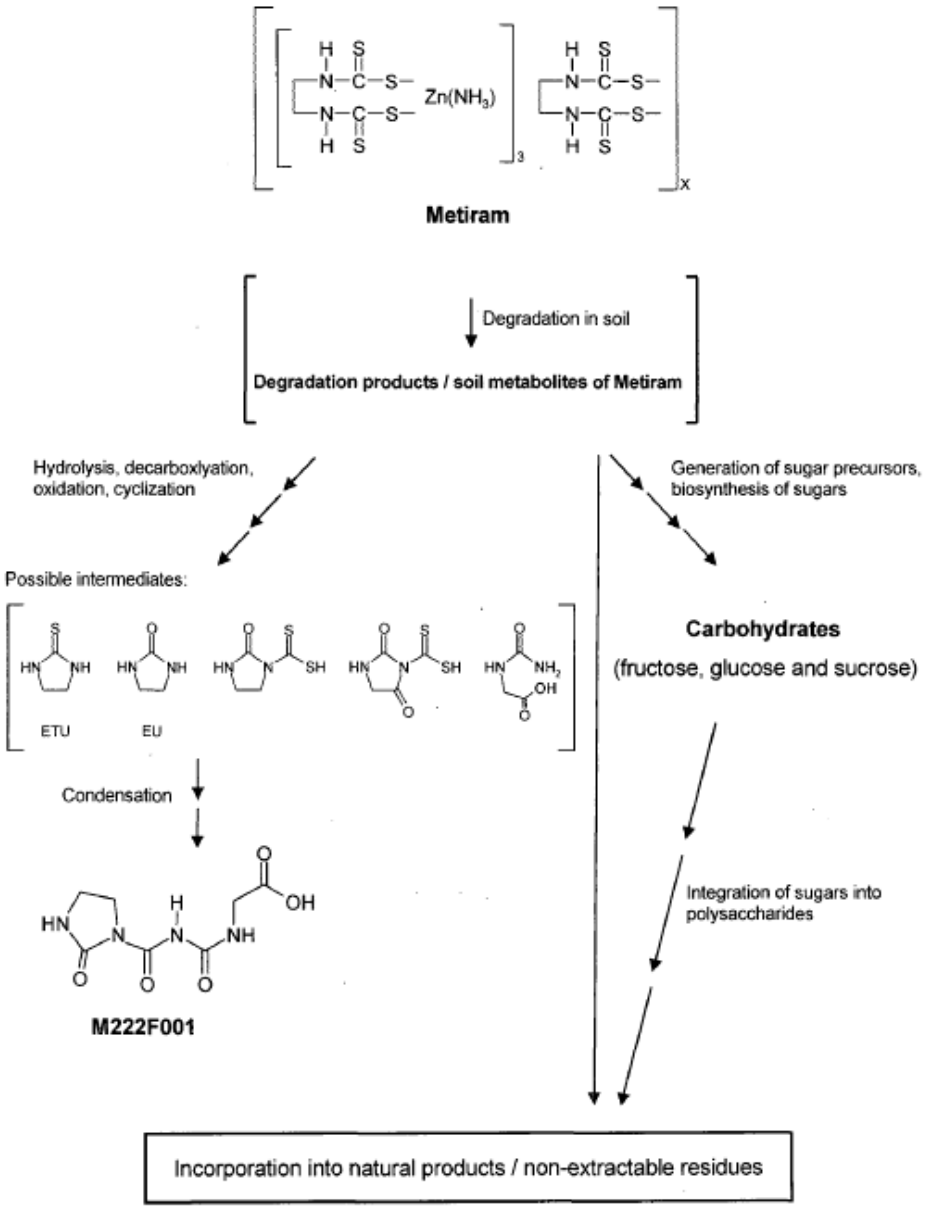
Matrix	DAP	Carbohydrates (glucose, fructose, sucrose)		M222F001		Sum of identified components		Total characterized	
		[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Plant back interval: 30 DAT*									
Lettuce leaf	38	0.307	40.1	0.137	17.9	0.444	58.0	0.197	25.7
Lettuce head	59	0.328	50.0	0.125	19.0	0.453	69.0	0.074	11.3
White radish top	88	0.286	31.6	0.082	9.0	0.368	40.7	0.356	39.4
White radish root	88	0.236	60.1	0.022	5.7	0.258	65.8	0.054	13.7
Spring wheat forage	54	0.550	32.6	0.138	8.2	0.688	40.7	0.565	33.4
Spring wheat straw	131	1.051	24.8	0.417	9.8	1.468	34.6	1.416	33.4
Spring wheat chaff	131	1.000	26,5	0.218	5.8	1.218	32.3	1.158	30.7
Spring wheat grain	131	1.726	62.7	0.123	4.5	1.849	67.2	0.701	25.5
Plant back interval: 121 DAT									
Lettuce leaf	41	0.060	33.1	0.011	6.1	0.071	39.2	0.075	41.3
Lettuce head	55	0.085	38.3	0.022	9.8	0.107	48.2	0.072	32.7
White radish top	109	0.046	16.4	0.008	2.8	0.054	19.2	0.156	55.2
White radish root	109	0.052	38.4	0.004	2.7	0.056	41.0	0.053	38.8
Spring wheat forage	67	0.091	21.9	0.014	3.3	0.104	25.1	0.198	47.8
Spring wheat straw	146	0.378	21.7	0.075	4.3	0.452	26.0	0.688	39.6
Spring wheat chaff	146	0.208	20.4	0.019	1.8	0.227	22.2	0.456	44.6
Spring wheat grain	146	0.328	61.9	0.007	1.3	0.335	63.2	0.151	28.5
Plant back interval: 365 DAT									
Lettuce leaf	29	0.011	10.0	0.002	2.2	0.014	12.1	0.076	67.8
Lettuce head	56	0.044	47.9	0.002	2.0	0.045	49.9	0.032	35.2
White radish top	77	0.011	12.1	0.002	2.3	0.013	14.4	0.081	86.8
White radish root	77	0.020	33.5	0.002	3.0	0.022	36.5	0.027	45.1
White radish plant	13	0.008	8.7	0.001	0.8	0.009	9.4	0.070	73.8
Spring wheat forage	49	0.045	22.3	0.002	1.0	0.047	23.3	0.102	50.9
Spring wheat straw	109	0.373	26.2	0.054	3.8	0.427	30.0	0.720	50.5
Spring wheat chaff	109	0.360	25.8	0.039	2.8	0.399	28.6	0.690	49.4
Spring wheat grain	109	0.586	49.6	0.046	3.9	0.632	53.5	0.454	38.4

* Sum of ammonia solubilizate after solvent extraction residues and extractable radioactive residues

3. Metabolic pathway

Since metiram is a water-insoluble complex, the metabolism in crops implies the decomposition of the complex and formation of soluble degradation products in soil prior plant uptake. The soil metabolites of metiram are taken up and transformed in rotational crops primarily into carbohydrates (fructose, glucose and sucrose) and to a lower extend to metabolite M222F001. Incorporation of metiram moieties into sugar molecules requires the transformation of the soil metabolites into suitable compounds for the biosynthesis of carbohydrates. As a consequence of the incorporation of metiram moieties into sugars, they are also incorporated into biopolymers (e.g. amylopectin and cellulose). Another transformation path of metiram leads to the condensation product M222F001. The formation of M222F001 from metiram presumes a series of transformation steps, which include hydrolysis, decarboxylation, cyclization, oxidation and condensation. In the present study neither ETU nor any other known degradation product of metiram was found.

Figure 6.6.1-1: Metabolic Pathway of BAS 222 F in Rotational Crops



4. Storage stability

All samples were stored in a freezer at approximately -18 °C or below during the course of the study. A comparison of the extractabilities and of the metabolite patterns (HPLC analyses) obtained at the beginning and at the end of the investigation period (representative samples of lettuce head 30 DAT and spring wheat straw 30 DAT) showed that there was no relevant change in the nature of the radioactive residues during storage of the plant samples over a period of at least three years. The stability in stored extracts was demonstrated for at least 30 months.

III. CONCLUSION

The metabolism of ^{14}C-BAS 222 F (metiram) in representative succeeding crops was investigated after application to bare soil at a single rate of 1 x 12.500 kg as/ha. After ageing of the soil for 30, 121 and 365 days, the crops lettuce, white radish and spring wheat were cultivated. In brief, the parent metiram was not detected in the crop plants. Metiram is a metal ion complex which desintegrates upon contact with water and therefore cannot be taken up from soil into the plant. Furthermore, none of the known degradation products of metiram were found in the plant. In contrast, the radioactive residue consisted predominantly of natural plant constituents such as sugars indicating that radioactive residue taken up from the soil into the plant is quantitatively entering primary metabolism followed by incorporation of the radiocarbon into plant constituents such as polysaccharides. In addition, the metabolite M222F001 was identified in all matrices. Considering its molecular structure this compound is a condensation product of various low molecular weight intermediates formed by degradation in soil. As-yet this condensation compound has not been detected in any other metiram metabolism study, and therefore is considered an incidential finding due to the laboratory conditions of this present study (an indicative assessment of exposure is provided in section 6.10 of the present dossier).

Regarding total radioactive residues, the TRR in unripe lettuce leaf did not exceed 0.766 mg/kg for all plant back intervals. The total residues in ripe lettuce head were comparable and reached up to 0.656 mg/kg. The TRR in immature white radish plant and mature white radish top ranged from 0.093 to 0.906 mg/kg. In mature white radish root, the residue levels ranged from 0.059 to 0.393 mg/kg. In spring wheat, the highest residue levels were measured in straw (ranging from 1.424 to 4.245 mg/kg) and chaff (1.023 to 3.775 mg/kg). The total radioactive residues in grain were somewhat lower and accounted for 0.530 to 2.752 mg/kg, and concentrations of 0.200 to 1.690 mg/kg were found in forage. After aging and ploughing, the residue concentrations in the soil decreased from the first plant back interval to the second and third plant back interval, respectively.

Regarding extractability of the radioactive residues with methanol and water generally above 50 % of the TRR were obtained for the lettuce samples, around 50 % for white radish top and root and up to 50 % or below for unripe white radish plant, spring wheat forage, straw and chaff. The extractability of spring wheat grain was approximately 10 to 20 %. With the exception of spring wheat grain, the main part of the radioactive residue was extracted with methanol.

Regarding composition of the residue, the parent compound metiram was not detected by HPLC analyses of the extracts or solubilizates. Also, neither ETU nor any other known degradation product of metiram were found. Uptake of metiram by crops implies the decomposition of the metiram complex and formation of soluble degradation products in soil, as it was previously described (Staudenmaier H.: Aerobic Metabolism of BAS 222 F (Metiram) in Soil, BASF Doc ID 2002/1012954 and Staudenmaier H.: Aerobic Metabolism of BAS 222 F (Metiram) in Cashmere Soil, BASF Doc ID 2002/1011913). The soil metabolites of metiram were taken up and transformed in the rotational crops primarily into sugars (glucose, fructose and sucrose), which were without exception the most abundant components in all matrices (in methanol/ water extracts and solubilizates after solvent extraction). Due to the incorporation of metiram moieties into sugars, they were finally also integrated into polysaccharides (e.g. amylopectin and cellulose). The incorporation of radioactive residues into polysaccharides was proven by treatment of the spring wheat grain (30 DAT) extraction residues with macerozyme and amylase / amyloglucosidase, whereby virtually all released components were identified as sugars (a smaller portion was identified as metabolite M222F001). The metabolite M222F001 was identified in all matrices and represented in the majority of cases the second most abundant component. Noteworthy, the metabolite M222F001 was not identified in previous investigations on metabolism of metiram.

CA 6.6.2 Magnitude of residues in rotational crops

According to Reg. 283/2013, studies on the magnitude of residues in rotational crops are required under the following circumstances:

If the metabolism studies indicate that residues of the active substance or of relevant metabolites or breakdown products either from plant or soil metabolism may occur (> 0.01 mg/kg), limited field studies and, if necessary, field trials shall be carried out.

Studies shall not be required in the following cases:

- no metabolism studies on rotational crops are to be performed, or
- metabolism studies on rotational crops show that no residues of concern are to be expected in rotational crops

A magnitude of the residue study is not required for metiram, based on results of the metabolism study on rotational crops for metiram (see section 6.6.1)
In brief, the parent metiram was not detected in the plant. Metiram is a metal ion complex which desintegrates upon contact with water and therefore cannot be taken up from soil into the plant. Furthermore, none of the known degradation products of metiram were found in the plant. In contrast, the radioactive residue consisted predominantly of natural plant constituents such as sugars indicating that radioactive residue taken up from the soil into the plant is quantitatively entering primary metabolism followed by incorporation of the radiocarbon into plant constituents such as polysaccharides. In addition, the metabolite M222F001 was identified in all matrices. Considering its molecular structure this compound is a condensation product of various low molecular weight intermediates formed by degradation in soil (for example see Staudenmaier H.: Aerobic Metabolism of BAS 222 F (Metiram) in Soil, BASF Doc ID 2002/1012954 and Staudenmaier H.: Aerobic Metabolism of BAS 222 F (Metiram) in Cashmere Soil, BASF Doc ID 2002/1011913). As-yet this condensation compound has not been detected in any other metiram metabolism study, and therefore is considered an incidential finding due to the laboratory conditions of this present study. An indicative assessment of exposure is provided in section 6.10 of the present dossier.

Considering the metabolism on rotation crop study has been conducted under worst case conditions, notably at an overdosed rate (factor >3) to bare soil under laboratory conditions, it can be concluded that in practice the application of metiram does not lead to uptake of residue of concern from soil by succeeding crops.

CA 6.7 Proposed residue definitions and maximum residue levels

CA 6.7.1 Proposed residue definitions

CA 6.7.1.1 Plant commodities

The definition of the relevant residue in commodities of plant origin both for MRL establisment as well as risk assessment has been extensively discussed within the peer review under Directive 91/414/EEC based on metabolism of metiram in the two crop groups of fruit/fruiting vegetable and root/tuber. This residue definition, as established by the peer review, is further supported by metabolism in leafy vegetables (additional new data submitted as part of the present dossier).

Residue definition for establishment of MRLs and enforcement: In the European Union, MRLs are established only for the raw agricultural commodities of crops (RAC, as opposed to the processed fractions thereof). In plant RAC, the parent compound metiram is the predominant portion of the residue and therefore a suitable marker compound. The terminal residue is the result of significant incorporation of metiram transformation products into various naturally occurring plant constituents which as such are not relevant for a residue definition. In the RAC, metiram transformation products notably EBIS, ETU, EU and others, are detected only in low amounts. They are dynamic intermediates leading to other metabolites of low or no toxicological concern.
Due to these facts, metiram is regarded as the only relevant component of the residue in plants (RAC) for MRL setting and enforcement purposes

MRLs in the European Union (and internationally) are not set specifically for metiram, but for the group of dithiocarbamates including also maneb, mancozeb, propineb, thiram, and ziram.
Metiram as a metal ion complex cannot be detected directly, e.g. by chromatographic means. However, determination is feasible with a multi-residue method analysing residues of dithiocarbamates measured as CS_2.
In addition, metiram can be determined with an "EBDC specific method" which is based on hydrolysis to ethylene diamine, derivatisation and final HPLC/MS-MS quantitation (see section MCA 4.3). This method, as it allows to distinguish EBDC fungicides from other CS_2 sources, is suitable as a higher tier analytical method.
Regarding enforcement of metiram the following definition of the relevant residue has been established by the peer review. As part of the present dossier it is proposed to maintain the established definition of the relevant residue for establishment of MRLs and enforcement:

Metiram, expressed as CS_2

Residue definition for data generation and risk assessment: In plant RAC, the parent compound metiram is the predominant portion of the residue (see above). The terminal residue is the result of significant incorporation of metiram transformation products into various naturally occurring plant constituents which as such are not relevant for a residue definition. Metiram transformation products noteably EBIS, ETU, EU and others, are detected only in low amounts. A potential relevance of these transformation products can be ruled out based on a detailed assessment (see sections MCA 6.7.1.3 and MCA 6.10.1).
Under food processing conditions metiram can rapidly degrade to ETU. Considering its toxicological properties, ETU has to be considered in consumer dietary risk assessment as far as processed commodities are concerned. Regarding the risk assessment of metiram the following definition of the relevant residue has been established by the peer review. As part of the present dossier it is proposed to maintain the established residue definition:

Metiram, expressed as CS_2 *ETU (only for processed commodities)*

CA 6.7.1.2 Animal commodities

The definition of the relevant residue in commodities of animal origin both for MRL establisment as well as risk assessment has been extensively discussed within the peer review under Directive 91/414/EEC based on metabolism of metiram in poultry and ruminants. The definition of the relevant residue established by the peer review is further supported by metabolism in rat (notably additional new data submitted as part of the present dossier).

The metabolism studies indicate that the parent compound metiram, as a metal ion complex, is not resorbed in the gastrointestinal tract of rat, goat, or hen. Bioavailable are only the desintegration products : dynamic intermediates formed upon solvolysis of the metal ion complex. Their significant incorporation results in various naturally occurring cell constituents as the terminal residue (these product fractions as such are not relevant for a residue definition).
These dynamic intermediates are occurring at variable levels. Under realistic conditions, levels are expected to be below the quantitation limit and therefore not suitable for a residue definition. A potential relevance of these transformation products can be ruled out based on a detailed exposure assessment (see sections MCA 6.7.1.3 and MCA 6.10.1).

By default, the parent compound is considered suitable for the residue definition. A multi-residue method is available which allows the determination of metiram as well as metiram transformation products which release CS_2 (notably EBIS). Under food processing conditions metiram can rapidly degrade to ETU. Considering its toxicological properties, ETU has to be considered in consumer dietary risk assessment as far as processed commodities are concerned.

Regarding enforcement of metiram the following definition of the relevant residue has been established by the peer review. As part of the present dossier it is proposed to maintain the established residue definition:

Metiram, expressed as CS_2

Regarding risk assessment of metiram the following definition of the relevant residue has been established previously. As part of the present dossier it is proposed to maintain the established residue definition:

Metiram, expressed as CS_2 *ETU (only for processed commodities)*

The list of agreed EU endpoints is summarised below.

Table 6.7.1.2- 1: EU End-points - Metiram

End-Point	Active Substance: Metiram	
	EU Agreed Endpoints (SANCO/4059/2001 - rev. 3-3, Monograph as of July 2000)	**Endpoints Used in Risk Assessment**
Residue definition in plant matrices for risk assessment	Metiram, expressed as CS_2 , ETU (only for processed commodities)	Metiram, expressed as CS_2 ETU (only for processed commodities)
Residue definition in plant matrices for monitoring	Metiram, expressed as CS_2	Metiram, expressed as CS_2
Residue definition in animal matrices for risk assessment	Metiram, expressed as CS_2 ETU (only for processed commodities)	Metiram, expressed as CS_2 ETU (only for processed commodities)
Residue definition in animal matrices for monitoring	Metiram, expressed as CS_2	Metiram, expressed as CS_2
Conversion factor between both residue definitions in animal matrices	Not applicable	Not applicable

CA 6.7.1.3 Relevance assessment of further transformation products of metiram

As part of the current metiram re-registration process, the dietary risk assessment for the consumer resulting from the use of metiram has to take into account the actual toxicological burden of the components of the residue. Therefore, the establishment of the residue definition for risk assessment purposes involves a decision on which transformation products of metiram are of toxicological concern. To achieve robustness of such a residue definition, the data base considered should be reasonably broad. Thus, first, any metiram transformation product identified in a *nature of the residue* study is to be included (i.e. crop metabolism, rotational crop metabolism, livestock metabolism, high temperature hydrolysis). And second, dietary exposure is assessed for two crop scopes, first scope, the representative uses supported in the AIR3 dossier (grape, potato) and second scope, all uses registered in EU including import tolerances.

For an initial evaluation of relevance of transformation products, the estimated human exposure can be compared with a safe threshold derived using the assumptions of the TTC concept and information on the transformation product (i.e. molecular structure and genotoxic potential). To this end, a stepwise approach is envisaged (see decision tree in *Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment, EFSA Journal 2012;10(07):2799*). The threshold of toxicological concern (TTC) is based on the concept that exposure levels can be defined (pending the molecular structure) below which human exposure to the chemical results in "no appreciable risk to human health".
A further refined evaluation is to be done for transformation products with calculated exposure exceeding the corresponding TTC or specific reference values. The initial estimations generally result in considerable overestimations of exposure since typically based on various worst case assumptions, in particular in the absence of data from *magnitude of the residue* studies. (In general, all intake for the crop considered is from treated crop, which is an overestimation as market share is well below 100%. For a certain diet all included food items are assumed to have residues at the upper limit which is an overestimation as most crops have residues well below the MRL. Data generation such as crop field trials are conducted to represent the worst case condition as far as residues are concerned.) Therefore, on a case-by-case basis further detailed considerations allow to refine to more realistic exposure scenarios.

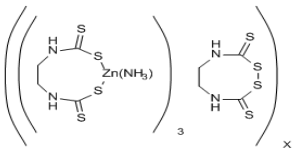
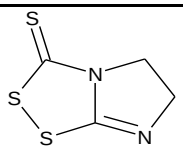
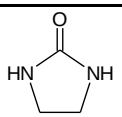
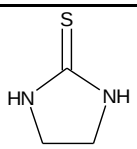
For metiram, a total of eleven potentially relevant transformation products has been identified in *nature of the residue* studies (M222F004=EBIS, M222F003=EU, M222F002=ETU, M222F001, M222F007, M222F008, M222F013, M222F021, M222F022, M222F023, and glycine).

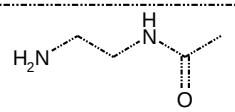
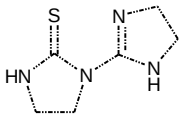
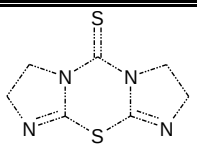
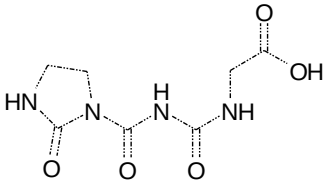
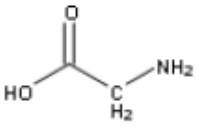
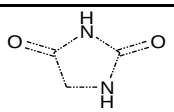
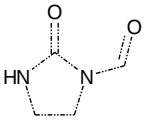
For two of these transformation products, no evaluation of relevance is provided in the context of the present assessment: first, glycine is a naturally occuring amino acid. Second, M222F002 (=ETU) is already defined a relevant metabolite and thus, is included in the existing definition of the residue for risk assessment (processed commodities).

For nine of these transformation products, dietary exposure has been estimated and expressed in percentage of the corresponding toxicological reference value (TTC or specific value, see Table 6.7.1.3- 2). To allow to reproduce the exposure calculations for each of the metiram transformation products, the detailed steps are provided in a separate document (DocID 2015/1087922, see section MCA6.10.1 for a summary). For all of them, the indicative exposure calculations both chronic and acute is below (or at) the corresponding toxicological reference value (see Table 6.7.1.3- 3 and Table 6.7.1.3- 4) indicating non-significant contribution to the overall toxicological burden.
Detailed considerations for each of the eleven transformation products are provided below. In brief, the available information, noteably molecular structure, genotoxicological investigations, occurrence in food/feed commodities, exposure estimations etc was evaluated. For each transformation product sufficient information is available to exclude relevance the compond for the purpose of dietary risk assessment. Moreover, they are not suitable as marker compounds. Thus, none of them has to be included in the existing definition of the relevant residue both for for risk assessment as wellas MRL setting.

In conclusion, this relevance assessment confirms the definition of the relevant residue for risk assessment, presently established, is sufficiently protective for dietary risk assessment (see section 6.7.1 and 6.7.2).

Table 6.7.1.3- 1: Overview metabolites: occurrence, molecular structure and molecular mass

Parent			
Name	**Occurrence**	**Structure**	**Molecular mass [g/mol]**
Metiram (BAS 222 F)	not relevant		1088.7
Metabolites			
Name	**Occurrence**	**Structure**	**Molecular mass [g/mol]**
M222F004 (EBIS)	crop (lettuce, apple, potato)* goat** poultry***		176.3
M222F003 (EU)	crop (lettuce, apple, potato)* goat** poultry***		86.1
M222F002 (ETU)	crop (lettuce, apple, potato)* goat** poultry***		102.2

M222F023 (EDA)	crop (apple)* goat** poultry***		60.1
M222F021 (N-AcEDA)	crop (apple)* goat** poultry***		102.1
M222F022 (Jaffe`s Base)	crop (apple)* goat** poultry***		170.2
M222F007 (TDIT)	crop (lettuce)*		212.3
M222F001	rotational crop****		230.2
Glycine	crop (apples, potato)* goat** poultry***		75.1
M222F008 (Hydantoin)	crop (apple)* goat** poultry***		100.1
M222F013	crop (lettuce)*		114.1

* 'Metabolism of 14C-Metiram (14C-BAS 222 F) in lettuce', BASF DocID 2009/1049027
'Metiram: Nature of Residues in Apples', BASF DocID 1990/10669
'Metabolism of 14C-Metiram Complex in Potatoes', BASF DocID 1990/10668
** 'Metabolism of 14C-Metiram Complex in Lactating Goats', BASF DocID 1989/10487
*** 'Metabolism of 14C-Metiram Complex in Laying Hens', BASF DocID 1990/5080
**** 'Confined rotational crop study with 14C-BAS 222 F', BASF DocID 2009/1017248

The following toxicological reference values were used for chronic assessments (ADI) and acute assessments (ARfD).

Table 6.7.1.3- 2: Toxicological reference values used

Name	End-Point		Study	Safety factor	Reference
	Acceptable Daily Intake (ADI)	Acute Reference Dose (ARfD)			
Metiram	0.03 mg/kg bw/d		2-year study in rats	100	SANCO/4059/2001-rev 3.3 (03.06.2005)
		not necessary - not allocated	-	-	SANCO/4059/2001-rev 3.3 (03.06.2005)
ETU	0.002 mg/kg bw/d		2-year study in rats	100	SANCO/4059/2001-rev 3.3 (03.06.2005)
		0.05 mg/kg bw/d	-	-	SANCO/4059/2001-rev 3.3 (03.06.2005)
EU	0.06 mg/kg bw/d		90 day study, rat	200	M-CA 5.8
		0.06 mg/kg bw/d	90 day study, rat	200	M-CA 5.8
EBIS	0.02 mg/kg bw/d		90 day study, rat	200	M-CA 5.8
		0.15 mg/kg bw/d	90 day study, rat	200	M-CA 5.8
EDA / NAcEDA	0.2 mg/kg bw/d		90 day study, rat	200	M-CA 5.8
		0.5 mg/kg bw/d	90 day study, rat	200	M-CA 5.8
TTC approach	0.0015 mg/kg bw/d		none	not relevant	TTC Cramer class III*
		0.005 mg/kg bw/d	none	not relevant	recommended by EFSA PPR*

* Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment (EFSA Journal 2012;10(07):2799), page 32

Consideration on M222F004 (EBIS)

M222F004 is a dynamic intermediate which is formed from metiram when this metal ion complex is exposed to water (solvolysis). EBIS itself is unstable and breaks down into compounds such as EU and ETU (as indicated by results of freezer storage stability investigations, see section MCA6.1). The transient formation of EBIS from metiram can occur under abiotic conditions as well as does occur generally in metabolism studies with metiram in plants and animals (livestock, rat). Noteworthy, it is a metabolite in common with fungicides of the dithiocarbamate group.

In rat, EBIS can be considered as being present in significant amounts based on the finding of a methylated derivative of EBIS, M222F024. Levels in bile amounted to 5.1% of applied dose, lower levels were found in faeces and urine (section MCA5.1). Thus, the toxicity of EBIS can be considered as covered by studies with the parent metiram. As a more conservative alternative to applying the metiram toxicological reference values, EBIS specific toxicological reference can be derived based on the available toxicological data (section MCA5.8, 0.02 mg/kg bw/d (ADI) and 0.15 mg/kg bw (ARfD).

In order to provide an indicative assessment of dietary exposure, the chronic and acute exposure was calculated based on residue data calculated from nature of the residue studies. EBIS levels determined in crop residue trials are not covered by storage stability (instability even under freezer storage conditions, section MCA6.1). Therefore, residue levels were estimated based on EBIS/metiram ratio (*nature of the residue* studies) and metiram field residue data. For animal commodities, EBIS levels (*nature of the residue* studies) were normalized to a realistic feed burden.
These calculations confirmed that the exposure is below the toxicological reference values, not only for (a) the uses supported in the present dossier but also when (b) all registered uses of metiram including import tolerances are included:

chronic	(a) up to 3.9 % ADI,	(b) up to 8.6% ADI,
acute	(a) up to 17.8 %ARfD,	(b) up to 33.7% ARfD.

Considering that conservative assumptions were used both for estimating dietary exposure as well as for deriving a toxicological reference value (see above), these results indicate, with a large margin of safety, the absence of a health concern.
It should be noted that metiram residue data was generated using a common moiety method detecting CS_2. In addition to metiram, CS_2 is also released from EBIS. Therefore, transient amounts of EBIS can be considered included in the residue of metiram, expressed as CS_2.
In conclusion, absence of a health concern under very conservative assumptions as well as instability of the molecule show that the transformation product EBIS is not relevant for the residue definition, both regarding risk assessment as well as enforcement.
Result: no further consideration for M222F004 (EBIS) is necessary.

Consideration on M222F003 (EU)

EU is a dynamic intermediate which is formed from metiram when this metal ion complex is exposed to water (solvolysis). EU is converted further to ETU. Stability investigations indicated that EU also has limited stability (up to 90d under freezer storage conditions, section MCA6.1). The transient formation of EU from metiram can occur under abiotic conditions as well as is does occur generally in metabolism studies with metiram in plants and animals (livestock, rat). Noteworthy, it is a metabolite in common with fungicides of the dithiocarbamate group.

In rat, EU can be considered as being present in significant amounts based on the finding levels in urine up to 5.8% of applied dose. EU was also found in faeces, albeit at lower level (section MCA5.1). As a polar low molecular weight molecule, EU is rapidly excreted in addition to effective elimination by incorporation into natural cell constituents (rat metabolism, section MCA5.1 and livestock metabolism, section MCA6.2). Based on the available toxicological data EU specific toxicological reference can be derived (section MCA5.8, 0.02 mg/kg bw/d (ADI) and 0.15 mg/kg bw (ARfD).

In order to provide an indicative assessment of dietary exposure, the chronic and acute exposure was calculated based on residue data calculated from nature of the residue studies. For two crops grape and potato, EU levels determined in crop residue trials are available. For other crops, residue levels were estimated based on EU/metiram ratio (*nature of the residu*e studies) and metiram field residue data. For animal commodities, EU levels (*nature of the residue* studies) were normalized to a realistic feed burden.
These calculations confirmed that the exposure is below the toxicological reference values, not only for (a) the uses supported in the present dossier but also when (b) all registered uses of metiram including import tolerances are included:

chronic	(a) up to 0.1 % ADI,	(b) up to 1.4% ADI,
acute	(a) up to 7.7 %ARfD,	(b) up to 73.6% ARfD).

Considering that conservative assumptions were used (see above), these results indicate absence of a health concern.

For enforcement purpose in commodities of plant origin, the parent metiram can be determined using a common moiety method measuring CS_2 as well as an "EBDC specific method" (section MCA4.3). Determination of EU is not possible with the analytical method for metiram, thus requiring application of a separate method. However, the available data shows that residue levels of metiram are generally severalfold higher than EU, and therefore better suited as a marker compound for enforcement. For enforcement purpose in commodities of animal origin, EU is not a suitable marker compound as residue levels resulting from the use of metiram are at the LOQ of 0.01 mg/kg if quantifyable at all. In light of the fact that conservative exposure estimations indicate absence of a health concern for EU, the metiram transformation product EU is considered non-relevant for the residue definition for MRL setting.

For risk assessment purpose, the parent metiram is generally the predominant component of the residue in crops. Under practical conditions, levels of EU are considerably lower than metiram levels as exemplarily shown by analysis of metiram as well as metabolite EU in crop field trials with grape. Extrapolation of EU residue levels in other crops (based on EU/metiram ratios observed in metabolism studies) are including very conservative assumptions. In commodities of animal origin, residue levels resulting from the use of metiram are at the LOQ of 0.01 mg/kg if quantifyable at all. Taken together, the data shows that under realistic conditions, the metabolite EU does not contribute significantly to the toxicological burden. In conclusion, the metiram transformation product EU is considered non-relevant for the residue definition for risk assessment.
Result: no further consideration for M222F003 (EU) is necessary.

Consideration on M222F002 (ETU)

M222F002 (ETU) is a transformation product found in plant and livestock metabolism studies. It is formed in significant amounts from metiram under food processing conditions. Consequently, ETU has been included in the residue definition for processed commodities. A detailed dietary exposure assessment is provided in section MCA 6.9 of the present dossier.
Result: no further consideration for M222F002 (ETU) is necessary.

Consideration on M222F023 / M222F021 (EDA / N-AcEDA)

The compound M222F023 and its acetylated derivative M222F021 are dynamic intermediates formed after desintegration of the metiram metal ion complex, which is then further transformed into glycine thereby channeling metiram derived carbon into metabolic carbon pool. This pair of compounds has structural characteristics similar to the ligand of metiram complex. It is found in metiram metabolism studies in plant and livestock (tissues, milk, egg).
To provide an indicative assessment of dietary exposure, the chronic and acute exposure scenarios were calculated and compared with compound specific toxicological reference values (see MCA 5.8, Table 6.7.1.3-1). For chronic assessment an ADI of 0.02 mg/kg bw/d was used as toxicological reference value and for acute assessment 0.5 mg/kg bw was used. Calculations are provided for two crop scopes: first, the uses supported in the present dossier (grape, potato) and second, the entirety of all registered EU uses of metiram. For all scenarios exposure was less than 1% of the toxicological reference value.

In conclusion, the contribution of M222F023/M222F021 to the toxicological burden resulting from the uses of metiram is insignificant. Therefore, M222F023/M222F021 is not relevant for the definition of the relevant residue both regarding MRL setting and dietary risk assessment.
Result: no further consideration for both M222F023 and M222F021 (EDA / NAcEDA) is necessary.

Consideration on M222F022 (Jaffes Base)

This compound has structural characteristics similar to ETU with an addition of an ethylene diamine moiety. M222F022 is found in metiram metabolism studies in plant and livestock (tissues, milk, egg).
To provide an indicative assessment of dietary exposure, the chronic and acute exposure scenarios were calculated and compared with default toxicological reference values according to the TTC approach. For chronic assessment the Cramer class III trigger of 0.0015 mg/kg bw/d was used as toxicological reference value and for acute assessment 0.005 mg/kg bw was used. Both genotox studies as well as a QSAR (DEREK) evaluation did not indicate any carcinogenic, genotoxic or neurotoxic effect (see section MCA 5.1), thereby confirming the applicability of the default toxicological reference values. Considering the uses supported in the present dossier (and in addition, all registered uses of EU metiram) for the chronic scenario exposures 1.9 (and 9.0 %) of the toxicological reference value were obtained. For the acute scenario exposures of 1.7% (and 14.3 %) of the toxicoloical reference value were obtained.
In conclusion, the contribution of M222F022 to the toxicological burden resulting from the uses of metiram is insignificant. Therefore, M222F022 is not relevant for the definition of the relevant residue both regarding MRL setting and dietary risk assessment.
Result: no further consideration for M222F022 (Jaffes base) is necessary.

Consideration on M222F007 (TDIT)

The compound M222F007 was identified in only one of the nature of the residue studies of metiram metabolism in lettuce). In the only matrix analysed in this study, M222F007 was found at 1.4% TRR, thus at only low proportion of the overall residue. Considering the artificial conditions of the laboratory study, it can be assumed that under realistic conditions the proportion of M222F007 would be even lower. While this compound has not been identified in other nature of the residue studies (apple, potato, goat, hen), it has previously been reported in soil and is known to undergo fast degradation. In addition, it was identified in low amounts in a rat excretion study (see section MCA 5.1). Taken together, the incidental occurrence in the metiram studies available, indicates that M222F007 is not a ubiquitous transformation product of metiram.
To provide an indicative assessment of dietary exposure, the chronic and acute exposure scenarios were calculated and compared with default toxicological reference values according to the TTC approach. For chronic assessment the Cramer class III trigger of 0.0015 mg/kg bw/d was used as toxicological reference value and for acute assessment 0.005 mg/kg bw was used. Both genotox studies as well as a QSAR (DEREK) evaluation did not indicate any carcinogenic, genotoxic or neurotoxic effect (see MCA 5.1), thereby confirming the applicability of the default toxicological reference values.

Chronic exposure calculations resulted in a value of 0% of the toxicological reference value (for both crop scopes, representative uses and all registered uses). The acute exposure calculations for grape and potato resulted in a value of 0% of the toxicological reference value. If all EU registered uses, i.e. including leafy vegetables, were considered values at the toxicological threshold were obtained (100.9% for scarole, children, 31.0% for lettuce). This however is an overestimation since considering these artificial conditions of the laboratory study, M222F007 levels under realistic conditions are expected to be much lower. Therefore, these calculations indicate absence of an appreciable dietary risk (chronic and acute) to human health. The contribution to the toxicological burden is insignificant. In conclusion, M222F007 is not relevant for the definition of the relevant residue for dietary risk assessment as well as for MRL setting.
Result: no further consideration for M222F007 (TDIT) is necessary.

Consideration on M222F001

This transformation product of metiram was identified only in one of the nature of the residue studies with metiram hinting at the likelihood of only incidental occurrence (rotational crop metabolism. After bare soil treatment at 3X (dose 12.5 kg ai/ha compared with 4.2 kg ai/ha maximal seasonal application rate) M222F001 was found in edible commodities at levels up to 0.137 mg/kg (lettuce leaf).
Based on its molecular structure this compound is a condensation product of EU (M222F003) with various low molecular weight intermediates formed by degradation in soil (see section MCA 6.6.2). The rotational crop study was conducted under laboratory conditions with plants cultivated in plastic boxes where elimination from root zone of such low molecular weight molecules is restricted resulting in an artificial concentration in the root zone.
Radiolabelled metiram at a dose of 3X of the seasonal application rate was applied to bare soil. The purpose is to study qualitatively the nature of the residue. It only provides limited knowledge on the quantity of components of the residue. Even if an overdosing factor of 3 is considered, this study design does not account for the effect of crop interception (study design: bare soil application) as well as the effect of degradation between the applications (study design: simultaneous application) which both would result in reduction of residue levels under realistic conditions. Considering these artificial conditions of the laboratory study, it can be concluded that under realistic conditions M222F001 residue would be much lower if present at all.
However, in order to provide an indicative assessment of dietary exposure, the chronic and acute exposure scenarios were calculated and compared with default toxicological reference values according to the TTC approach. For chronic assessment the Cramer class III trigger of 0.0015 mg/kg bw/d was used as toxicological reference value and for acute assessment 0.005 mg/kg bw was used. QSAR (DEREK) evaluation did not indicate any carcinogenic, genotoxic or neurotoxic effect (see MCA 5.1), thereby confirming the applicability of the default toxicological reference values.
Taking into account the representative uses supported in the present dossier (or, in addition, all registered uses of EU metiram) for the chronic scenario, exposures up to 2.8% (or 5.3%) of the toxicological reference value were obtained. For the acute scenario, exposures up to 21.5% (or 80.4%) of the toxicological reference value were obtained.
Considering the significant overestimation of estimated residue levels used in these calculations, the contribution of M222F001 to the dietary burden is insignificant. Therefore, M222F001 is not relevant for the definition of the relevant residue both regarding MRL setting and dietary risk assessment.
Result: no further consideration for M222F001 is necessary.

Consideration on glycine

Glycine is an amino acide normally present in the diet. Therefore further consideration of this compound is not required. The detection of glycine in the radioactive residue in metabolism studies with radiolabeled metiram indicates that the radiocarbon is eventually entering the metabolic carbon pool which is in accordance with naturally occurring cell constituents as the terminal residue of metiram.
Result: no further consideration for glycine is necessary.

Consideration on M222F008

This compound was identified in metabolism studies conducted in plant and livestock, however only in few matrices and in low proportions (goat liver <1% TRR, goat muscle 3.7% TRR, hen muscle 8.1% TRR, hen skin 2.7%). It can be considered a transient intermediate derived by oxidation from EU towards glycine and thus entry into the metabolic carbon pool. Considering that M222F008 was found in livestock studies which were considerably overdosed, levels under realistic conditions can be expected to be insignificant (see TTC position paper, DocID201571087922, table 18 provides overdosing factors, tables 21 and 22 list input values).
To provide an indicative assessment of dietary exposure, the chronic and acute exposure scenarios were calculated and expressed as toxicological reference values according to the TTC approach both considering the uses supported in the present dossier as well as considering all registered uses of EU metiram. For all scenarios exposure was less than 1% of the toxicological reference value.
In conclusion, the contribution of M222F008 to the dietary burden resulting from the uses of metiram is insignificant. Therefore, M222F008 is not relevant for the definition of the relevant residue both regarding MRL setting and dietary risk assessment.
Result: no further consideration for M222F008 is necessary.

Consideration on M222F013 (Formamid derivative)

This compound was identified only in one study (DocID 2009/1049027). As stated in the study report (page 53, footnote 4) this compound is "*probably an artefact formed of EU*" (formamide of EU). With 0.4 % TRR, the proportion of formamide derivative detected in this study is very low, noteably when compared to the level of EU (upper level at 14.7 % TRR, common EU/ETU fraction).
Based on its incidental occurrence, M222F013 does not need to be considered a metabolite of metiram. However, in order to be comprehensive in the context of the present dossier, an indicative assessment of exposure to this compound was calculated. In a first scenario, when grouping the formamid-derivative of EU (M222F013) with EU (M222F003), the exposure to M222F013 can be considered as covered by the exposure estimation for EU alone, as EU levels are much higher compared with the M222F013 levels (in particular as the estimate for EU is already an overestimation by using the 14.7% TRR value for EU). In a second scenario (separate assessment for M222F013), an indicative assessment for the representative uses (potato, grape) results in exposures of 0.8 % of the chronic toxicological reference point (TTC Cramer class III) and 7.8 % of the default ARfD.

Similar levels well below the corresponding toxicological reference points are obtained if all registered uses of metiram are considered (chronic 1.7%, acute 32.6%). Therefore, also this calculation using the TTC approach indicates that a hypothetical exposure to M222F013 would be insignificant.
Note, for chronic assessment the Cramer class III trigger of 0.0015 mg/kg bw/d was used as toxicological reference value and for acute assessment 0.005 mg/kg bw was used. QSAR (DEREK) evaluation did not indicate any carcinogenic, genotoxic or neurotoxic effect (see MCA 5.1), thereby confirming the applicability of the default toxicological reference values.
In conclusion, M222F013 (which most likely is an artefact limited to one metabolism study) is not relevant for the definition of the relevant residue both regarding MRL setting and dietary risk assessment.
Result: no further consideration for M222F013 is necessary.

Table 6.7.1.3- 3: Overview: chronic exposure assessments [1)]

Metabolite	Dietary exposure [% reference value], most critical diet		Commodity with highest contribution [% reference value]	
EBIS	8.6	DE child	Pome fruit	[6.1]
EU	1.4	DE child	Pome fruit	[1.0]
EDA/N-AcEDA	0.1	DE child	Pome fruit	[0.1]
Jaffe`s Base	9.1	FR toddler	Milk and cream	[8.7]
TDIT	0.0	IT adult	Lettuce and other salad	[0.0]
M222F001	5.3	WHO Cluster diet B	Tomatoes	[1.4]
M222F008	3.1	DE child	Pome fruit	[2.3]
M222F013	0.1	DK child	Cucurbits – edible peel	[0.0]

1) scope: uses registered in EU, including import tolerances

Table 6.7.1.3- 4: Overview: acute exposure assessments

Metabolite	Commodity with highest contribution [% reference value]	Commodity with 2nd highest contribution [% reference value]	Commodity with 3rd highest contribution [% reference value]
EBIS	33.7 (Melons, children)	27.1 (Watermelons, children)	17.8 (Table grapes, children)
EU	73.6 (Scarole, children)	57.0 (Melons, children)	45.9 (Watermelons, children)
EDA/N-AcEDA	1.2 (Melons, children)	1.0 (Watermelons, children)	0.6 (Table grapes, children)
Jaffe`s Base	14.3 (Cattle milk and milk products, children)	12.2 (Bovine kidney, children)	5.5 (Bovine kidney, adults)
TDIT	100.9 (Scarole, children)	31.0 (Lettuce, children)	12.7 (Lettuce, adults)
M222F001	80.4 (Scarole, children)	24.8 (Lettuce, children)	21.5 (Potatoes, children)
M222F008	28.7 (Melons, children)	23.2 (Watermelons, children)	15.2 (Table grapes, children)
M222F013	32.6 (Scarole, children)	14.7 (Melons, children)	11.8 (Watermelons, children)

1) scope: uses registered in EU, including import tolerances

Conclusion

The relevance assessment performed for the eleven metiram transformation products identified in *nature of the residue* studies, shows that for all componds no further consideration is necessary. This result confirms that the present definition of the relevant residue for risk assessment, is sufficiently protective for dietary risk assessment (see section 6.7.1 and 6.7.2). In addition, the none of these transformation products is suitable to be included in the residue definition for enforcement. In summary, this relevance assessment supports the proposal to maintain the currently established residue definitions for metiram (section MCA6.7.1.1 and MCA6.7.1.2).

CA 6.7.2 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed

In the European Union MRLs are not set specifically for metiram, but for the group of dithiocarbamates comprising maneb, mancozeb, propineb, thiram, ziram as well as metiram. The residues are expressed as carbon disulfide CS_2, which is the common moiety generated during the analytical procedure. Dithiocarbamate MRLs have been established in various commodities of plant and animal origin. An overview over the established EU MRLs for dithiocarbamates is given below (Table 6.7.3- 1).

For the representative use (potato) of metiram supported by the present dossier, the OECD calculator[1] was used to calculate MRLs based on the residue data (see section MCA 6.3) both for commodities of plant origin as well as commodities of animal origin. The calculated MRL proposals were below the established dithiocarbamate MRLs. Therefore, a change of existing MRLs for commodities of plant and animal origin is not required.

[1] OECD calculator (OECD calculator spreadsheet, taken from the OECD page: http://www.oecd.org/document/34/0,3746,en_2649_37465_48447010_1_1_1_37465,00.html

Commodities of plant origin

Potato

In support of the representative use in potato, a total 24 GAP compliant field residue trials on potato were conducted. The residue trials were conducted in various European Member States in S-EU and N-EU during the growing seasons 2012 to 2014 and thereby fulfill the requirements for seasonal and geographical distribution. The number of residue trials is sufficient to derive a MRL proposal.

The samples were stored under conditions for which integrity of the samples was demonstrated. The analytical methods used have been validated. All samples were analysed for metiram via the CS_2 method as well as via the EBDC specific method. Residues in untreated control samples were below the limit of quantitation (LOQ).

Expressed as CS_2 equivalent, residue levels were all $\leq$0.056 mg/kg, resulting in a MRL_{OECD} value for potato of 0.06 mg/kg. The existing EU MRL for dithiocarbamates in potato is established at 0.3 mg/kg. Therefore, there is no need to modify the existing EU MRL in potato.

The overview over the residue trials data, the related risk assessment input values (HR, STMR) and the MRL proposals are provided below (Table 6.7.2- 1).

In the meantime, specific methods exist which allow a differentiation between the EBDC fungicides and other plant protection products generating CS_2. The analytical method selective for the EBDC fungicides used (see section MCA 4.3) is based on hydrolysis to ethylene diamine, derivatisation and final HPLC/MS-MS quantitation. To facilitate future applicability as confirmatory method (higher tier analysis), field residue trials supporting the representive use in the present dossier do include analytical results obtained with the EBDC method: Expressed as EBDC equivalent, residue levels were all <0.05 mg/kg.

Commodities of animal origin

Estimation of residues in livestock feed

The previous estimation of residues in livestock feed (*Italy, 2010: Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174p.)* is covering the use supported in the present dossier. A new estimation is therefore not required. The rationale is as follows:
Residues resulting from the use of metiram in potato are below the LOQ if metiram is applied according to the cGAP supported in the present dossier. Therefore, a contribution to the livestock feed burden is insignificant.

Estimation of residues in livestock products

Since the previous estimation of residues in livestock feed is covering the use supported in the present dossier (potato), the established EU MRLs for commodities of animal origin are covering the use of BAS 222 28 F. These MRLs are established at the limit of quantitation of the relevant enforcement method (0.05 mg/kg).

Table 6.7.2- 1: MRL calculation for potatoes (calculation based on CS_2 detection)

Commodity	Region	Individual trial results [mg/kg][1, 2, 3]		Median residue [mg/kg]	Highest residue [mg/kg]	MRL calculated [mg/kg]	MRL established [mg/kg]
		Enforcement (metiram, expressed as CS_2)	**Risk assessment** (metiram, expressed as CS_2)				
Potatoes	NEU	Samples analysed as CS_2, **residues expressed as CS_2** All residues below LOQ (< 0.056 mg/kg)	Samples analysed as CS_2, **residues expressed as CS_2** All residues below LOQ (< 0.056 mg/kg) Samples analysed as CS_2, **residues recalculated to metiram[4]** All residues below LOQ (< 0.1 mg/kg)	0.056	0.056	0.06	0.3
	SEU	Samples analysed as CS_2, **residues expressed as CS_2** All residues below LOQ (< 0.056 mg/kg)	Samples analysed as CS_2, **residues expressed as CS_2** All residues below LOQ (< 0.056 mg/kg) Samples analysed as CS_2, **residues recalculated to metiram[4]** All residues below LOQ (< 0.1 mg/kg)	0.056	0.056	0.06	

1. if higher residues were determined at harvest intervals exceeding the PHI these values were used for the MRL calculation
2. Indicates that the MRL is set at the limit of analytical quantitation.
3. Individual residue levels considered for MRL calculation are reported in ascending order.
4. Metiram concentration derived by recalculating the CS_2 to metiram applying the molecular weight conversion factor of 1.79

Table 6.7.2- 2: MRL calculation for potatoes (calculation based on EBDC detection)

Commodity	Region	Individual trial results [mg/kg][1, 2, 3]		Median residue [mg/kg]	Highest residue [mg/kg]	MRL calculated [mg/kg]
		Enforcement (metiram, expressed as EBDC)	**Risk assessment** (metiram, expressed as EBDC)			
Potatoes	NEU	Samples analysed as EBDC, **residues of metiram** All residues below LOQ (< 0.05 mg/kg)	Samples analysed as EBDC, **residues of metiram** All residues below LOQ (< 0.05 mg/kg)	0.05	0.05	0.05
	SEU	Samples analysed as EBDC, **residues of metiram** All residues below LOQ (< 0.05 mg/kg)	Samples analysed as EBDC, **residues of metiram** All residues below LOQ (< 0.05 mg/kg)	0.05	0.05	0.05

1. If higher residues were determined at harvest intervals exceeding the PHI these values were used for the MRL calculation
2. Indicates that the MRL is set at the limit of analytical quantitation.
3. Individual residue levels considered for MRL calculation are reported in ascending order.

CA 6.7.3 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)

Not applicable for the use supported in the present dossier.

APPENDIX

Table 6.7.3- 1: EU MRLs set for the uses of metiram (BAS 222 F)

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
100000	. FRUITS, FRESH or FROZEN; TREE NUTS	
110000	. Citrus fruits	5
110010	. Grapefruits	5
110020	. Oranges	5
110030	. Lemons	5
110040	. Limes	5
110050	. Mandarins	5
110990	. Others (2)	5
120000	. Tree nuts	
120010	. Almonds	0.05*
120020	. Brazil nuts	0.05*
120030	. Cashew nuts	0.05*
120040	. Chestnuts	0.05*
120050	. Coconuts	0.05*
120060	. Hazelnuts/cobnuts	0.05*
120070	. Macadamias	0.05*
120080	. Pecans	0.05*
120090	. Pine nut kernels	0.05*
120100	. Pistachios	0.05*
120110	. Walnuts	0.1
120990	. Others (2)	0.05*
130000	. Pome fruits	5
130010	. Apples	5
130020	. Pears	5
130030	. Quinces	5
130040	. Medlars	5
130050	. Loquats/Japanese medlars	5
130990	. Others (2)	5
140000	. Stone fruits	
140010	. Apricots	2 (ft)
140020	. Cherries (sweet)	2 (ft)
140030	. Peaches	2 (ft)
140040	. Plums	2 (ft)

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
140990	. Others (2)	0.05*
150000	. Berries and small fruits	
151000	. (a) grapes	5 (ft)
151010	. Table grapes	5
151020	. Wine grapes	5
152000	. (b) strawberries	10 (ft)
153000	. (c) cane fruits	0.05*
153010	. Blackberries	0.05*
153020	. Dewberries	0.05*
153030	. Raspberries (red and yellow)	0.05*
153990	. Others (2)	0.05*
154000	. (d) other small fruits and berries	
154010	. Blueberries	5
154020	. Cranberries	5
154030	. Currants (black, red and white)	5 (ft)
154040	. Gooseberries (green, red and yellow)	5
154050	. Rose hips	0.05*
154060	. Mulberries (black and white)	0.05*
154070	. Azaroles/Mediterranean medlars	0.05*
154080	. Elderberries	0.05*
154990	. Others (2)	5
160000	. Miscellaneous fruits with	
161000	. (a) edible peel	
161010	. Dates	0.05*
161020	. Figs	0.05*
161030	. Table olives	5 (ft)
161040	. Kumquats	0.05*
161050	. Carambolas	0.05*
161060	. Kaki/Japanese persimmons	0.05*
161070	. Jambuls/jambolans	0.05*
161990	. Others (2)	0.05*
162000	. (b) inedible peel, small	0.05*
162010	. Kiwi fruits (green, red, yellow)	0.05*
162020	. Litchis/lychees	0.05*
162030	. Passionfruits/maracujas	0.05*
162040	. Prickly pears/cactus fruits	0.05*
162050	. Star apples/cainitos	0.05*
162060	. American persimmons/Virginia kaki	0.05*
162990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
163000	. (c) inedible peel, large	
163010	. Avocados	7 (ft)
163020	. Bananas	2 (ft)
163030	. Mangoes	2 (ft)
163040	. Papayas	7 (ft)
163050	. Granate apples/pomegranates	0.05*
163060	. Cherimoyas	0.05*
163070	. Guavas	0.05*
163080	. Pineapples	0.05*
163090	. Breadfruits	0.05*
163100	. Durians	0.05*
163110	. Soursops/guanabanas	0.05*
163990	. Others (2)	0.05*
200000	. VEGETABLES, FRESH or FROZEN	
210000	. Root and tuber vegetables	
211000	. (a) potatoes	0.3 (ft)
212000	. (b) tropical root and tuber vegetables	0.05*
212010	. Cassava roots/manioc	0.05*
212020	. Sweet potatoes	0.05*
212030	. Yams	0.05*
212040	. Arrowroots	0.05*
212990	. Others (2)	0.05*
213000	. (c) other root and tuber vegetables except sugar beets	
213010	. Beetroots	0.5 (ft)
213020	. Carrots	0.2 (ft)
213030	. Celeriacs/turnip rooted celeries	0.3 (ft)
213040	. Horseradishes	0.2 (ft)
213050	. Jerusalem artichokes	0.05*
213060	. Parsnips	0.2 (ft)
213070	. Parsley roots/Hamburg roots parsley	0.2 (ft)
213080	. Radishes	2 (ft)
213090	. Salsifies	0.2 (ft)
213100	. Swedes/rutabagas	0.05*
213110	. Turnips	0.05*
213990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
220000	. Bulb vegetables	
220010	. Garlic	0.6 (ft)
220020	. Onions	1 (ft)
220030	. Shallots	1 (ft)
220040	. Spring onions/green onions and Welsh onions	1 (ft)
220990	. Others (2)	0.05*
230000	. Fruiting vegetables	
231000	. (a) solanacea	
231010	. Tomatoes	3 (ft)
231020	. Sweet peppers/bell peppers	5 (ft)
231030	. Aubergines/eggplants	3 (ft)
231040	. Okra/lady's fingers	0.5 (ft)
231990	. Others (2)	0.05*
232000	. (b) cucurbits with edible peel	2 (ft)
232010	. Cucumbers	2
232020	. Gherkins	2
232030	. Courgettes	2
232990	. Others (2)	2
233000	. (c) cucurbits with inedible peel	1.5 (ft)
233010	. Melons	1.5 (ft)
233020	. Pumpkins	1.5 (ft)
233030	. Watermelons	1.5 (ft)
233990	. Others (2)	1.5 (ft)
234000	. (d) sweet corn	0.05*
239000	. (e) other fruiting vegetables	0.05*
240000	. Brassica vegetables (excluding brassica roots and brassica baby leaf crops)	
241000	. (a) flowering brassica	1 (ft)
241010	. Broccoli	1
241020	. Cauliflowers	1
241990	. Others (2)	1
242000	. (b) head brassica	
242010	. Brussels sprouts	2 (ft)
242020	. Head cabbages	3 (ft)
242990	. Others (2)	0.05*
243000	. (c) leafy brassica	0.5 (ft)
243010	. Chinese cabbages/pe-tsai	0.5
243020	. Kales	0.5
243990	. Others (2)	0.5
244000	. (d) kohlrabies	1 (ft)

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
250000	. Leaf vegetables, herbs and edible flowers	
251000	. (a) lettuces and salad plants	5 (ft)
251010	. Lamb's lettuces/corn salads	5
251020	. Lettuces	5
251030	. Escaroles/broad-leaved endives	5
251040	. Cresses and other sprouts and shoots	5
251050	. Land cresses	5
251060	. Roman rocket/rucola	5
251070	. Red mustards	5
251080	. Baby leaf crops (including brassica species)	5
251990	. Others (2)	5
252000	. (b) spinaches and similar leaves	
252010	. Spinaches	0.05*
252020	. Purslanes	5
252030	. Chards/beet leaves	0.05*
252990	. Others (2)	0.05*
253000	. (c) grape leaves and similar species	0.05*
254000	. (d) watercresses	0.3 (ft)
255000	. (e) witloofs/Belgian endives	0.5 (ft)
256000	. (f) herbs and edible flowers	5 (ft)
256010	. Chervil	5
256020	. Chives	5
256030	. Celery leaves	5
256040	. Parsley	5
256050	. Sage	5
256060	. Rosemary	5
256070	. Thyme	5
256080	. Basil and edible flowers	5
256090	. Laurel/bay leave	5
256100	. Tarragon	5
256990	. Others (2)	5
260000	. Legume vegetables	
260010	. Beans (with pods)	1 (ft)
260020	. Beans (without pods)	0.1 (ft)
260030	. Peas (with pods)	1 (ft)
260040	. Peas (without pods)	0.2 (ft)
260050	. Lentils	0.05*
260990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
270000	. Stem vegetables	
270010	. Asparagus	0.5 (ft)
270020	. Cardoons	0.05*
270030	. Celeries	0.05*
270040	. Florence fennels	0.05*
270050	. Globe artichokes	0.05*
270060	. Leeks	3 (ft)
270070	. Rhubarbs	0.5 (ft)
270080	. Bamboo shoots	0.05*
270090	. Palm hearts	0.05*
270990	. Others (2)	0.05*
280000	. Fungi, mosses and lichens	0.05*
280010	. Cultivated fungi	0.05*
280020	. Wild fungi	0.05*
280990	. Mosses and lichens	0.05*
290000	. Algae and prokaryotes organisms	0.05*
300000	. PULSES	
300010	. Beans	0.1 (ft)
300020	. Lentils	0.05*
300030	. Peas	0.1 (ft)
300040	. Lupins/lupini beans	0.05*
300990	. Others (2)	0.05*
400000	. OILSEEDS AND OIL FRUITS	
401000	. Oilseeds	
401010	. Linseeds	0.1*
401020	. Peanuts/groundnuts	0.1*
401030	. Poppy seeds	0.1*
401040	. Sesame seeds	0.1*
401050	. Sunflower seeds	0.1*
401060	. Rapeseeds/canola seeds	0.5 (ft)
401070	. Soya beans	0.1*
401080	. Mustard seeds	0.1*
401090	. Cotton seeds	0.1*
401100	. Pumpkin seeds	0.1*
401110	. Safflower seeds	0.1*
401120	. Borage seeds	0.1*
401130	. Gold of pleasure seeds	0.1*
401140	. Hemp seeds	0.1*
401150	. Castor beans	0.1*
401990	. Others (2)	0.1*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
402000	. Oil fruits	
402010	. Olives for oil production	5 (ft)
402020	. Oil palms kernels	0.1*
402030	. Oil palms fruits	0.1*
402040	. Kapok	0.1*
402990	. Others (2)	0.1*
500000	. CEREALS	
500010	. Barley	2 (ft)
500020	. Buckwheat and other pseudo-cereals	0.05*
500030	. Maize/corn	0.05*
500040	. Common millet/proso millet	0.05*
500050	. Oat	2 (ft)
500060	. Rice	0.05*
500070	. Rye	1 (ft)
500080	. Sorghum	0.05*
500090	. Wheat	1 (ft)
500990	. Others (2)	0.05*
600000	. TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS	0.1*
610000	. Teas	0.1*
620000	. Coffee beans	0.1*
630000	. Herbal infusions from	0.1*
631000	. (a) flowers	0.1*
631010	. Chamomile	0.1*
631020	. Hibiscus/roselle	0.1*
631030	. Rose	0.1*
631040	. Jasmine	0.1*
631050	. Lime/linden	0.1*
631990	. Others (2)	0.1*
632000	. (b) leaves and herbs	0.1*
632010	. Strawberry	0.1*
632020	. Rooibos	0.1*
632030	. Mate/maté	0.1*
632990	. Others (2)	0.1*
633000	. (c) roots	0.1*
633010	. Valerian	0.1*
633020	. Ginseng	0.1*
633990	. Others (2)	0.1*
639000	. (d) any other parts of the plant	0.1*
640000	. Cocoa beans	0.1*
650000	. Carobs/Saint John's breads	0.1*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
700000	. HOPS	25 (ft)
800000	. SPICES	
810000	. Seed spices	0.1*
810010	. Anise/aniseed	0.1*
810020	. Black caraway/black cumin	0.1*
810030	. Celery	0.1*
810040	. Coriander	0.1*
810050	. Cumin	0.1*
810060	. Dill	0.1*
810070	. Fennel	0.1*
810080	. Fenugreek	0.1*
810090	. Nutmeg	0.1*
810990	. Others (2)	0.1*
820000	. Fruit spices	0.1*
820010	. Allspice/pimento	0.1*
820020	. Sichuan pepper	0.1*
820030	. Caraway	0.1*
820040	. Cardamom	0.1*
820050	. Juniper berry	0.1*
820060	. Peppercorn (black, green and white)	0.1*
820070	. Vanilla	0.1*
820080	. Tamarind	0.1*
820990	. Others (2)	0.1*
830000	. Bark spices	0.1*
830010	. Cinnamon	0.1*
830990	. Others (2)	0.1*
840000	. Root and rhizome spices	0.1*
840010	. Liquorice	0.1*
840020	. Ginger	0.1*
840030	. Turmeric/curcuma	0.1*
840040	. Horseradish	(ft)
840990	. Others (2)	0.1*
850000	. Bud spices	
850010	. Cloves	0.1*
850020	. Capers	25
850990	. Others (2)	0.1*
860000	. Flower pistil spices	0.1*
860010	. Saffron	0.1*
860990	. Others (2)	0.1*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
870000	. Aril spices	0.1*
870010	. Mace	0.1*
870990	. Others (2)	0.1*
900000	. SUGAR PLANTS	
900010	. Sugar beet roots	2
900020	. Sugar canes	0.05*
900030	. Chicory roots	0.05*
900990	. Others (2)	0.05*
1000000	. PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS	0.05*
1010000	. Tissues from	0.05*
1011000	. (a) swine	0.05*
1011010	. Muscle	0.05*
1011020	. Fat tissue	0.05*
1011030	. Liver	0.05*
1011040	. Kidney	0.05*
1011050	. Edible offals (other than liver and kidney)	0.05*
1011990	. Others (2)	0.05*
1012000	. (b) bovine	0.05*
1012010	. Muscle	0.05*
1012020	. Fat tissue	0.05*
1012030	. Liver	0.05*
1012040	. Kidney	0.05*
1012050	. Edible offals (other than liver and kidney)	0.05*
1012990	. Others (2)	0.05*
1013000	. (c) sheep	0.05*
1013010	. Muscle	0.05*
1013020	. Fat tissue	0.05*
1013030	. Liver	0.05*
1013040	. Kidney	0.05*
1013050	. Edible offals (other than liver and kidney)	0.05*
1013990	. Others (2)	0.05*
1014000	. d) goat	0.05*
1014010	. Muscle	0.05*
1014020	. Fat tissue	0.05*
1014030	. Liver	0.05*
1014040	. Kidney	0.05*
1014050	. Edible offals (other than liver and kidney)	0.05*
1014990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
1015000	. (e) equine	0.05*
1015010	. Muscle	0.05*
1015020	. Fat tissue	0.05*
1015030	. Liver	0.05*
1015040	. Kidney	0.05*
1015050	. Edible offals (other than liver and kidney)	0.05*
1015990	. Others (2)	0.05*
1016000	. (f) poultry	0.05*
1016010	. Muscle	0.05*
1016020	. Fat tissue	0.05*
1016030	. Liver	0.05*
1016040	. Kidney	0.05*
1016050	. Edible offals (other than liver and kidney)	0.05*
1016990	. Others (2)	0.05*
1017000	. (g) other farmed terrestrial animals	0.05*
1017010	. Muscle	0.05*
1017020	. Fat tissue	0.05*
1017030	. Liver	0.05*
1017040	. Kidney	0.05*
1017050	. Edible offals (other than liver and kidney)	0.05*
1017990	. Others (2)	0.05*
1020000	. Milk	0.05*
1020010	. Cattle	0.05*
1020020	. Sheep	0.05*
1020030	. Goat	0.05*
1020040	. Horse	0.05*
1020990	. Others (2)	0.05*
1030000	. Birds eggs	0.05*
1030010	. Chicken	0.05*
1030020	. Duck	0.05*
1030030	. Geese	0.05*
1030040	. Quail	0.05*
1030990	. Others (2)	0.05*
1040000	. Honey and other apiculture products	0.05*
1050000	. Amphibians and Reptiles	0.05*
1060000	. Terrestrial invertebrate animals	0.05*
1070000	. Wild terrestrial vertebrate animals	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
Pesticide residue	**Legislation**	**Entry in to force**
Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)		
	Reg. (EU) 2017/171	03.02.2017

Pesticide residues and maximum residue levels (mg/kg)
*** indicates lower limit of analytical determination**

The MRLs expressed as CS_2 can arise from different dithiocarbamates and therefore they do not reflect a single Good Agricultural Practice (GAP). It is therefore not appropriate to use these MRLs to check compliance with a GAP.
(ft) Footnotes
In brackets the origin of the residue (ma: maneb mz: mancozeb me: metiram pr: propineb t: thiram z: ziram).

0110000 : Citrus fruits
(mz)
0110010 : Grapefruits
(mz)
0110020 : Oranges
(mz)
0110030 : Lemons
(mz)
0110040 : Limes
(mz)
0110050 : Mandarins
(mz)
0110990 : Others (2)
(mz)
0120110 : Walnuts
(mz)
0130000 : Pome fruits
(ma, mz, me, pr, t, z)
0130010 : Apples
(ma, mz, me, pr, t, z)
0130020 : Pears
(ma, mz, me, pr, t, z)
0130030 : Quinces
(ma, mz, me, pr, t, z)
0130040 : Medlars
(ma, mz, me, pr, t, z)
0130050 : Loquats/Japanese medlars
(ma, mz, me, pr, t, z)
0130990 : Others (2)
(ma, mz, me, pr, t, z)
0140010 : Apricots
(mz, t)
0140020 : Cherries (sweet)
(mz, me, pr, t, z)
0140030 : Peaches
(mz, t)
0140040 : Plums
(mz, me, t, z)
0151000 : (a) grapes
(ma, mz, me, pr, t, z)
0151010 : Table grapes
(ma, mz, me, pr, t, z)
0151020 : Wine grapes
(ma, mz, me, pr, t, z)
0152000 : (b) strawberries
(t)
0154010 : Blueberries
(mz)

0154020 : Cranberries
(mz)
0154030 : Currants (black
(mz)
0154040 : Gooseberries (green
(mz)
0161030 : Table olives
(mz, pr)
0161060 : Kaki/Japanese persimmons
(mz)
0163010 : Avocados
(t)
0163020 : Bananas
(mz, me, t)
0163030 : Mangoes
(mz)
0163040 : Papayas
(mz)
0211000 : (a) potatoes
(ma, mz, me, pr, z)
0213010 : Beetroots
(mz)
0213020 : Carrots
(mz)
0213030 : Celeriacs/turnip rooted celeries
(ma, mz, me, pr, t, z)
0213040 : Horseradishes
(mz)
0213060 : Parsnips
(mz)
0213070 : Parsley roots/Hamburg roots parsley
(mz)
0213080 : Radishes
(mz)
0213090 : Salsifies
(mz)
0220010 : Garlic
(me)
0220020 : Onions
(ma, me, mz)
0220030 : Shallots
(ma, me, mz)
0220040 : Spring onions/green onions and Welsh onions
(ma, mz)
0231010 : Tomatoes
(mz, pr)
0231020 : Sweet peppers/bell peppers
(mz, pr)
0231030 : Aubergines/eggplants
(me, mz)
0231040 : Okra/lady's fingers
(mz)
0232000 : (b) cucurbits with edible peel

(mz, me, pr)
0232010 : Cucumbers
(mz, me, pr)
0232020 : Gherkins
(mz, me, pr)
0232030 : Courgettes
(mz, me, pr)
0232990 : Others (2)
(mz, me, pr)
0233000 : (c) cucurbits with inedible peel
(me)
0233010 : Melons
(me)
0233020 : Pumpkins
(me)
0233030 : Watermelons
(me)
0233990 : Others (2)
(me)
0241000 : (a) flowering brassica
(mz)
0241010 : Broccoli
(mz)
0241020 : Cauliflowers
(mz)
0241990 : Others (2)
(mz)
0242010 : Brussels sprouts
(mz)
0242020 : Head cabbages
(mz)
0243000 : (c) leafy brassica
(mz)
0243010 : Chinese cabbages/pe-tsai
(mz)
0243020 : Kales
(mz)
0243990 : Others (2)
(mz)
0244000 : (d) kohlrabies
(mz)
0251000 : (a) lettuces and salad plants
(mz, me, t)
0251010 : Lamb's lettuces/corn salads
(mz, me, t)
0251020 : Lettuces
(mz, me, t)
0251030 : Escaroles/broad-leaved endives
(mz, me, t)
0251040 : Cresses and other sprouts and shoots
(mz, me, t)
0251050 : Land cresses
(mz, me, t)

0251060 : Roman rocket/rucola
(mz, me, t)
0251070 : Red mustards
(mz, me, t)
0251080 : Baby leaf crops (including brassica species)
(mz, me, t)
0251990 : Others (2)
(mz, me, t)
0252020 : Purslanes
(mz, me, t)
0254000 : (d) watercresses
(mz)
0255000 : (e) witloofs/Belgian endives
(mz)
0256000 : (f) herbs and edible flowers
(mz, me)
0256010 : Chervil
(mz, me)
0256020 : Chives
(mz, me)
0256030 : Celery leaves
(mz, me)
0256040 : Parsley
(mz, me)
0256050 : Sage
(mz, me)
0256060 : Rosemary
(mz, me)
0256070 : Thyme
(mz, me)
0256080 : Basil and edible flowers
(mz, me)
0256090 : Laurel/bay leaves
(mz, me)
0256100 : Tarragon
(mz, me)
0256990 : Others (2)
(mz, me)
0260010 : Beans (with pods)
(mz)
0260020 : Beans (without pods)
(mz)
0260030 : Peas (with pods)
(ma, mz)
0260040 : Peas (without pods)
(mz)
0270010 : Asparagus
(me, mz)
0270060 : Leeks
(ma, mz)
0270070 : Rhubarbs
(mz)
0300010 : Beans

(mz)
0300030 : Peas
(mz)
0401060 : Rapeseeds/canola seeds
(ma, mz)
0402010 : Olives for oil production
(mz, pr)
0500010 : Barley
(ma, mz)
0500050 : Oat
(ma, mz)
0500070 : Rye
(ma, mz)
0500090 : Wheat
(ma, mz)
0633020 : Ginseng
(mz)
0700000 : HOPS
(pr)
0810040 : Coriander
(mz)
0810070 : Fennel
(mz)
0820040 : Cardamom
(mz)
0820060 : Peppercorn (black
(mz)
0840040 : Horseradish (11)
The applicable maximum residue level for horseradish (Armoracia rusticana) in the spice group (code 0840040) is the one set for horseradish (Armoracia rusticana) in the Vegetables category, root and tuber vegetables group (code 0213040) taking into account changes in the levels by processing (drying) according to Art. 20 (1) of Regulation (EC) No 396/2005.

CA 6.8 Proposed safety intervals

Residue trials have been conducted with applications made at the latest recommended crop growth stage with harvest taking place at the time of crop maturity following good agricultural practice.

Pre-harvest interval
For potato, the PHI is 14 days. The formulation BAS 222 28 F is intended to be used between BBCH growth stages 21 and 89, whereby three applications are intended to be made.

Re-entry period for livestock to areas to be grazed
Because metiram is not intended to be used in areas to be grazed, no re-entry period for livestock has to be defined.

Re-entry period for man to treated crops
Re-entry assessment is given for the representative use in the supplemental product dossiers (M-CP 7.2). Re-entry is possible after the spray deposits on the crops have dried given the worker is wearing adequate work clothing.

Withholding period for animal feed stuffs
Due to the very favourable residue situation in potatoes with residues consistently below LOQ no withholding period needs to be considered for tubers.

Waiting period between application and crop sowing or planting the crop to be protected
No waiting period is necessary since metiram is not intended in a pre-emergence use.

Waiting period between application and handling treated produce
This is not relevant here since a post-harvest treatment is not intended for potatoes.

Waiting period between last application and sowing or planting succeeding crops
No accumulation of metiram (BAS 222 F) or any of its degradation products was observed in the confined rotational crop study. The metabolites of metiram were extensively incorporated into the carbon pool and into the natural products of plants.

CA 6.9 Estimation of the potential and actual exposure through diet and other sources

For assessing the dietary risk for the consumer resulting from the potato use supported in the present dossier, dietary risk assessment according to the parent compound metiram (expressed as CS_2) was performed.
For metiram an assessment of acute exposure was not performed due to the low acute toxicity of the active substance (ARfD is not allocated).

The newest version of PRIMo3.1 was used (EFSA (European Food Safety Authority), 2019. Technical report on the Pesticide Residue Intake Model- EFSA PRIMo revision 3.1 (update of EFSA PRIMo revision 3). EFSA supporting publication 2019:EN-1605, 15 pp, doi:10.2903/sp.efsa.2019.EN-1605.

Toxicological reference values used

The following toxicological reference value was used for the chronic assessment (ADI).

Table 6.9- 1: Toxicological reference values: Metiram

End-Point	Value	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.03 mg/kg bw/d	2-year study in rats	100	SANCO/4059/2001-rev 3.3 (03.06.2005)
Acute Reference Dose (ARfD)	0.4 mg/kg bw	-	-	-

Acceptable Daily Intake (ADI) and Dietary Exposure Calculation

Metiram exposure calculations

Metiram: TMDI

For the assessment, the STMR value for Metiram (expressed as CS_2 equivalent) of the potato use (<0.056 mg/kg) can be used as input value for the exposure assessment (TMDI).

Using an ADI for metiram of 0.03 mg/kg bw/d (Table 6.9- 1), intake calculations result in ADI utilization of 0.1 to 1.0% (see Table 6.9- 3 in appendix).

Metiram: NEDI

Considering the potato use, refinement of intake calculations using STMR or STMRp are not required since the TMDI calculations result in ADI utilizations below 100%.

The exposure assessment indicates that the metiram use (potato) supported in the present dossier do not pose a chronic safety concern for the consumer.

Acute Reference Dose (ARfD) and Dietary Exposure Calculation

NESTI calculations

For the acute assessment, the HR value for Metiram (expressed as CS_2 equivalent) of the potato use (0.056 mg/kg) can be used as input value for the exposure assessment (NESTI).

Using an ARfD for metiram of 0.4 mg/kg bw (Table 6.9-1), intake calculations result in ARfD utilization of 2.0% for potatoes, 1% for potatoes/fried and 0.8% for potatoes / dried (flakes) (see Table 6.9- 4 in appendix).

The acute exposure assessment indicates that the metiram use (potato) supported in the present dossier do not pose a safety concern for the consumer.

Overall conclusion on dietary exposure

For the use of Metiram on potatoes according to the GAP included in the present dossier, calculations of dietary exposure reveal a very low exposure: **chronic:** 0.1 to 1.0% (see Table 6.9-3 in appendix); **acute:** 2.0% for potatoes, 1% for potatoes/fried and 0.8% for potatoes / dried (flakes) (see Table 6.9- 4in appendix).

Considering that this value was calculated assuming various worst-case assumptions, a realistic dietary exposure can be considered as insignificant, i.e. negligible.

NESTI calculations

For the acute assessment, the HR value for Metiram (expressed as CS_2 equivalent) of the potato use (0.056 mg/kg) can be used as input value for the exposure assessment (NESTI).

Using an ARfD for metiram of 0.4 mg/kg bw (Table 6.9- 1), intake calculations result in ARfD utilization of 2.0% for potatoes, 1% for potatoes/fried and 0.8% for potatoes / dried (flakes) (see Table 6.9- 4 in appendix).

The acute exposure assessment indicates that the metiram use (potato) supported in the present dossier do not pose a safety concern for the consumer.

Overall conclusion on dietary exposure

For the use of Metiram on potatoes according to the GAP included in the present dossier, calculations of dietary exposure reveal a very low exposure: **chronic:** 0.1 to 1.0% (see Table 6.9-3 in appendix); **acute:** 2.0% for potatoes, 1% for potatoes/fried and 0.8% for potatoes / dried (flakes) (see Table 6.9- 4 in appendix).

Considering that this value was calculated assuming various worst-case assumptions, a realistic dietary exposure can be considered as insignificant, i.e. negligible.

APPENDIX

Table 6.9- 2: EU MRLs set for the uses of metiram (BAS 222 F) / dithiocarbamate fungicides

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
100000	. FRUITS, FRESH or FROZEN; TREE NUTS	
110000	. Citrus fruits	5
110010	. Grapefruits	5
110020	. Oranges	5
110030	. Lemons	5
110040	. Limes	5
110050	. Mandarins	5
110990	. Others (2)	5
120000	. Tree nuts	
120010	. Almonds	0.05*
120020	. Brazil nuts	0.05*
120030	. Cashew nuts	0.05*
120040	. Chestnuts	0.05*
120050	. Coconuts	0.05*
120060	. Hazelnuts/cobnuts	0.05*
120070	. Macadamias	0.05*
120080	. Pecans	0.05*
120090	. Pine nut kernels	0.05*
120100	. Pistachios	0.05*
120110	. Walnuts	0.1
120990	. Others (2)	0.05*
130000	. Pome fruits	5
130010	. Apples	5
130020	. Pears	5
130030	. Quinces	5
130040	. Medlars	5
130050	. Loquats/Japanese medlars	5
130990	. Others (2)	5
140000	. Stone fruits	
140010	. Apricots	2 (ft)
140020	. Cherries (sweet)	2 (ft)
140030	. Peaches	2 (ft)
140040	. Plums	2 (ft)
140990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
150000	. Berries and small fruits	
151000	. (a) grapes	5 (ft)
151010	. Table grapes	5
151020	. Wine grapes	5
152000	. (b) strawberries	10 (ft)
153000	. (c) cane fruits	0.05*
153010	. Blackberries	0.05*
153020	. Dewberries	0.05*
153030	. Raspberries (red and yellow)	0.05*
153990	. Others (2)	0.05*
154000	. (d) other small fruits and berries	
154010	. Blueberries	5
154020	. Cranberries	5
154030	. Currants (black, red and white)	5 (ft)
154040	. Gooseberries (green, red and yellow)	5
154050	. Rose hips	0.05*
154060	. Mulberries (black and white)	0.05*
154070	. Azaroles/Mediterranean medlars	0.05*
154080	. Elderberries	0.05*
154990	. Others (2)	5
160000	. Miscellaneous fruits with	
161000	. (a) edible peel	
161010	. Dates	0.05*
161020	. Figs	0.05*
161030	. Table olives	5 (ft)
161040	. Kumquats	0.05*
161050	. Carambolas	0.05*
161060	. Kaki/Japanese persimmons	0.05*
161070	. Jambuls/jambolans	0.05*
161990	. Others (2)	0.05*
162000	. (b) inedible peel, small	0.05*
162010	. Kiwi fruits (green, red, yellow)	0.05*
162020	. Litchis/lychees	0.05*
162030	. Passionfruits/maracujas	0.05*
162040	. Prickly pears/cactus fruits	0.05*
162050	. Star apples/cainitos	0.05*
162060	. American persimmons/Virginia kaki	0.05*
162990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
163000	. (c) inedible peel, large	
163010	. Avocados	7 (ft)
163020	. Bananas	2 (ft)
163030	. Mangoes	2 (ft)
163040	. Papayas	7 (ft)
163050	. Granate apples/pomegranates	0.05*
163060	. Cherimoyas	0.05*
163070	. Guavas	0.05*
163080	. Pineapples	0.05*
163090	. Breadfruits	0.05*
163100	. Durians	0.05*
163110	. Soursops/guanabanas	0.05*
163990	. Others (2)	0.05*
200000	. VEGETABLES, FRESH or FROZEN	
210000	. Root and tuber vegetables	
211000	. (a) potatoes	0.3 (ft)
212000	. (b) tropical root and tuber vegetables	0.05*
212010	. Cassava roots/manioc	0.05*
212020	. Sweet potatoes	0.05*
212030	. Yams	0.05*
212040	. Arrowroots	0.05*
212990	. Others (2)	0.05*
213000	. (c) other root and tuber vegetables except sugar beets	
213010	. Beetroots	0.5 (ft)
213020	. Carrots	0.2 (ft)
213030	. Celeriacs/turnip rooted celeries	0.3 (ft)
213040	. Horseradishes	0.2 (ft)
213050	. Jerusalem artichokes	0.05*
213060	. Parsnips	0.2 (ft)
213070	. Parsley roots/Hamburg roots parsley	0.2 (ft)
213080	. Radishes	2 (ft)
213090	. Salsifies	0.2 (ft)
213100	. Swedes/rutabagas	0.05*
213110	. Turnips	0.05*
213990	. Others (2)	0.05*

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
220000	. Bulb vegetables	
220010	. Garlic	0.6 (ft)
220020	. Onions	1 (ft)
220030	. Shallots	1 (ft)
220040	. Spring onions/green onions and Welsh onions	1 (ft)
220990	. Others (2)	0.05*
230000	. Fruiting vegetables	
231000	. (a) solanacea	
231010	. Tomatoes	3 (ft)
231020	. Sweet peppers/bell peppers	5 (ft)
231030	. Aubergines/eggplants	3 (ft)
231040	. Okra/lady's fingers	0.5 (ft)
231990	. Others (2)	0.05*
232000	. (b) cucurbits with edible peel	2 (ft)
232010	. Cucumbers	2
232020	. Gherkins	2
232030	. Courgettes	2
232990	. Others (2)	2
233000	. (c) cucurbits with inedible peel	1.5 (ft)
233010	. Melons	1.5 (ft)
233020	. Pumpkins	1.5 (ft)
233030	. Watermelons	1.5 (ft)
233990	. Others (2)	1.5 (ft)
234000	. (d) sweet corn	0.05*
239000	. (e) other fruiting vegetables	0.05*
240000	. Brassica vegetables (excluding brassica roots and brassica baby leaf crops)	
241000	. (a) flowering brassica	1 (ft)
241010	. Broccoli	1
241020	. Cauliflowers	1
241990	. Others (2)	1
242000	. (b) head brassica	
242010	. Brussels sprouts	2 (ft)
242020	. Head cabbages	3 (ft)
242990	. Others (2)	0.05*
243000	. (c) leafy brassica	0.5 (ft)
243010	. Chinese cabbages/pe-tsai	0.5
243020	. Kales	0.5
243990	. Others (2)	0.5

Pesticides - Web Version - EU MRLs (File created on 09/05/2019)		
Code number	**Groups and examples of individual products to which the MRLs apply (a)**	**Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)**
244000	. (d) kohlrabies	1 (ft)
250000	. Leaf vegetables, herbs and edible flowers	
251000	. (a) lettuces and salad plants	5 (ft)
251010	. Lamb's lettuces/corn salads	5
251020	. Lettuces	5
251030	. Escaroles/broad-leaved endives	5
251040	. Cresses and other sprouts and shoots	5
251050	. Land cresses	5
251060	. Roman rocket/rucola	5
251070	. Red mustards	5
251080	. Baby leaf crops (including brassica species)	5
251990	. Others (2)	5
252000	. (b) spinaches and similar leaves	
252010	. Spinaches	0.05*
252020	. Purslanes	5
252030	. Chards/beet leaves	0.05*
252990	. Others (2)	0.05*
253000	. (c) grape leaves and similar species	0.05*
254000	. (d) watercresses	0.3 (ft)
255000	. (e) witloofs/Belgian endives	0.5 (ft)
256000	. (f) herbs and edible flowers	5 (ft)
256010	. Chervil	5
256020	. Chives	5
256030	. Celery leaves	5
256040	. Parsley	5
256050	. Sage	5
256060	. Rosemary	5
256070	. Thyme	5
256080	. Basil and edible flowers	5
256090	. Laurel/bay leave	5
256100	. Tarragon	5
256990	. Others (2)	5
260000	. Legume vegetables	
260010	. Beans (with pods)	1 (ft)
260020	. Beans (without pods)	0.1 (ft)
260030	. Peas (with pods)	1 (ft)
260040	. Peas (without pods)	0.2 (ft)
260050	. Lentils	0.05*
260990	. Others (2)	0.05*

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270000	. Stem vegetables	
270010	. Asparagus	0.5 (ft)
270020	. Cardoons	0.05*
270030	. Celeries	0.05*
270040	. Florence fennels	0.05*
270050	. Globe artichokes	0.05*
270060	. Leeks	3 (ft)
270070	. Rhubarbs	0.5 (ft)
270080	. Bamboo shoots	0.05*
270090	. Palm hearts	0.05*
270990	. Others (2)	0.05*
280000	. Fungi, mosses and lichens	0.05*
280010	. Cultivated fungi	0.05*
280020	. Wild fungi	0.05*
280990	. Mosses and lichens	0.05*
290000	. Algae and prokaryotes organisms	0.05*
300000	. PULSES	
300010	. Beans	0.1 (ft)
300020	. Lentils	0.05*
300030	. Peas	0.1 (ft)
300040	. Lupins/lupini beans	0.05*
300990	. Others (2)	0.05*
400000	. OILSEEDS AND OIL FRUITS	
401000	. Oilseeds	
401010	. Linseeds	0.1*
401020	. Peanuts/groundnuts	0.1*
401030	. Poppy seeds	0.1*
401040	. Sesame seeds	0.1*
401050	. Sunflower seeds	0.1*
401060	. Rapeseeds/canola seeds	0.5 (ft)
401070	. Soya beans	0.1*
401080	. Mustard seeds	0.1*
401090	. Cotton seeds	0.1*
401100	. Pumpkin seeds	0.1*
401110	. Safflower seeds	0.1*
401120	. Borage seeds	0.1*
401130	. Gold of pleasure seeds	0.1*
401140	. Hemp seeds	0.1*
401150	. Castor beans	0.1*
401990	. Others (2)	0.1*

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402000	. Oil fruits	
402010	. Olives for oil production	5 (ft)
402020	. Oil palms kernels	0.1*
402030	. Oil palms fruits	0.1*
402040	. Kapok	0.1*
402990	. Others (2)	0.1*
500000	. CEREALS	
500010	. Barley	2 (ft)
500020	. Buckwheat and other pseudo-cereals	0.05*
500030	. Maize/corn	0.05*
500040	. Common millet/proso millet	0.05*
500050	. Oat	2 (ft)
500060	. Rice	0.05*
500070	. Rye	1 (ft)
500080	. Sorghum	0.05*
500090	. Wheat	1 (ft)
500990	. Others (2)	0.05*
600000	. TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS	0.1*
610000	. Teas	0.1*
620000	. Coffee beans	0.1*
630000	. Herbal infusions from	0.1*
631000	. (a) flowers	0.1*
631010	. Chamomile	0.1*
631020	. Hibiscus/roselle	0.1*
631030	. Rose	0.1*
631040	. Jasmine	0.1*
631050	. Lime/linden	0.1*
631990	. Others (2)	0.1*
632000	. (b) leaves and herbs	0.1*
632010	. Strawberry	0.1*
632020	. Rooibos	0.1*
632030	. Mate/maté	0.1*
632990	. Others (2)	0.1*
633000	. (c) roots	0.1*
633010	. Valerian	0.1*
633020	. Ginseng	0.1*
633990	. Others (2)	0.1*
639000	. (d) any other parts of the plant	0.1*
640000	. Cocoa beans	0.1*
650000	. Carobs/Saint John's breads	0.1*

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700000	. HOPS	25 (ft)
800000	. SPICES	
810000	. Seed spices	0.1*
810010	. Anise/aniseed	0.1*
810020	. Black caraway/black cumin	0.1*
810030	. Celery	0.1*
810040	. Coriander	0.1*
810050	. Cumin	0.1*
810060	. Dill	0.1*
810070	. Fennel	0.1*
810080	. Fenugreek	0.1*
810090	. Nutmeg	0.1*
810990	. Others (2)	0.1*
820000	. Fruit spices	0.1*
820010	. Allspice/pimento	0.1*
820020	. Sichuan pepper	0.1*
820030	. Caraway	0.1*
820040	. Cardamom	0.1*
820050	. Juniper berry	0.1*
820060	. Peppercorn (black, green and white)	0.1*
820070	. Vanilla	0.1*
820080	. Tamarind	0.1*
820990	. Others (2)	0.1*
830000	. Bark spices	0.1*
830010	. Cinnamon	0.1*
830990	. Others (2)	0.1*
840000	. Root and rhizome spices	0.1*
840010	. Liquorice	0.1*
840020	. Ginger	0.1*
840030	. Turmeric/curcuma	0.1*
840040	. Horseradish	(ft)
840990	. Others (2)	0.1*
850000	. Bud spices	
850010	. Cloves	0.1*
850020	. Capers	25
850990	. Others (2)	0.1*
860000	. Flower pistil spices	0.1*
860010	. Saffron	0.1*
860990	. Others (2)	0.1*

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870000	. Aril spices	0.1*
870010	. Mace	0.1*
870990	. Others (2)	0.1*
900000	. SUGAR PLANTS	
900010	. Sugar beet roots	2
900020	. Sugar canes	0.05*
900030	. Chicory roots	0.05*
900990	. Others (2)	0.05*
1000000	. PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS	0.05*
1010000	. Tissues from	0.05*
1011000	. (a) swine	0.05*
1011010	. Muscle	0.05*
1011020	. Fat tissue	0.05*
1011030	. Liver	0.05*
1011040	. Kidney	0.05*
1011050	. Edible offals (other than liver and kidney)	0.05*
1011990	. Others (2)	0.05*
1012000	. (b) bovine	0.05*
1012010	. Muscle	0.05*
1012020	. Fat tissue	0.05*
1012030	. Liver	0.05*
1012040	. Kidney	0.05*
1012050	. Edible offals (other than liver and kidney)	0.05*
1012990	. Others (2)	0.05*
1013000	. (c) sheep	0.05*
1013010	. Muscle	0.05*
1013020	. Fat tissue	0.05*
1013030	. Liver	0.05*
1013040	. Kidney	0.05*
1013050	. Edible offals (other than liver and kidney)	0.05*
1013990	. Others (2)	0.05*
1014000	. d) goat	0.05*
1014010	. Muscle	0.05*
1014020	. Fat tissue	0.05*
1014030	. Liver	0.05*
1014040	. Kidney	0.05*
1014050	. Edible offals (other than liver and kidney)	0.05*
1014990	. Others (2)	0.05*

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1015000	. (e) equine	0.05*
1015010	. Muscle	0.05*
1015020	. Fat tissue	0.05*
1015030	. Liver	0.05*
1015040	. Kidney	0.05*
1015050	. Edible offals (other than liver and kidney)	0.05*
1015990	. Others (2)	0.05*
1016000	. (f) poultry	0.05*
1016010	. Muscle	0.05*
1016020	. Fat tissue	0.05*
1016030	. Liver	0.05*
1016040	. Kidney	0.05*
1016050	. Edible offals (other than liver and kidney)	0.05*
1016990	. Others (2)	0.05*
1017000	. (g) other farmed terrestrial animals	0.05*
1017010	. Muscle	0.05*
1017020	. Fat tissue	0.05*
1017030	. Liver	0.05*
1017040	. Kidney	0.05*
1017050	. Edible offals (other than liver and kidney)	0.05*
1017990	. Others (2)	0.05*
1020000	. Milk	0.05*
1020010	. Cattle	0.05*
1020020	. Sheep	0.05*
1020030	. Goat	0.05*
1020040	. Horse	0.05*
1020990	. Others (2)	0.05*
1030000	. Birds eggs	0.05*
1030010	. Chicken	0.05*
1030020	. Duck	0.05*
1030030	. Geese	0.05*
1030040	. Quail	0.05*
1030990	. Others (2)	0.05*
1040000	. Honey and other apiculture products	0.05*
1050000	. Amphibians and Reptiles	0.05*
1060000	. Terrestrial invertebrate animals	0.05*
1070000	. Wild terrestrial vertebrate animals	0.05*

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Pesticide residue	**Legislation**	**Entry in to force**
Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)		
	Reg. (EU) No 2017/171	03.02.2017

Pesticide residues and maximum residue levels (mg/kg)
*** indicates lower limit of analytical determination**

The MRLs expressed as CS_2 can arise from different dithiocarbamates and therefore they do not reflect a single Good Agricultural Practice (GAP). It is therefore not appropriate to use these MRLs to check compliance with a GAP.
(ft) Footnotes
In brackets the origin of the residue (ma: maneb mz: mancozeb me: metiram pr: propineb t: thiram z: ziram).

0110000 : Citrus fruits
(mz)
0110010 : Grapefruits
(mz)
0110020 : Oranges
(mz)
0110030 : Lemons
(mz)
0110040 : Limes
(mz)
0110050 : Mandarins
(mz)
0110990 : Others (2)
(mz)
0120110 : Walnuts
(mz)
0130000 : Pome fruits
(ma, mz, me, pr, t, z)
0130010 : Apples
(ma, mz, me, pr, t, z)
0130020 : Pears
(ma, mz, me, pr, t, z)
0130030 : Quinces
(ma, mz, me, pr, t, z)
0130040 : Medlars
(ma, mz, me, pr, t, z)
0130050 : Loquats/Japanese medlars
(ma, mz, me, pr, t, z)
0130990 : Others (2)
(ma, mz, me, pr, t, z)
0140010 : Apricots
(mz, t)
0140020 : Cherries (sweet)
(mz, me, pr, t, z)
0140030 : Peaches
(mz, t)
0140040 : Plums
(mz, me, t, z)

0151000 : (a) grapes
(ma, mz, me, pr, t, z)
0151010 : Table grapes
(ma, mz, me, pr, t, z)
0151020 : Wine grapes
(ma, mz, me, pr, t, z)
0152000 : (b) strawberries
(t)
0154010 : Blueberries
(mz)
0154020 : Cranberries
(mz)
0154030 : Currants (black
(mz)
0154040 : Gooseberries (green
(mz)
0161030 : Table olives
(mz, pr)
0161060 : Kaki/Japanese persimmons
(mz)
0163010 : Avocados
(t)
0163020 : Bananas
(mz, me, t)
0163030 : Mangoes
(mz)
0163040 : Papayas
(mz)
0211000 : (a) potatoes
(ma, mz, me, pr, z)
0213010 : Beetroots
(mz)
0213020 : Carrots
(mz)
0213030 : Celeriacs/turnip rooted celeries
(ma, mz, me, pr, t, z)
0213040 : Horseradishes
(mz)
0213060 : Parsnips
(mz)
0213070 : Parsley roots/Hamburg roots parsley
(mz)
0213080 : Radishes
(mz)
0213090 : Salsifies
(mz)
0220010 : Garlic
(me)
0220020 : Onions
(ma, me, mz)
0220030 : Shallots
(ma, me, mz)
0220040 : Spring onions/green onions and Welsh onions

(ma, mz)
0231010 : Tomatoes
(mz, pr)
0231020 : Sweet peppers/bell peppers
(mz, pr)
0231030 : Aubergines/eggplants
(me, mz)
0231040 : Okra/lady's fingers
(mz)
0232000 : (b) cucurbits with edible peel
(mz, me, pr)
0232010 : Cucumbers
(mz, me, pr)
0232020 : Gherkins
(mz, me, pr)
0232030 : Courgettes
(mz, me, pr)
0232990 : Others (2)
(mz, me, pr)
0233000 : (c) cucurbits with inedible peel
(me)
0233010 : Melons
(me)
0233020 : Pumpkins
(me)
0233030 : Watermelons
(me)
0233990 : Others (2)
(me)
0241000 : (a) flowering brassica
(mz)
0241010 : Broccoli
(mz)
0241020 : Cauliflowers
(mz)
0241990 : Others (2)
(mz)
0242010 : Brussels sprouts
(mz)
0242020 : Head cabbages
(mz)
0243000 : (c) leafy brassica
(mz)
0243010 : Chinese cabbages/pe-tsai
(mz)
0243020 : Kales
(mz)
0243990 : Others (2)
(mz)
0244000 : (d) kohlrabies
(mz)
0251000 : (a) lettuces and salad plants
(mz, me, t)

0251010 : Lamb's lettuces/corn salads
(mz, me, t)
0251020 : Lettuces
(mz, me, t)
0251030 : Escaroles/broad-leaved endives
(mz, me, t)
0251040 : Cresses and other sprouts and shoots
(mz, me, t)
0251050 : Land cresses
(mz, me, t)
0251060 : Roman rocket/rucola
(mz, me, t)
0251070 : Red mustards
(mz, me, t)
0251080 : Baby leaf crops (including brassica species)
(mz, me, t)
0251990 : Others (2)
(mz, me, t)
0252020 : Purslanes
(mz, me, t)
0254000 : (d) watercresses
(mz)
0255000 : (e) witloofs/Belgian endives
(mz)
0256000 : (f) herbs and edible flowers
(mz, me)
0256010 : Chervil
(mz, me)
0256020 : Chives
(mz, me)
0256030 : Celery leaves
(mz, me)
0256040 : Parsley
(mz, me)
0256050 : Sage
(mz, me)
0256060 : Rosemary
(mz, me)
0256070 : Thyme
(mz, me)
0256080 : Basil and edible flowers
(mz, me)
0256090 : Laurel/bay leaves
(mz, me)
0256100 : Tarragon
(mz, me)
0256990 : Others (2)
(mz, me)
0260010 : Beans (with pods)
(mz)
0260020 : Beans (without pods)
(mz)
0260030 : Peas (with pods)

(ma, mz)
0260040 : Peas (without pods)
(mz)
0270010 : Asparagus
(me, mz)
0270060 : Leeks
(ma, mz)
0270070 : Rhubarbs
(mz)
0300010 : Beans
(mz)
0300030 : Peas
(mz)
0401060 : Rapeseeds/canola seeds
(ma, mz)
0402010 : Olives for oil production
(mz, pr)
0500010 : Barley
(ma, mz)
0500050 : Oat
(ma, mz)
0500070 : Rye
(ma, mz)
0500090 : Wheat
(ma, mz)
0633020 : Ginseng
(mz)
0700000 : HOPS
(pr)
0810040 : Coriander
(mz)
0810070 : Fennel
(mz)
0820040 : Cardamom
(mz)
0820060 : Peppercorn (black
(mz)
0840040 : Horseradish (11)
The applicable maximum residue level for horseradish (Armoracia rusticana) in the spice group (code 0840040) is the one set for horseradish (Armoracia rusticana) in the Vegetables category, root and tuber vegetables group (code 0213040) taking into account changes in the levels by processing (drying) according to Art. 20 (1) of Regulation (EC) No 396/2005.

Table 6.9- 3: Metiram: TMDI calculation based on input values of representative commodities (potatoes)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Metiram

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	**0,03**	ARfD (mg/kg bw):	**not necessary**
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	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	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
	1,0%	PT general	0,30	1,0%	Potatoes						
	0,9%	FI 3 yr	0,26	0,9%	Potatoes		FRUIT AND TREE NUTS				
	0,8%	NL toddler	0,24	0,8%	Potatoes		FRUIT AND TREE NUTS				
	0,8%	SE general	0,23	0,8%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	GEMS/Food G11	0,22	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	GEMS/Food G08	0,22	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	FI 6 yr	0,22	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	GEMS/Food G07	0,21	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	RO general	0,21	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	GEMS/Food G15	0,20	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,7%	UK toddler	0,20	0,7%	Potatoes		FRUIT AND TREE NUTS				
	0,6%	NL child	0,19	0,6%	Potatoes		FRUIT AND TREE NUTS				
	0,6%	PL general	0,19	0,6%	Potatoes		FRUIT AND TREE NUTS				
	0,6%	UK infant	0,18	0,6%	Potatoes		FRUIT AND TREE NUTS				
	0,6%	LT adult	0,18	0,6%	Potatoes		FRUIT AND TREE NUTS				
	0,6%	GEMS/Food G10	0,17	0,6%	Potatoes		FRUIT AND TREE NUTS				
	0,5%	DE child	0,15	0,5%	Potatoes		FRUIT AND TREE NUTS				
	0,5%	DK child	0,14	0,5%	Potatoes		FRUIT AND TREE NUTS				
	0,5%	NL general	0,14	0,5%	Potatoes		FRUIT AND TREE NUTS				
	0,4%	IE adult	0,13	0,4%	Potatoes		FRUIT AND TREE NUTS				
	0,4%	GEMS/Food G06	0,11	0,4%	Potatoes		FRUIT AND TREE NUTS				
	0,4%	FR infant	0,11	0,4%	Potatoes		FRUIT AND TREE NUTS				
	0,3%	FR toddler 2 3 yr	0,10	0,3%	Potatoes		FRUIT AND TREE NUTS				
	0,3%	ES child	0,10	0,3%	Potatoes		FRUIT AND TREE NUTS				
	0,3%	FR child 3 15 yr	0,08	0,3%	Potatoes		FRUIT AND TREE NUTS				
	0,3%	UK adult	0,08	0,3%	Potatoes		FRUIT AND TREE NUTS				
	0,3%	UK vegetarian	0,08	0,3%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	DK adult	0,07	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	DE general	0,07	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	FI adult	0,07	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	DE women 14-50 yr	0,06	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	ES adult	0,05	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,2%	IT toddler	0,05	0,2%	Potatoes		FRUIT AND TREE NUTS				
	0,1%	FR adult	0,04	0,1%	Potatoes		FRUIT AND TREE NUTS				
	0,1%	IE child	0,03	0,1%	Potatoes		FRUIT AND TREE NUTS				
	0,1%	IT adult	0,03	0,1%	Potatoes		FRUIT AND TREE NUTS				

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Metiram is unlikely to present a public health concern.

Table 6.9- 4: Metiram: NEST calculation based on input value of representative commodity (potatoes)

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Results for children				Results for adults			
No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	No. of commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Potatoes	0 / 0,06	8,6	0,4%	Potatoes	0 / 0,06	1,7
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

Results for children				Results for adults			
No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Potatoes / fried	0 / 0,06	5,2	0,1%	Potatoes / chips	0 / 0,06	0,47
0,8%	Potatoes / dried (flakes)	0 / 0,26	3,3	0,08%	Potatoes / dried (flakes)	0 / 0,26	0,32
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Metiram is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

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Italy, 2010a. Pesticide Residues Overview File (PROFile) on propineb prepared by the rapporteur Member State Italy. Submitted to EFSA on 20 April 2010.

Italy, 2010b. Evaluation report on the setting of MRLs for metiram in plant commodities prepared by the evaluating Member State Italy under Article 8 of Regulation (EC) No 396/2005, 15 November 2010, 174 p.

CA 6.10 Other studies

Report: CA 6.10/1
Schopfer C.,Wenzel M., 2015a
Metiram (BAS 222 F): Transformation products: Assessment of dietary exposure including application of TTC concept (threshold of toxicological concern)
2015/1087922
Guidelines: none
GLP: no

1. OBJECTIVE

As part of the metiram re-registration process (Metiram AIR3 Dossier, 2015), the dietary risk assessment for consumers resulting from the use of metiram has to take into account the actual toxicological burden of the components making up the residue. Therefore, the establishment of the residue definition for risk assessment purposes involves a decision on which transformation products of metiram are of toxicological concern. To achieve robustness of such a residue definition, the data base considered should be reasonably broad. Thus, first, any metiram transformation product identified in a *nature of the residue* study is included (i.e. crop metabolism, rotational crop metabolism, livestock metabolism, high temperature hydrolysis). And second, dietary exposure is assessed for two crop scopes, first scope, the representative uses supported in the AIR3 dossier (grape, potato) and second scope, all uses registered in EU including import tolerances.
All nature of the residue studies taken together, a total of eleven potentially relevant transformation products were identified (M222F004=EBIS, M222F003=EU, M222F002=ETU, M222F001, M222F007, M222F008, M222F013, M222F021, M222F022, M222F023, and glycine).
To allow to reproduce the exposure calculations for each of the metiram transformation products, the detailed steps are provided in a separate document: the present report (CA6.10/1) provides a summary of the relevant data base, derivation of estimated residue levels and result of the calculations for dietary exposure.

2. EVALUATION APPROACH

For an initial evaluation of relevance of transformation products, the estimated human exposure can be compared with a safe threshold derived using the assumptions of the TTC concept and information on the transformation product (i.e. molecular structure and genotoxic potential). To this end, a stepwise approach is envisaged (see decision tree in *Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment, EFSA Journal 2012;10(07):2799*). The threshold of toxicological concern (TTC) is based on the concept that exposure levels can be defined (pending the molecular structure) below which human exposure to the chemical results in "no appreciable risk to human health". In consequence, a transformation product with calculated exposure lower than the corresponding TTC does not need to be considered further. In particular, regarding the exposure threshold of 0.0025 µg/kg bw/day: if the human exposure is estimated to be below this threshold, only absence of certain structural elements (exclusion citeria) has to be confirmed. Alternatively, if the human exposure is estimated to exceed this threshold, any genotoxic concern has to be excluded via (computational) QSAR or (experimental) testing. The transformation products considered in this document were all assessed or tested for genotoxicity. In conclusion, the Cramer class III threshold of 1.5 µg/kg bw/day is considered to represent a safe value covering all toxicological endpoints. In thoses cases, where toxicological information is available for the transformation product, compound specific reference values are derived. The specific derivation can be found in the metiram AIR3 Dossier, section MCA5.8.

A further refined evaluation is to be done for transformation products with calculated exposure exceeding the corresponding TTC or specific reference values. The initial estimations generally result in considerable overestimations of exposure since typically based on various worst case assumptions, in particular in the absence of data from *magnitude of the residue* studies. (In general, all intake for the crop considered is from treated crop, which is an overestimation as market share is well below 100%. For a certain diet all included food items are assumed to have residues at the upper limit which is an overestimation as most crops have residues well below the MRL. Data generation such as crop field trials are conducted to represent the worst case condition as far as residues are concerned.) Therefore, on a case-by-case basis further detailed considerations allow to refine to more realistic exposure scenarios.

3. RESULTS OF EVALUATION

3.1 Initial evaluations

Metiram belongs to the class of dithiocarbamate fungicides. The parent molecule is neither carcinogenic nor genotoxic in vivo. The ADI is 0.03 mg/kg bw/d. An ARfD is not allocated due to low acute toxicity. Based on nature of the residue studies (crop metabolism, rotational crop metabolism, high temperature hydrolysis study, livestock metabolism) the pathway of metiram is well elucidated (metiram AIR3 dossier MCA6.2): desintegration of the parent complex results in dynamic intermediates, their incorporation into the carbon pool of primary metabolism with natural constituents as the terminal residue. All nature of the residue studies taken together, a total of eleven potentially relevant transformation products were identified (M222F004=EBIS, M222F003=EU, M222F002=ETU, M222F001, M222F007, M222F008, M222F013, M222F021, M222F022, M222F023, and glycine). The molecular structure is provided in Table 6.10-5.

For all nine of these transformation products dietary exposure is estimated and expressed in percentage of the corresponding toxicological reference value (see Table 6.10-1 to Table 6.10-4). The exposure calculation model used is EFSA PRIMo vers.2. The residue levels in food commodities is estimated based on available data from *nature and magnitude of the residue studies* (metabolism and residue studies, see section MCA6.2 and MCA6.3). No evaluation of relevance is provided in the context of the present document for two of the listed transformation products: first, glycine is a naturally occurring amino acid. Second, M222F002 (=ETU) is a relevant metabolite and is included in the existing definition of the residue for risk assessment (processed commodities).

For all nine of these transformation products, the indicative exposure calculation is below ot at the corresponding chronic and acute toxicological reference value. Results of the chronic exposure calculations are provided in Table 6.10-1 (scope: representative uses of metiram) and Table 6.10-2 (scope: entirety of metiram uses registered in EU including import tolerances).

Results of the acute exposure calculations are provided in Table 6.10-3 (scope: representative uses of metiram) and Table 6.10-4 (scope: entirety of metiram uses registered in EU including import tolerances).

Table 6.10- 1: Results of chronic exposure assessments (potatoes and grapes, AIR3 dossier)

Metabolite	Dietary exposure [% reference value], most critical diet		Commodity with highest contribution [% reference value]	
EBIS	3.9	FR all population	Table and wine grapes	[3.8]
EU*	0.6	FR all population	Table and wine grapes	[0.6]
EU**	0.1	PT General population	Potatoes	[0.1]
EDA/N-AcEDA	0.0	FR all population	Table and wine grapes	[0.0]
Jaffe`s Base	1.9	FR toddler	Milk and cream	[1.8]
TDIT	0.0	not measurable	not applicable	[0.0]
M222F001	2.8	NL child	Potatoes	[2.8]
M222F008	1.5	FR all population	Table and wine grapes	[1.4]
M222F013	0.0	not measurable	not applicable	[0.0]

EU* using residue estimated based on metabolism data
EU** using residue data obtained in crop field trials (grape, potato, see chapter 2.2)

Table 6.10- 2: Results of chronic exposure assessments (entirety of EU-registered uses*)

Metabolite	Dietary exposure [% reference value], most critical diet		Commodity with highest contribution [% reference value]	
EBIS	8.6	DE child	Pome fruit	[6.1]
EU	1.4	DE child	Pome fruit	[1.0]
EDA/N-AcEDA	0.1	DE child	Pome fruit	[0.1]
Jaffe`s Base	9.1	FR toddler	Milk and cream	[8.7]
TDIT	0.0	IT adult	Lettuce and other salad	[0.0]
M222F001	5.3	WHO Cluster diet B	Tomatoes	[1.4]
M222F008	3.1	DE child	Pome fruit	[2.3]
M222F013	0.1	DK child	Cucurbits – edible peel	[0.0]

* including import tolerances

Table 6.10- 3: Overview: acute exposure assessments (potatoes, grapes, AIR3 dossier)

Metabolite	Commodity with highest contribution [% reference value]	Commodity with 2nd highest contribution [% reference value]	Commodity with 3rd highest contribution [% reference value]
EBIS	17.8 (Table grapes, children)	8.6 (Table grapes, adults)	6.5 (Wine grapes, adults)
EU*	21.4 (Table grapes, children)	10.4 (Table grapes, adults)	7.7 (Wine grapes, adults)
EU**	7.7 (Potatoes, children)	6.7 (Table grapes, children)	3.2 (Table grapes, adults)
EDA/N-AcEDA	0.6 (Table grapes, children)	0.3 (Table grapes, adults)	0.2 (Wine grapes, adults)
Jaffe`s Base	1.9 (Table grapes)	1.7 (Cattle milk and milk products, children)	1.0 (Bovine kidney, children)
TDIT	0.0 (not measurable)	0.0 (not measurable)	0.0 (not measurable)
M222F001	21.5 (Potatoes, children)	4.2 (Potatoes, adults)	0.0 (not measurable)
M222F008	15.2 (Table grapes, children)	7.4 (Table grapes, adults)	5.5 (Wine grapes, adults)
M222F013	0.0 (not measurable)	0.0 (not measurable)	0.0 (not measurable)

EU* using residue estimated based on metabolism data
EU** using residue data obtained in crop field trials (grape, potato, see chapter 2.2)

Table 6.10- 4: Overview: acute exposure assessments (uses registered in EU)

Metabolite	Commodity with highest contribution [% reference value]	Commodity with 2nd highest contribution [% reference value]	Commodity with 3rd highest contribution [% reference value]
EBIS	33.7 (Melons, children)	27.1 (Watermelons, children)	17.8 (Table grapes, children)
EU	73.6 (Scarole, children)	57.0 (Melons, children)	45.9 (Watermelons, children)
EDA/N-AcEDA	1.2 (Melons, children)	1.0 (Watermelons, children)	0.6 (Table grapes, children)
Jaffe`s Base	14.3 (Cattle milk and milk products, children)	12.2 (Bovine kidney, children)	5.5 (Bovine kidney, adults)
TDIT	100.9 (Scarole, children)	31.0 (Lettuce, children)	12.7 (Lettuce, adults)
M222F001	80.4 (Scarole, children)	24.8 (Lettuce, children)	21.5 (Potatoes, children)
M222F008	28.7 (Melons, children)	23.2 (Watermelons, children)	15.2 (Table grapes, children)
M222F013	32.6 (Scarole, children)	14.7 (Melons, children)	11.8 (Watermelons, children)

4. CONCLUSION

In order to assess the contribution of eleven metiram transformation products to the actual toxicological burden, indicative exposure calculations are provided including the TTC approach (*Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment, EFSA Journal 2012;10(07):2799*). Dietary exposure is assessed for two crop scopes, first scope, the representative uses supported in the metiram AIR3 dossier (grape, potato) and second scope, all metiram uses registered in EU including import tolerances.

For nine of these transformation products dietary exposure is estimated and expressed as percentage of the corresponding toxicological reference value or the TTC. The exposure calculation model used is EFSA PRIMo vers.2. The residue levels in food commodities is estimated based on available data from *nature and magnitude of the residue studies* (metabolism and residue studies).

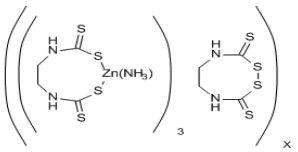
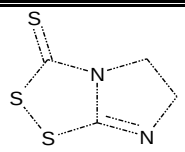
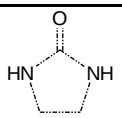
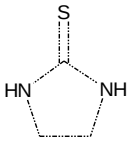
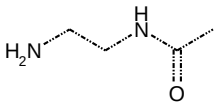
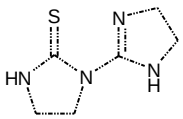
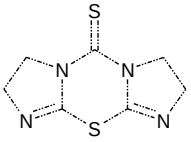
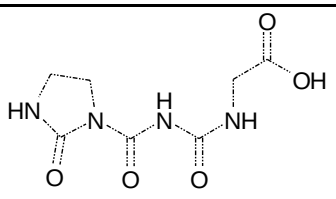
For two of the listed transformation products no evaluation of relevance is provided in the context of the present document: first, glycine is a naturally occurring amino acid. Second, M222F002 (=ETU) is a relevant metabolite and is included in the existing definition of the residue for risk assessment (processed commodities). A detailed dietary exposure assessment is provided as part of the metiram AIR3 dossier (section MCA6.9).

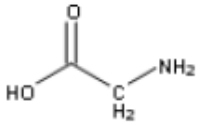
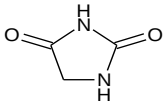
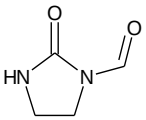
For all of these transformation products, the indicative exposure calculation provide results at or below the corresponding toxicological reference value. In summary, the relevance of nine transformation products of metiram has been assessed (M222F004, M222F003, M222F0023, M222F021, M222F022, M222F007, M222F001, M222F008, M222F013). The results show for each transformation product that its contribution to the overall toxicological burden is insignificant. Therefore no further compound has to be included in the definition of the relevant residue for risk assessment.

In conclusion, this relevance assessment confirms the present established definition of the metiram residue for risk assessment (section MCA6.7). This definition of the residue is robust in that it applies not only to the representative uses supported in the metiram AIR3 dossier, but also to the entirety of metiram uses currently registered in EU including established import tolerances.

5. APPENDIX

Table 6.10- 5: Overview metabolites: occurrence, molecular structure and molecular mass

Parent			
Name	**Occurrence**	**Structure**	**Molecular mass [g/mol]**
Metiram (BAS 222 F)	not relevant		1088.7
Metabolites			
Name	**Occurrence**	**Structure**	**Molecular mass [g/mol]**
M222F004 (EBIS)	crop (lettuce, apple, potato)* goat** poultry***		176.3
M222F003 (EU)	crop (lettuce, apple, potato)* goat** poultry***		86.1
M222F002 (ETU)	crop (lettuce, apple, potato)* goat** poultry***		102.2
M222F023 (EDA)	crop (apple)* goat** poultry***		60.1
M222F021 (N-AcEDA)	crop (apple)* goat** poultry***		102.1
M222F022 (Jaffe`s Base)	crop (apple)* goat** poultry***		170.2
M222F007 (TDIT)	crop (lettuce)*		212.3
M222F001	rotational crop****		230.2

Glycine	crop (apples, potato)* goat** poultry***		75.1
M222F008 (Hydantoin)	crop (apple)* goat** poultry***		100.1
M222F013	crop (lettuce)*		114.1

* 'Metabolism of 14C-Metiram (14C-BAS 222 F) in lettuce', BASF DocID 2009/1049027
'Metiram: Nature of Residues in Apples', BASF DocID 1990/10669
'Metabolism of 14C-Metiram Complex in Potatoes', BASF DocID 1990/10668
** 'Metabolism of 14C-Metiram Complex in Lactating Goats', BASF DocID 1989/10487
*** 'Metabolism of 14C-Metiram Complex in Laying Hens', BASF DocID 1990/5080
**** 'Confined rotational crop study with 14C-BAS 222 F', BASF DocID 2009/1017248

Table 6.10- 6:Transformation products of metiram: molecular weight correction factors

Metabolite	Units[1)]	Total molecular weight[2)]	Molecular weight correction factor[3)]
M222F004 (EBIS)	4	705.2	0.65
M222F003 (EU)	4	344.4	0.32
M222F002 (ETU)	n.a.[4)]	n.a.	n.a.
M222F023 (EDA)	4	240.4	0.22
M222F021 (N-AcEDA)	4	408.4	0.38
M222F022 (Jaffe`s Base)	2	340.4	0.31
M222F007 (TDIT)	2	426.6	0.39
M222F001	2	460.4	0.42
Glycine	n.a.	n.a.	n.a.
M222F008	4	400.4	0.37
M222F013	4	456.4	0.42

1) number of molecules that may potentially be formed from one molecule metiram (= n)
2) n x molecular weight [g/mol]
3) calculated as (n x molecular weight)/1088.7 g/mol)
4) n.a. not applicable Rationale: the transformation product M222F002=ETU is a relevant metabolite and since included in the existing definition of the residue for risk assessment is subject to a dietary risk assessment (see Metiram AIR3 dossier, in preparation). The transformation product glycine is a naturally occurring amino acid. Therefore, in the context of the present document, both for ETU and for glycine, no further evaluation of relevance for the metiram residue definitions is performed.

Table 6.10- 7: Toxicological reference values used for chronic dietary exposure calculations

Metabolite	Reference value [mg/kg bw/d]	Source
EBIS	0.02	AIR3 dossier, MCA 06.09
EU	0.06	AIR3 dossier, MCA 06.09
EDA/N-AcEDA	0.2	AIR3 dossier, MCA 06.09
Jaffe`s Base	0.0015	TTC Cramer class III*
TDIT	0.0015	TTC Cramer class III*
M222F001	0.0015	TTC Cramer class III*
M222F008	0.0015	TTC Cramer class III*
M222F013	0.0015	TTC Cramer class III*

The following reference values were used for the assessment of acute exposure to metiram metabolites:

Table 6.10- 8: Toxicological reference values used for acute dietary exposure calculations

Metabolite	Reference value [mg/kg bw]	Source
EBIS	0.15	AIR3 dossier, MCA 06.09
EU	0.06	AIR3 dossier, MCA 06.09
EDA/N-AcEDA	0.5	AIR3 dossier, MCA 06.09
Jaffe`s Base	0.005	recommended by EFSA PPR*
TDIT	0.005	recommended by EFSA PPR*
M222F001	0.005	recommended by EFSA PPR*
M222F008	0.005	recommended by EFSA PPR*
M222F013	0.005	recommended by EFSA PPR*

* Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment (EFSA Journal 2012;10(07):2799), page 32

CA 6.10.1 Effect on the residue level in pollen and bee products

The objective of these studies would be to determine the residue in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.

So far, for metiram no study for pollen and bee products was conducted as official published guideline for such a study is as-yet not available. Moreover, the representative uses supported in the present dossier, grape and potato are not considered as important for honey production. Metiram is a non-systemic fungicide non-soluble in water. In summary, the dietary risk resulting from the supported uses of metiram is considered negligible.

Tier 1 Summaries of the Supervised Field Residue Trials for the Representative Crops

Potato

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation (common name and content)**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)		
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2), BAS 222 F (by EBDC)
Region	**Central and Northern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
2012/1272625 Ormersheimerhof 4 67227 Frankenthal Germany L120524	VR0589 Marabell	1. 27.03.2012 2. n.a. 3. 21.09.2012	plot-sprayer with boom	0.7	200	1.4	3 01.08.2012	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 22	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Oggersheimer Str. 60 67227 Studernheim Germany L120525	VR0589 Quarta	1. 17.04.2012 2. 15.06.-11.07.2012 3. 24.08.-21.09.2012	plot-sprayer with boom	0.7	200	1.4	3 31.07.2012	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Kings New ham, Rugby Warwickshire CV 23 0JT United Kingdom L120526	VR0589 Markies	1. 21.04.2012 2. 25.07.-20.08.2012 3. 12.10.2012	Pulv-exper boom sprayer	0.56	250	1.4	3 20.09.2012	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 13 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Stradford Road, Banbury Oxfordshire OX 15 6EP United Kingdom L120527	VR0589 Markies	1. 06.05.2012 2. 01.-09.08.2012 3. 19.10.2012	Pulv-exper boom sprayer	0.56	250	1.4	3 04.10.2012	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 15 22	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No.

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2),
Region	**Central and Northern Zone**		BAS 222 F (by EBDC)

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
														L0089/01
2014/1000222 Ormsheimerhof 4 67227 Frankenthal Germany L130118	VR0589 Marabell	1. 11.03.2013 2. n.a. 3. 14.08.2013	mono-cycle plot-sprayer with boom	0.7	200	1.4	3 16.07.2013	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 Oggersheimer Str. 60 67227 Studernheim Germany L130119	VR0589 Alians	1. 18.04.2013 2. 06.06.-11.07.2013 3. 30.08.-12.09.2013	plot-sprayer with boom	0.7	200	1.4	3 08.08.2013	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 La Bonde, 49850 Albnes France (N) L130120	VR0589 Spunta	1. 22.04.2013 2. 20.06.-15.07.2013 3. 15.-22.08.2013	Pulv-exper boom sprayer	0.7	200	1.4	3 29.07.2013	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 22	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 The Meadows Alkerton Oaks Business Park Stratford Road Banbury, OX156EP United Kingdom L130121	VR0589 Harmony	1. 17.04.2013 2. 01.-29.07.2013 3. 20.-30.08.2013	Pulv-exper boom sprayer	0.7	200	1.4	3 09.08.2013	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 6 13 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 Omersheimerhof 4 67227 Frankenthal	VR0589 Musica	1. 21.03.2014 2. n.a. 3. 21.08.2014	Boom sprayer BASF	0.7	200	1.4	3 17.06.2014	46	potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05	0 8 14	metiram (CS_2): BASF method No. L0234/01

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2),
Region	**Central and Northern Zone**		BAS 222 F (by EBDC)

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
Germany L140382			Gloria						potato (tuber)	< 0.056	< 0.1	< 0.05	22	metiram (EBDC): BASF method No. L0089/01
2015/1000321 Oggersheimer Str. 60 67227 Studernheim Germany L140383	VR0589 Toscana	1. 11.04.2014 2. 23.06.-16.07.2014 3. 21.08.-30.09.2014	Boom sprayer BASF Gloria	0.7	200	1.4	3 31.07.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 6 13 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 Akerton Oaks Buisness Park Upton Estate, Stradford Road Banbury, OX 15 6EP United Kingdom L140384	VR0589 Home guard	1. 26.03.2014 2. 19.05.-13.06.2014 3. 07.08.2014	Pulv-exper boom sprayer	0.7	200	1.4	3 16.07.2014	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 13 22	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 De Streek 13 9414 VL Hooghalen The Netherlands L140385	VR0589 Lady Claire	1. 28.04.2014 2. 10.-17.07.2014 3. 28.08.-03.09.2014	Boom sprayer	0.7	200	1.4	2* 14.08.2014	47	potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05	7 14 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01

1) conversion factor from metiram to CS_2 is 1.79

n.a. not applicable

* due to an infection with phytophtora infestans only two applications could be carried out and not all sampling were possible (no 0 DALA sampling)

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Central and Northern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I ETU**	**II EU**	**III EBIS**		
2012/1272625 Ormersheimerhof 4 67227 Frankenthal Germany L120524	VR0589 Marabell	1. 27.03.2012 2. n.a. 3. 21.09.2012	plot-sprayer with boom	0.7	200	1.4	3 01.08.2012	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	0.019 0.022 0.026 0.021	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Oggersheimer Str. 60 67227 Studernheim Germany L120525	VR0589 Quarta	1. 17.04.2012 2. 15.06.-11.07.2012 3. 24.08.-21.09.2012	plot-sprayer with boom	0.7	200	1.4	3 31.07.2012	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Kings New ham, Rugby Warwickshire CV 23 0JT United Kingdom L120526	VR0589 Markies	1. 21.04.2012 2. 25.07.-20.08.2012 3. 12.10.2012	Pulv-exper boom sprayer	0.56	250	1.4	3 20.09.2012	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 13 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Stradford Road, Banbury Oxfordshire OX 15 6EP United Kingdom L120527	VR0589 Markies	1. 06.05.2012 2. 01.-09.08.2012 3. 19.10.2012	Pulv-exper boom sprayer	0.56	250	1.4	3 04.10.2012	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 15 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Central and Northern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I ETU**	**II EU**	**III EBIS**		
2014/1000222 Ormsheimerhof 4 67227 Frankenthal Germany L130118	VR0589 Marabell	1. 11.03.2013 2. n.a. 3. 14.08.2013	mono-cycle plot-sprayer with boom	0.7	200	1.4	3 16.07.2013	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	0.037 0.028 0.038 0.031	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2014/1000222 Oggersheimer Str. 60 67227 Studernheim Germany L130119	VR0589 Alians	1. 18.04.2013 2. 06.06.-11.07.2013 3. 30.08.-12.09.2013	plot-sprayer with boom	0.7	200	1.4	3 08.08.2013	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	0.011 0.020 0.017 0.013	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2014/1000222 La Bonde, 49850 Albnes France (N) L130120	VR0589 Spunta	1. 22.04.2013 2. 20.06.-15.07.2013 3. 15.-22.08.2013	Pulv-exper boom sprayer	0.7	200	1.4	3 29.07.2013	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2014/1000222 The Meadows Alkerton Oaks Business Park Stratford Road Banbury, OX156EP United Kingdom L130121	VR0589 Harmony	1. 17.04.2013 2. 01.-29.07.2013 3. 20.-30.08.2013	Pulv-exper boom sprayer	0.7	200	1.4	3 09.08.2013	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 6 13 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Central and Northern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I ETU**	**II EU**	**III EBIS**		
2015/1000321 Omersheimerhof 4 67227 Frankenthal Germany L140382	VR0589 Musica	1. 21.03.2014 2. n.a. 3. 21.08.2014	Boom sprayer BASF Gloria	0.7	200	1.4	3 17.06.2014	46	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 14 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 Oggersheimer Str. 60 67227 Studernheim Germany L140383	VR0589 Toscana	1. 11.04.2014 2. 23.06.-16.07.2014 3. 21.08.-30.09.2014	Boom sprayer BASF Gloria	0.7	200	1.4	3 31.07.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 6 13 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 Akerton Oaks Buisness Park Upton Estate, Stradford Road Banbury, OX 15 6EP United Kingdom L140384	VR0589 Home guard	1. 26.03.2014 2. 19.05.-13.06.2014 3. 07.08.2014	Pulv-exper boom sprayer	0.7	200	1.4	3 16.07.2014	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 13 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 De Streek 13 9414 VL Hooghalen The Netherlands L140385	VR0589 Lady Claire	1. 28.04.2014 2. 10.-17.07.2014 3. 28.08.-03.09.2014	Boom sprayer	0.7	200	1.4	2* 14.08.2014	47	potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	7 14 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg

* due to an infection with phytophtora infestans only two applications could be carried out and not all sampling were possible (no 0 DALA sampling)

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation (common name and content)**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)		
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2), BAS 222 F (by EBDC)
Region	**Southern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
2012/1272625 Platahos, Imathia, Central Macedonia GR-59032 Greece L120528	VR0589 Agria	1. 04.04.2012 2. 05.-30.05.2012 3. 10.-30.07.2012	boom sprayer AZO	0.47	300	1.4	3 02.07.2012	45-47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 22	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Polymilos, Kozani, West Macedonia GR-50100 Greece L120529	VR0589 Agria	1. 05.05.2012 2. 01.07.-05.08.2012 3. 20.08.-15.09.2012	boom sprayer AZO	0.35	400	1.4	3 03.08.2012	45-47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Entrada de Velez No. 7 Zafarraya Spain L120530	VR0589 Kennebec	1. 24.05.2012 2. n.a. 3. 19.09.2012	boom sprayer Agrar-test	0.56	250	1.4	3 05.09.2012	46	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 6 14 20	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2012/1272625 Hermanos Pinzon No. 22 29700 Velez-Malaga Spain L120531	VR0589 Kennebec	1. 24.05.2012 2. n.a. 3. 26.09.2012	boom sprayer Agrar-test	0.56	250	1.4	3 13.09.2012	46	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 13 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2),
Region	**Southern Zone**		BAS 222 F (by EBDC)

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
2014/1000222 84480 Bonnieux France (S) L130122	VR0589 Jaerla	1. 20.06.2013 2. 15.08.-01.09.2013 3. 24.09.2013	plot-sprayer with boom	0.7	200	1.4	3 10.09.2013	44	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 8 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 Nea Magnisia, Thessaloniki Central Macedonia, GR-57008 Greece L130123	VR0589 Spunta	1. 18.04.2013 2. 01.-20.06.2013 3. 05.-20.07.2013	AZO boom-sprayer	0.7	200	1.4	3 21.06.2013	42-45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 Via Giugni 3 23010 Albosaggia Italy L130124	VR0589 Primura	1. 28.05.2013 2. 25.06.-04.07.2013 3. 16.-23.08.2013	backpack sprayer with boom	0.7	200	1.4	3 02.08.2013	47-48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	0.07 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2014/1000222 Cale Olivio No. 50 14400 Pozoblanco Spain L130125	VR0589 Condor	1. 02.03.2013 2. 22.05.-03.06.2013 3. 03.06.2013	knapsack boom-sprayer	0.7	200	1.4	3 20.06.2013	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 6 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	CS_2, BAS 222 F (by CS_2),
Region	**Southern Zone**		BAS 222 F (by EBDC)

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./h L	**Water L/ha**	**kg a.s./ha**				**CS_2[1]**	**metiram (by CS_2)**	**metiram (by EBDC)**		
2015/1000321 C/San Francisco No 6 14412 Pedrpche Cordoba Spain L140386	VR0589 Carlita	1. 10.02.2014 2. n.a. 3. 02.-09.06.2014	Boom sprayer	0.7	200	1.4	3 19.06.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 57008 Nea Magnisis Greece L140387	VR0589 Jaerla	1. 19.03.2014 2. 05.-25.05.2014 3. 05.-25.06.2014	AZO Boom sprayer	0.7	200	1.4	3 26.05.2014	45/47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 6 15 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 23036 Teglio Italy L140388	VR0589 Kennebeck	1. 24.04.2014 2. 07.-23.07.2014. 3. 11.09.2014	Boom sprayer	0.7	200	1.4	3 28.08.2014	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	0.064 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01
2015/1000321 C/Union Del Iano No 3 18128 Zafarraya Spain L140389	VR0589 Kennebeck	1. 14.05.2014 2. 21.-28.07.2014 3. 18.-25.08.2014	Boom sprayer	0.7	200	1.4	3 04.08.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.056 < 0.056 < 0.056 < 0.056	< 0.1 < 0.1 < 0.1 < 0.1	< 0.05 < 0.05 < 0.05 < 0.05	0 7 14 21	metiram (CS_2): BASF method No. L0234/01 metiram (EBDC): BASF method No. L0089/01

1) conversion factor from metiram to CS_2 is 1.79
n.a. not applicable

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation (common name and content)**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)		
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Southern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I** **ETU**	**II** **EU**	**III** **EBIS**		
2012/1272625 Platahos, Imathia, Central Macedonia GR-59032 Greece L120528	VR0589 Agria	1. 04.04.2012 2. 05.-30.05.2012 3. 10.-30.07.2012	boom sprayer AZO	0.47	300	1.4	3 02.07.2012	45-47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 22	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Polymilos, Kozani, West Macedonia GR-50100 Greece L120529	VR0589 Agria	1. 05.05.2012 2. 01.07.-05.08.2012 3. 20.08.-15.09.2012	boom sprayer AZO	0.35	400	1.4	3 03.08.2012	45-47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Entrada de Velez No. 7 Zafarraya Spain L120530	VR0589 Kennebec	1. 24.05.2012 2. n.a. 3. 19.09.2012	boom sprayer Agrar-test	0.56	250	1.4	3 05.09.2012	46	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 6 14 20	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01
2012/1272625 Hermanos Pinzon No. 22 29700 Velez-Malaga Spain L120531	VR0589 Kennebec	1. 24.05.2012 2. n.a. 3. 26.09.2012	boom sprayer Agrar-test	0.56	250	1.4	3 13.09.2012	46	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 13 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Southern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I ETU**	**II EU**	**III EBIS**		
2014/1000222 84480 Bonnieux France (S) L130122	VR0589 Jaerla	1. 20.06.2013 2. 15.08.-01.09.2013 3. 24.09.2013	plot-sprayer with boom	0.7	200	1.4	3 10.09.2013	44	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 0.011 0.013	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 8 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2014/1000222 Nea Magnisia, Thessaloniki Central Macedonia, GR-57008 Greece L130123	VR0589 Spunta	1. 18.04.2013 2. 01.-20.06.2013 3. 05.-20.07.2013	AZO boom-sprayer	0.7	200	1.4	3 21.06.2013	42-45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2014/1000222 Via Giugni 3 23010 Albosaggia Italy L130124	VR0589 Primura	1. 28.05.2013 2. 25.06.-04.07.2013 3. 16.-23.08.2013	backpack sprayer with boom	0.7	200	1.4	3 02.08.2013	47-48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Southern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
										I	**II**	**III**		
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**ETU**	**EU**	**EBIS**		
2014/1000222 Cale Olivio No. 50 14400 Pozoblanco Spain L130125	VR0589 Condor	1. 02.03.2013 2. 22.05.-03.06.2013 3. 03.06.2013	knapsack boom-sprayer	0.7	200	1.4	3 20.06.2013	45	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 0.018 0.023 0.023	< 0.01 < 0.01 0.010 0.010	< 0.01 < 0.01 < 0.01 < 0.01	0 6 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 C/San Francisco No 6 14412 Pedrpche Cordoba Spain L140386	VR0589 Carlita	1. 10.02.2014 2. n.a. 3. 02.-09.06.2014	Boom sprayer	0.7	200	1.4	3 19.06.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 57008 Nea Magnisis Greece L140387	VR0589 Jaerla	1. 19.03.2014 2. 05.-25.05.2014 3. 05.-25.06.2014	AZO Boom sprayer	0.7	200	1.4	3 26.05.2014	45/47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 6 15 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg

RESIDUE DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)

b

Active substance (common name)	Metiram	**Commercial Product (name)**	Polyram DF, Polyram WG
Crop/crop group:	Potato / Root and Tuber Vegetables	**Producer of commercial product**	BASF SE, Ludwigshafen, Germany
Responsible body for reporting (name, address)	BASF SE, 67056 Ludwigshafen	**Indoor/Glasshouse/Outdoor**	outdoor
Country	Germany	**Other active substance in the formulation**	none
Content of active substance (g/kg or g/L)	700 g/kg (metiram)	**(common name and content)**	
Formulation (e.g. WP)	BAS 222 28 F (WG)	**Residues calculated as:**	ETU, EU, EBIS
Region	**Southern Zone**		

1	2	3	4	5			6	7	8	9			10	11
Report-No. Location (trial no.)	**Commo-dity/ Variety**	**Date of 1. Sowing / planting 2. Flowering 3. Harvest**	**Method of treat-ment**	**Application rate per treatment**			**No of treat-ment(s) and last date**	**Growth stage at last treat. or date**	**Portion analysed**	**Residues (mg/kg parent equiv.)**			**PHI (days)**	**Remarks**
				kg a.s./hL	**Water L/ha**	**kg a.s./ha**				**I** **ETU**	**II** **EU**	**III** **EBIS**		
2015/1000321 23036 Teglio Italy L140388	VR0589 Kennebeck	1. 24.04.2014 2. 07.-23.07.2014 3. 11.09.2014	Boom sprayer	0.7	200	1.4	3 28.08.2014	48	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg
2015/1000321 C/Union Del Iano No 3 18128 Zafarraya Spain L140389	VR0589 Kennebeck	1. 14.05.2014 2. 21.-28.07.2014 3. 18.-25.08.2014	Boom sprayer	0.7	200	1.4	3 04.08.2014	47	potato (tuber) potato (tuber) potato (tuber) potato (tuber)	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01	0 7 14 21	ETU: BASF method No. L0176/01 EU and EBIS: BASF method No. L0233/01 LOQ: 0.01 mg/kg