Environmental Chemistry Method for SYN508210, SYN508211, CSCC210616, CSCD465008, and CSAA798670 in Water (Method GRM023.06A)

Reports:

ECM: Braid S and Hayward, G. (2010). SYN545192 – Analytical Method for the Determination of Residues of SYN508210 and SYN508211 and the Metabolites CSCC210616, CSCD465008, and CSAA798670 in Water. Syngenta Ltd., Jealott's Hill International Research Centre, Bracknell, United Kingdom. Issued February 2010. Unpublished Method No. GRM023.06A (Syngenta Regulatory Document No. GRM023.06A), EPA MRID No 47473348.

Oppilliart, S. (2010). SYN524464 – Validation of the Analytical Method GRM023.06A for the Determination of Residues of SYN508210 and SYN508211 and the Metabolites CSCC210616, CSCD465008,and CSAA798670 IN Water. Syngenta Ltd., Jealott's Hill International Research Centre, Bracknell, United Kingdom. Issued February 2010. Unpublished Method No. GRM023.06A (Syngenta Regulatory Document No. GRM023.06A), EPA MRID No 47473348.

ILV: None

Document No.: MRIDs 47473348 & 47473349

Guideline: USEPA 850.6100

PMRA 8.2.2.3

Statements: The study was conducted in accordance with USEPA FIFRA Good

Laboratory Practice (GLP) Standards, 40 CFR Part 160 (pp. 3, 16). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements

were provided (p. 3).

Classification: This analytical method is classified as Acceptable. However, there has been

no independent laboratory validation submitted accompanying the method. There are two reports provided for the method which appear to convey identical information (MRID Nos. 47473348 and 47473349). Overall mean recoveries for SYN508210 and SYN508211 were less than 90 percent in some instances, but never lower than 83 percent. Overall mean recoveries for CSCC210616 were less than 90 percent in some instances, but never lower than 85 percent. Overall mean recoveries for CSCD465008 were less

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than 90 percent in some instances, but never lower than 87 percent.

PC Code: 122305

Reviewer:
Gabe Rothman
Signature:

Environmental Scientist **Date:** August 29, 2013

Executive Summary

Residues of SYN508210 and, SYN508211 in water may be diluted with methanol and quantified by direct injection by LC-MS/MS, where instrument sensitivity is sufficient. Residues of CSCC210616 in water may be quantified by LC-MS/MS directly without any sample manipulation, where instrument sensitivity is sufficient.

Alternatively, for analysis of SYN508210, SYN508211 and CSCC210616 the water samples are taken through a solid-phase extraction (SPE) procedure using Oasis TM HLB cartridges. The SPE cartridges are washed with water and the anlytes are eluted with acetonitrile. The final volume is adjusted to 5 mL with acetonitrile. Aliquots of the eluate are diluted with ultra pure water, as required.

For the analysis of CSCD465008 and CSAA798670, water samples are acidified then taken through a solid-phase extraction (SPE) procedure using Oasis TM HLB cartridges. The SPE cartridges are washed with water and CSCD465008 and CSAA798670 are eluted with acetonitrile. The column eluates are evaporated to remove the acetonitrile and then redissolved in ultra pure water.

For all analytes, final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). The limit of quantification of the method is 0.05 mg/L for SYN508210, SYN508211, CSCD465008, CSAA798670 and CSCC210616.

I. Recovery Findings

<u>Initial Validation of Method</u>: (Tables 10 -25 from Study Report, MRID No. 47473348)

Table 10: Recovery Data for SYN508210 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 330.2 → 131.1

	SYN	508210 (Transition m	2 330.2 → 131.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	83, 78, 84, 78, 83	81	3	78-84
Groundwater	0.5	88, 84, 83, 83, 83	84	2	83-88
	Overall		83	3	78-88
	0.05	93, 96, 90, 96, 93	94	3	90-96
Surface water	0.5	94, 93, 93, 93, 93	93	1	93-94
	Ove	rall	93	2	90-96
	0.05	86, 78, 89, 86, 89	86	5	78-89
Drinking water	0.5	87, 86, 86, 86, 85	86	1	85-87
	Ove	rall	86	3	78-89

Limit of quantification is defined by the lowest validated fortification level.

Residues in duplicate control samples and reagent blanks were less than 30% of the LOQ.

Table 11: Recovery Data for SYN508210 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 330.2 → 91.1

	SY	N508210 (Transition m	z 330.2 → 91.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	83, 78, 78, 81, 87	81	RSD (%) 5 3 4 2 2 4 5 2	78-87
Groundwater	0.5	87, 83, 83, 81, 85	84		81-87
	Ou	erall	83	4	78-87
	0.05	102, 100, 100, 103, 98	101	2	98-103
Surface water	0.5	93, 95, 93, 96, 96	95	2	93-96
	On	erall	98	4	93-103
	0.05	81, 82, 81, 90, 84	84	5 3 4 2 2 2 4 5	81-90
Drinking water	0.5	88, 87, 85, 88, 87	87	2	85-88
	On	erall	85	4	81-90
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Table 12: Recovery Data for SYN508210 (SPE Procedure) Obtained During Method Validation. Transition m/z 330.2 → 131.1

	SYN	508210 (Transition m	2 330.2 → 131.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	89, 85, 87, 95, 91	89	4	85-95
Groundwater	0.5	82, 83, 82, 81, 81	82	1	81-83
	Ow	rall	86	RSD (%) 4 1 6 2 2 3 2 3 5	81-95
	0.05	87, 84, 83, 86, 85	85	2	83-87
Surface water	0.5	92, 88, 87, 89, 88	89	2	87-92
	Ow	rall	87	3	83-92
	0.05	93, 87, 90, 92, 91	91	2	87-93
Drinking water	0.5	88, 82, 86, 85, 81	84	3	81-88
	Ove	rall	87	5	81-93

Table 13: Recovery Data for SYN508210 (SPE Procedure) Obtained During Method Validation. Transition m/z 330.2 → 91.1

	SY	N508210 (Transition m	/z 330.2 → 91.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	89, 92, 91, 93, 88	91	2	88-93
Groundwater	0.5	82, 79, 82, 80, 79	81	2	79-82
	Ow	rall	86	RSD (%) 2 2 7 3 2 3 4 3 7	79-93
	0.05	87, 83, 89, 84, 88	86	3	83-89
Surface water	0.5	91, 88, 88, 88, 89	89	2	88-91
	Ow	rall	88	3	83-91
	0.05	96, 92, 89, 96, 98	94	4	89-98
Drinking water	0.5	87, 84, 86, 83, 80	84	3	80-87
	Ow	rall	89	7	80-98

Table 14: Recovery Data for SYN508211 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 330.2 → 131.1

	SYN	508211 (Transition m	z 330.2 → 131.1)	(
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	81, 83, 76, 86, 83	Mean (%) RSD (%) 82 4 85 2 83 3 92 4 92 2 92 3 88 4 87 1	76-86	
Groundwater	0.05 81, 83, 76, 86, 83 82 andwater 0.5 85, 87, 83, 83, 84 85 Overall 83 0.05 94, 92, 92, 86, 96 92	2	83-87		
	Ove	Overall		3	76-87
	0.05	94, 92, 92, 86, 96	92	4 NO NO 10 TO	86-96
Surface water	0.5	92, 91, 93, 90, 94	92	2	90-94
	Ove	rall	92	3	86-96
	0.05	90, 93, 89, 84, 88	88	4	84-93
Drinking water	0.5	88, 88, 87, 86, 85	87	1	85-88
	Ove	rall	88	3	84-93

Table 15: Recovery Data for SYN508211 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 330.2 → 91.1

	SYN	508211 (Transition m	$(z 330.2 \rightarrow 91.1)$		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	91, 89, 85, 88, 98	91, 89, 85, 88, 98 90 89, 86, 85, 84, 85 86 II 88 96, 105, 91, 91, 97 96 90, 90, 89, 93, 90 91 II 93 92, 90, 86, 91, 100 92 87, 89, 90, 88, 89 89	6	85-98
Groundwater	0.5	89, 86, 85, 84, 85	86	2	84-89
	Overall		88	5	84-98
Surface water	0.05	96, 105, 91, 91, 97	96	6	91-105
Surface water	0.5	90, 90, 89, 93, 90	91	2	89-93
	One	rall	93	5	89-105
	0.05	92, 90, 86, 91, 100	92	5	86-100
Drinking water	0.5	87, 89, 90, 88, 89	89	1	87-90
	Ove	rall	90	4	86-100

Table 16: Recovery Data for SYN508211 (SPE Procedure) Obtained During Method Validation. Transition m/z 330.2 → 131.1

	SYN	508211 (Transition m	z 330.2 → 131.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	87, 91, 89, 91, 94	90	Ì	87-94
Groundwater	0.5	80, 80, 80, 79, 79	80	1	79-80
	Overall		85	7	79-94
	0.05	80, 80, 80, 79, 79 80	3	82-89	
Surface water	0.5	91, 88, 88, 88, 88	89	2	88-91
	One	rall	87	3	82-91
	0.05	91, 92, 86, 91, 88	90	3	86-92
Drinking water	0.5	87, 83, 85, 85, 81	84	3	81-87
	One	rall	87	4	81-92

Table 17: Recovery Data for SYN508211 (SPE Procedure) Obtained During Method Validation. Transition m/z 330.2 → 91.1

	SYN	N508211 (Transition n	v⁄z 330.2 → 91.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	94, 93, 91, 93, 88	92	3	88-94
Groundwater	0.5	82, 81, 81, 80, 78	80	2	78-82
	Ove	rall	86		78-94
	0.05	91, 88, 87, 85, 83	87	3	83-91
Surface water	0.5	90, 86, 86, 88, 89	88	2	86-90
	Ove	rall	87	3	83-91
	0.05	93, 93, 94, 92, 91	93	1	91-94
Drinking water	0.5	86, 82, 85, 84, 79	83	3	79-86
	Ove	rall	88	6	79-94

Table 18: Recovery Data for CSCC210616 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 176.0 → 136.1

	csc	C210616 (Transition m/	2 176.0 → 136.1)	
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	103, 113, 102, 97, 102	103	6	97-113
Groundwater	0.5	107, 103, 61, 91, 91	90	20	61 - 107
Crotmawater	0.5	96, 96, 96, 96, 94	95	1	94-96
	Overall		96	12	61-113
	0.05	99, 99, 107, 97, 102	101	4	97-107
Surface water	0.5	96, 97, 93, 79, 86	90	8	79-97
	O	erall	96	8	79-107
1000	0.05	94, 92, 89, 97, 98	94	4	89-98
Drinking water	0.5	98, 97, 95, 96, 95	96	1	95-98
	O	erall	95	3	89-98

For groundwater, a second series was performed only for the recoveries at 10 LOQ as the first one was invalidated for the transition m/z 176.0 \rightarrow 156.1. Therefore there are two sets of data for CSCC210616 at 10 LOQ for the transition m/z 176.0 \rightarrow 136.1.

Limit of quantification is defined by the lowest validated fortification level.

Residues in duplicate control samples and reagent blanks were less than 30% of the LOQ.

Table 19: Recovery Data for CSCC210616 (Direct Injection Procedure)
Obtained During Method Validation. Transition m/z 176.0 → 156.1

	CSC	C210616 (Transition m/	2 176.0 → 156.1)	
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	107, 111, 100, 103, 95	103	6	95-111
Groundwater	0.5	94, 100, 99, 97, 97	98	2	94-100
	O)	erall	100	5	94-111
	0.05	101, 108, 96, 99, 107	102	5	96-108
Surface water	0.5	96, 97, 96, 80, 87	91	8	80-97
	O)	erall	97	9	80-108
	0.05	97, 97, 89, 92, 96	94	4	89-97
Drinking water	0.5	96, 97, 98, 97, 96	97	1	96-98
	Ov	erall	95	3	89-98

Table 20: Recovery Data for CSCC210616 (SPE Procedure) Obtained During Method Validation. Transition m/z 176.0 → 136.1

	CSC	C210616 (Transition m	z 176.0 → 136.1)	
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
	0.05	91, 75, 76, 73, 69	77	11	69-91
Groundwater	0.5	94, 88, 91, 97, 92	92	4	88-97
	Overall		85	12	69-97
	0.05	106, 100, 99, 95, 94	99	5	94-106
Surface water	0.5	93, 82, 80, 75, 78	82	9	75-93
	Ove	rall	90	12	75-106
	0.05	102, 91, 97, 99, 102	98	5	91-102
Drinking water	0.5	93, 99, 95, 101, 98	97	3	93-101
	Ove	rall	98	4	91-102

Table 21: Recovery Data for CSCC210616 (SPE Procedure) Obtained During Method Validation. Transition m/z 176.0 → 156.1

	csc	C210616 (Transition m/	2 176.0 → 156.1)	
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	104, 99, 96, 104, 113	103	6	96-113
Groundwater	0.5	87, 93, 90, 94, 92	91	3	87-94
	Overall		97	S	87-113
	0.05	105, 106, 85, 76, 101	95	14	76-106
Surface water	0.5	83, 79, 77, 64, 80	77	10	64-83
	Oil	erall	36	16	64-106
	0.05	95, 118, 99, 103, 91	101	10	91-118
Drinking water	0.5	89, 101, 96, 102, 100	98	6	89-102
	Ov	erall	99	8	89-118

Table 22: Recovery Data for CSCD465008 (SPE Procedure) Obtained During Method Validation. Transition m/z 161.0 → 141.0

	CSC	D465008 (Transition m/s	2 161.0 → 141.0)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	91, 91, 90, 87, 98	92	4	87-98
	0.5	94, 94, 93, 96, 103	96	4	93-103
	Overall		94	5	87-103
Surface water	0.05	90, 87, 87, 96, 81	88	6	81-96
	0.5	85, 85, 93, 85, 82	86	5	82-93
	Overall		87	5	81-96
Drinking water	0.05	96, 108, 102, 96, 102	101	5	96-108
	0.5	98, 96, 98, 97, 100	98	1	96-100
	Overall		99	4	96-108

Table 23: Recovery Data for CSCD465008 (SPE Procedure) Obtained During Method Validation. Transition m/z 161.0 → 65.9

	CS	CD465008 (Transition m/	161.0 → 65.9)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	73, 74, 89, 81, 101	84	14	73-101
	0.5	93, 91, 92, 95, 99	94	3	91-99
	Overall		89	11	73-101
Surface water	0.05	87, 91, 89, 93, 88	90	3	87-93
	0.5	87, 87, 90, 86, 79	86	5	79-90
	Overail		88	4	79-93
Drinking water	0.05	100, 107, 118, 105, 106	107	6	100-118
	0.5	94, 98, 103, 99, 99	99	3	94-103
	Overali		103	ő	94-118

Table 24: Recovery Data for CSAA798670 (SPE Procedure) Obtained During Method Validation. Transition m/z 175.0 → 91.1

	CSA	A798670 (Transition m	\sqrt{z} 175.0 \rightarrow 91.1)		
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	83, 83, 84, 88, 90	86	4	83-90
	0.5	93, 94, 91, 98, 102	96	5	91-102
	Overall		91	7	83-102
Surface water	0.05	89, 89, 89, 95, 84	89	4	84-95
	0.5	90, 91, 98, 89, 89	91	4	89-98
	Overall		90	4	84-98
Drinking water	0.05	92, 98, 85, 94, 95	93	5	85-98
	0.5	95, 100, 97, 98, 100	98	2	95-100
	Overall		95	5	85-100

Table 25: Recovery Data for CSAA798670 (SPE Procedure) Obtained During Method Validation. Transition m/z 175.0 → 111.1

	CSA	A798670 (Transition m	z 175.0 → 111.1)	
Matrix	Fortification Level (µg/L)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Groundwater	0.05	79, 83, 83, 89, 81	83	4	79-89
	0.5	95, 99, 100, 102, 106	100	4	95-106
	Overall		92	11	79-106
Surface water	0.05	89, 90, 89, 94, 84	89	4	84-94
	0.5	89, 87, 98, 90, 89	91	4	87-98
	Overall		90	4	84-98
Drinking water	0.05	88, 98, 93, 95, 92	93	4	88-98
	0.5	102, 100, 103, 97, 101	101	2	97-103
	Overall		97	5	88-103

II. Method Characteristics

Specificity

LC-MS/MS is a highly specific detection technique and therefore a further confirmatory technique is not required. The method includes a primary and a confirmatory MS/MS transition, both of which have been validated for representative water samples.

Linearity

The response of the LC-MS/MS instrument was shown to be linear for:

- SYN508210 and SYN508211 at concentrations ranging from 0.0125 to 0.5 μg/L (equivalent to 0.625 to 25 pg of SYN508210 and SYN508211 injected on to the column, based on a 50 μL injection)
- CSCC210616 at concentrations ranging from 0.025 to 1 μg/L (equivalent to 1.25 to 50 pg of CSCC210616 injected on to the column, based on a 50 μL injection)
- CSCD465008 and CSAA798670 at concentrations ranging from 1.25 to 50 μg/L (equivalent to 12.5 to 500 pg for CSCD465008 and CSAA798670 injected on to the column, based on a 10 μL injection),

Accuracy and Precision

Acceptable mean recoveries of between 70% and 110% with a relative standard deviationless than 20% were found on all matrices tested for each transitions:

- the m/z 330.2 \rightarrow 131.1 and m/z 330.2 \rightarrow 91.1 for SYN508210 and SYN508211,
- the m/z $176.0 \rightarrow 136.1$ and m/z $176.0 \rightarrow 156.1$ for CSCC210616,
- the m/z $161.0 \rightarrow 141.0$ and m/z $161.0 \rightarrow 65.9$ for CSCD465008,
- the m/z $175.0 \rightarrow 91.1$ and m/z $175.0 \rightarrow 111.1$ for CSAA798670.

Limit of Quantification

The limit of quantification (LOQ) of the analytical method in water was established at $0.05~\mu g/L$ for SYN508210 and SYN508211 and its degradates CSCC210616, CSCD465008 and CSAA798670.

III. Method Deficiencies and Reviewer's Comments

1. There has been no independent laboratory validation submitted accompanying the method. There are two reports provided for the method which appear to convey identical information (MRID Nos. 47473348 and 47473349).

- 2. Overall mean recoveries of SYN508210 from municipal drinking water and ground water were less than 90 percent in all cases, but always greater than 83 percent in the initial validation of the method. In surface water, overall mean recoveries of SYN508210 were always above 90 percent except for transitions m/z = 330/131 and m/z = 330/91 for the SPE method. However, overall mean recoveries were always above 87 percent.
- 3. Overall mean recoveries of SYN508211 from ground water were less than 90 percent in all cases, but always greater than 83 percent in the initial validation of the method. In surface water, overall mean recoveries of SYN508211 were always above 90 percent except for transitions m/z = 330/131 and m/z = 330/91 for the SPE method. However, overall mean recoveries were always above 87 percent. In drinking water, overall mean recoveries of SYN508211 were always above 90 percent except for transitions m/z = 330/91 for the direct injection method. However, overall mean recoveries were always above 87 percent.
- 4. Overall mean recoveries of CSCC210616 from ground water were always above 90 percent except for transition m/z = 176/136 for the SPE method. However, in these instances, overall mean recoveries were always above 87 percent. In drinking water, overall mean recoveries of CSCC210616 were always above 90 percent except for transitions m/z = 330/91 for the SPE method. However, overall mean recoveries were always above 85 percent.
- Overall mean recoveries of CSCD465008 from surface water were less than 90 percent in all cases, but always greater than 87 percent in the initial validation of the method. In ground water, overall mean recoveries of CSCD465008 were always above 90 percent except for transitions m/z = 161/66 for the SPE method. However, overall mean recoveries were always above 89 percent.

IV. References

- 1. Luxon S G (1992): Hazards in the Chemical Laboratory 5th Edition. The Royal Society of Chemistry. Thomas Graham House, The Science Park, Cambridge CB4 4WF, UK. ISBN 0-85186-229-2.
- 2. Cardone M J, Palermo P J and Sybrand L B (1980): Potential error in single point ratio calculations based on linear calibration curves with a significant intercept. Anal.Chem., 52 pp 1187-1191
- 3. Oppilliart S. (2009), Eurofins ADME Bioanalyses Validation Report TK0009674-REG SYN524464 Validation of the Analytical Method GRM023.06A for the Determination of Residues of SYN508210 and SYN508211 and the Metabolites CSCC210616, CSCD465008 and CSAA798670 in Water.