CRL for Cereals and Feedingstuff
National Food Institute
Danish Technical University

Validation Report

Determination of pesticide residues in cereals by LC-MS/MS

Internal method no. FP086.1

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1. Introduction

This report describes the validation of 51 pesticide residues in cereals, internal method no. FP086 - ’Determination of pesticide residues in fruit, vegetables and cereals by LC-MS/MS’. The validated pesticides are ionised both by positive and negative electrospray. The method is a multiresidue method, which is quick and easy, due to the low amount of sample preparation.

2. Principle of analysis

The sample was milled and homogenised. 3 g of sample was weighed and added 7 g of water. The sample was left for about 30 min. The sample was then added a mixture of methanol-ammoniumacetat-acetic acid and extracted by ultrasonication for 30 min. Extraction was followed by centrifugation and the supernatant filtered into HPLC vials. The pesticide residues were separated on a reversed-phase column and detected by tandem mass spectrometry (MS/MS) by electrospray (ESI). The validation includes pesticides determined with both positive and negative ESI. $^{13}C_6$-carbaryl was used as internal standard for quantification. All pesticides were detected in the multiple reaction monitoring mode (MRM). For each pesticide precursor ion and 2 product ions (where possible) were determined, one product ion for quantification and one for qualification.

The MRM transitions for the pesticides and degradation products sought validated are given in appendix 1.

3. Validation design

The method was validated on wheat. The recovery tests were all on organic grown wheat flour. In total, 98 pesticides and degradations products were included in the validation (appendix 1). The pesticides were divided into two standard mixtures, one for the ESI positive ionisation and one for the ESI negative ionisation. It was decided not to measure both positive and negative ionisation in the same run, because the MS/MS system might loose sensitivity when changing from positive to negative in the same run.

Every recovery test was performed as double determinations at three concentration levels, 6 samples and 1 blank, in total 7 samples. This was repeated four times. The tests were done on different days by two different technicians.

Table 1. Validation design, spike levels and matrices

Experiment	0 mg/kg	0.02 mg/kg		0.04 mg/kg		0.2 mg/kg	
1	x	x	x	x	x	x	x
2	x	x	x	x	x	x	x
3	x	x	x	x	x	x	x
4	x	x	x	x	x	x	x

4. Chromatogrammes and calibration curves

The MRM detection of the pesticide residues was divided into 7 retention time windows, partly overlapping. Examples of chromatograms are given in Figure 1.

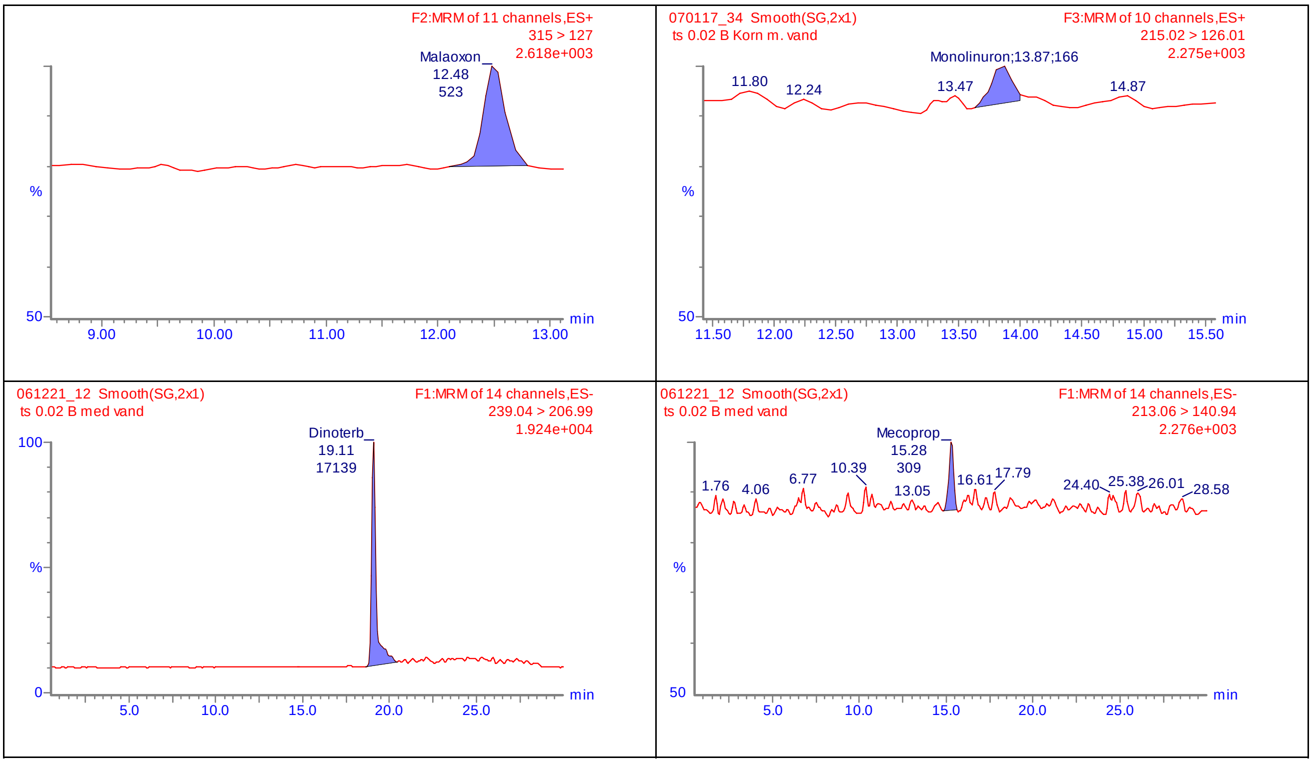

Figure 1. Chromatograms of malaoxon, monolinuron, dinoterb and mecoprop at spiking level 0.02 mg/kg.

Five-point matrix-matched calibration curves were used for quantification. The concentrations were 0.0015, 0.003, 0.01, 0.025 and 0.050 µg/ml. The quantification was performed from the mean of two calibration curves bracketing the samples. $^{13}C_6$-carbaryl was used as internal standard. Examples of calibration curves are given in Figure 2.

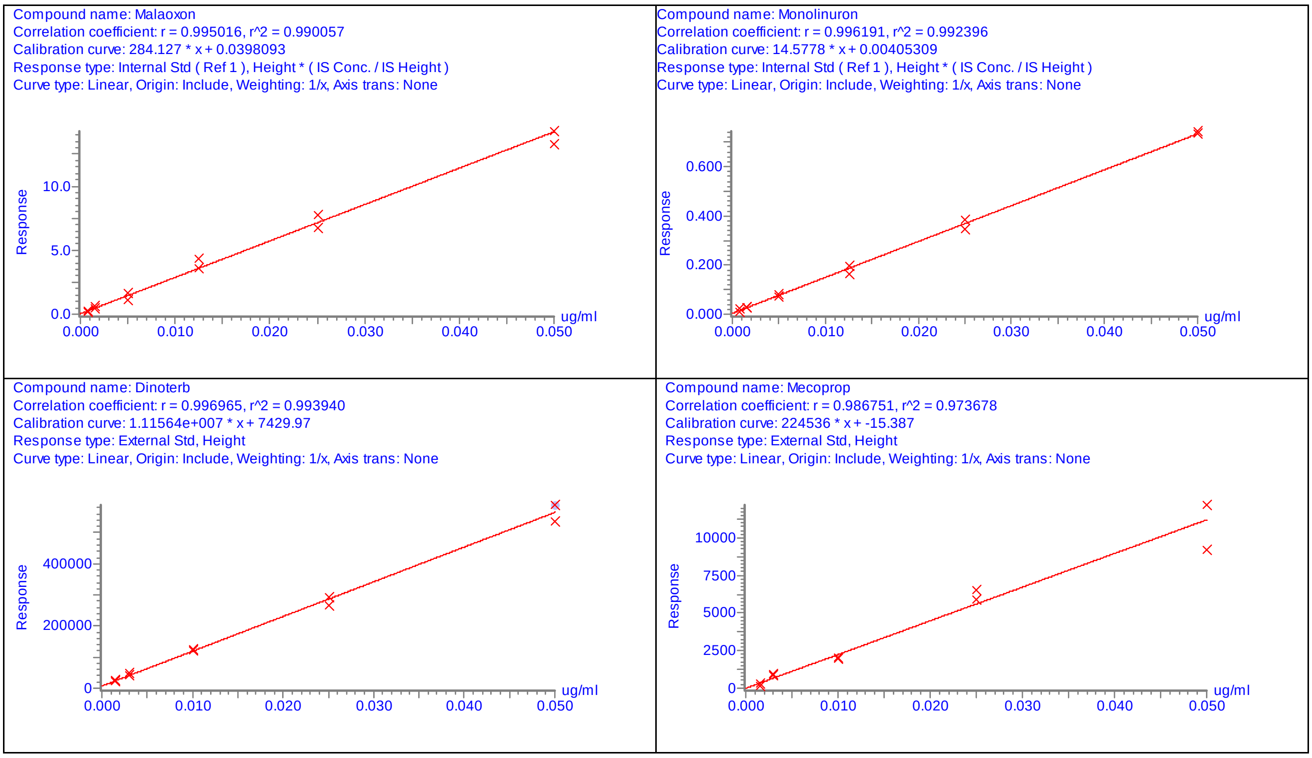

Figure 2. Examples of calibration curves for malaoxon, monolinuron, dinoterb and mecoprop (concentrations from 0.0015-0.05µg/ml)

5. Precision – Repeatability and reproducibility

Repeatability and in-house reproducibility were calculated for all pesticides and degradation products on all three spiking levels.

Repeatability is given as the relative standard deviation on the result from two or more analysis at the same sample, done by the same technician, on the same instrument and within a short period of time. Repeatability in this validation was calculated from the double determinations.

In-house reproducibility is the relative standard deviation on the result from two or more analysis performed on the same sample but by different technicians and within a larger period of time. Reproducibility includes the variation between double determination and variations between the different series of analysis.

Repeatability and reproducibility were calculated as given in ISO 5725-2[1].

Appendix 2 shows the relative repeatability and the in-house reproducibility for the validated pesticides and degradation products.

6. Accuracy – Recovery.

The accuracy was determined by recovery, samples were spiked at three concentration levels. In appendix 2 recovery, repeatability, reproducibility and limit of detection (LOD) are given for the validated pesticides and degradation products.

Recoveries may be seen in appendix 2.

7. Criteria to accept of validation results

For the pesticides to be accepted as validated the following criteria for precision and accuracy must to be fulfilled:

1. The relative standard deviation of the repeatability and reproducibility must be less than or equal to the standard deviation proposed by Horwitz[2].
2. The average relative recovery must be between 70 and 110%[3].

If the above mentioned criteria have been meet, the detection limits has been calculated.

8. Limit of detection, LOD

Detection limits (LOD) was calculated from the results at the lowest accepted spike level, as 3 times the standard deviation (absolute recovery). The detection limits are given in appendix 2.

9. Selectivity and specificity

LC-MS/MS is a highly selective detector, and thereby highly specific. For quantification of the pesticide residues a secondary product ion was used. Transitions are given in appendix 1. First transition was used for quantification, whereas second transition was used for qualification.

10. Results

The LC-MS/MS method for the determination of pesticide residues in cereals has been validated for 51 pesticides and degradation products. The method was based on methanol-ammoniumiumacetat-acetic acid extraction by ultrasonication. For 40 pesticides the ionization was done by ESI in the positive mode, and for 11 pesticides the ionization was ESI in the negative mode. An overview is given below. It should be mentioned that it was not possible to distinguish between dichlorprop and dichlorprop-P, nor was it possible to distinguish between mecoprop and mecoprop-P. Therefore these compounds are only counted for one.

The relative repeatability (RSD_r) and reproducibility (RSD_R) varied between 10>30%, however most of the values were around 20%. In general, the repeatability's and reproducibility's at the lowest spike level 0.02 mg/kg were higher than at higher spike levels (0.04 and 0.2 mg/kg). Some pesticides had reproducibility >30% and one explanation may be that the sensitivity of the instrument fluctuated throughout the analytical series, and that this was not completely compensated for by the use of internal standard. Standard addition would properly improve the fluctuation but for a high number of samples to be analysed by this method this will not be possible. However, it should be considered for samples with exceedances of the MRL. Moreover, it may be seen that the results of the validation were much better for ESI negative compounds. This are properly because the mass spectrometer with this method only analysed few compounds in the negative mode (13 pesticides), while in the positive mode it analysed 86 pesticides. The more compound to analyse the lesser time instrument has to acquire data for each compound. The problem could be overcome by dividing the compounds into more standard solution, however more standard solution will increase the time of analysis per sample.

For most of the pesticides the recovery were in the range of 70-110% for all three concentration levels (0.02mg/kg, 0.04 mg/kg and 0.2 mg/kg), but for some pesticide at one of the concentration levels the range were in the range 57-128% and for methacrifos and MCPA, the recoveries were 146 and 148% respectively. In general, the recoveries are not very good, which might be due to the low amount of sample, i.e. 3 gram. Furthermore dry matrices like wheat flour may be difficult matrices in pesticide residue analysis, due to larger matrix effect. Previous experiments (not published) have shown that there might be a connection between the time the samples are stored in the refrigerator or at room temperature before LC-MS/MS detection (and recovery). Therefore it is recommended that 1) The time where the samples are not frozen should be minimised; 2) That time from extraction to transfer to vials is as short as possible and 3) That samples either are analysed directly or stored in freezer until analysis. Moreover many of the pesticides sought validated showed weak response on the LC-MS/MS and were therefore not detectable in the diluted extract (no concentration in the sample preparation). Furthermore, many of the GC-troublesome pesticides and the non-polar pesticides were not extracted by the polar extraction solvent, and thereby giving poor recoveries.

The detection limits were in the range 0.006 mg/kg - 0.135 mg/kg with a median at 0.02 mg/kg. The lowest calibration level (LCL) was 0.0015µg/ml corresponding to LOD at 0.006 mg/kg. However, the method need to be optimized if use for control of MRL in baby foods.

The pesticides which were validated in ESI- and ESI+ as well as the pesticides that were not accepted are listed in Table 2. For the latter, further work will be done to include the method.

Table 2. Pesticides validated or not accepted.

ESI-, Validated (11 pesticides)

2-naphtoxy acetic acid
2,4-D
4-Chlorphenoxyacetic acid
Bentazone
Bromoxynil
Dichlorprop
Dinoterb
DNOC
MCPA
Mecoprop
Thifensulfuron-methyl

Not accepted (2 pesticides)

Malein hydrazide
Triforine (might be analysed in the posivive mode)

ESI+, Validated (40 pesticides)

Acetimiprid
Azimsulfuron
Bitertanol
Bupirimate
Buprofezin
Clethodim
Clomazone
Demeton-S-methyl
Demeton-S-methyl sulfoxid
Demeton-S-sulfon
Dimethomorph
Ethoxyquin
Fenazaquin
Fluazafop-p-buthyl
Fluoxastrobin
Iodosulfuron-methyl
Iprovalicarb
Isoproturon
Malaoxon
Methalaxyl-M
Methacrifos
Methiocab sulfoxid
Methiocarb sulfon
Metsulfuron-methyl
Monocrotophos
Monolinuron
Ofurace
Omethoate
Oxycarboxim
Pendimethalin
Pirimicarb
Propamocarb
Pymetrozine
Pyraclostrobin
Pyridaben
Pyridaphenthion
Pyridate
Pyrimethanil
Spiroxamin
Tebufenpyrad

Not validated (46 pesticides)

Amitrole (Aminotriazole)
Azocyclotin
Cinidon-ethyl
Clodinafoppropargyl
Clopyralid
Cyazofamid
Cycloxydim
Cyhalofop-buthyl
Cyromazine
Dichlofenthion
Diethofencarb
Epoxyconazole
Fenamiphos
Floroxypur
Fluazifop-p-buthyl
Flumioxazin
Fluroxypyr
Flusilazole
Flutolanil
Hexaconazole
Hexythiazox
Imidacloprid
Jodfenphos
Lufenuron
Mepanipyrim
Metribuzin
Molinate
Nuarimol
Oxadixyl
Phosmet
Picolinafen
Propargite
Prothioconazole
Pyraflufen-ethyl
Pyriproxyfen
Resmethrin
Rimsulfuron
Tebufenozide
Tetraconazole
Thiodicarb
Triallate
Triasulfuron
Tribenuron-methyl
Tridemorph
Triflumuron
Trinexepac-ethyl

11. Conclusions and remarks

In conclusion, 51 of 98 pesticides and degradation products were validated. In present method it is not possible to distinguish between dichlorprop and dichlorprop-P. Likewise it was not possible to distinguish between mecoprop and mecoprop-P. It should be pointed out that because this method is very quick and easy, due to low sample preparation and clean up, however the pesticides and degradation products not included in present validation may be tried to be included in the future expansions of the method along with new pesticides. Due to the relatively few pesticides validated, the work with the method will continue.

12. References

1. ISO 5725-2:1994. Accuracy (trueness and precision) of measurement methods and results – Part 2. Basic method for the determination of repeatability and reproducibility of standard measurement method. First edition. December 1994.
2. W. Horwitz, *Anal. Chem.*, 1982; **54**, 67A.
3. Quality Control Procedures for Pesticide Residue Analysis, Document No SANCO/10232/2006, 24/March/2006, European Commission, Brussels, 2006.

13. Appendices

Appendix 1. MRM transitions for the pesticides sought validated.

Pesticide/Metabolite	Molecular formula	Ionisation, ESI +/-	Molecular ion	Precursor	Transition 1			Transition 2		
					Product	Cone voltage (V)	Collision energy (eV)	Product	Cone voltage (V)	Collision energy (eV)
2,4-D	$C_8H_6Cl_2O_3$	ESI-	[M-H]-	219	161	9	13	125	10	26
2-Naphtoxy acetic acid	$C_{12}H_{10}O_3$	ESI-	[M-H]-	201	143	45	26	115	45	26
4-Chlorphenoxyacetic acid	$C_8H_7ClO_3$	ESI-	[M-H]-	185	127	24	17	123	24	19
Acetamiprid	$C_{10}H_{11}ClN_4$	ESI +	[M+H]+	223	126	27	20	90	27	35
Amitrole (Aminotriazole)	$C_2H_4N_4$	ESI+	[M+H]+	85	57	15	15	58	15	17
Azimsulfuron	$C_{13}H_{16}N_{10}O_5S$	ESI+	[M+H]+	425	182	52	11	156	52	25
Azocyclotin	$C_{20}H_{35}N_3Sn$	ESI +	[M+NH4]+	455	209	31	29	81	31	35
Bentazone	$C_{10}H_{12}N_2O_3S$	ESI-	[M-H]-	239	132	38	29	196	38	21
Bitertanol	$C_{20}H_{23}N_3O_2$	ESI+	[M+H]+	338	99	31	17	70	31	17
Bromoxynil	$C_7H_3Br_2NO$	ESI-	[M-H]-	274	79	10	11			
Bupirimat	$C_{13}H_{24}N_4O_3S$	ESI +	[M+H]+	317	166	27	23	108	25	25
Buprofenzin	$C_{16}H_{23}N_3OS$	ESI+	[M+H]+	306	201	10	11	106	10	23
Cinidon-ethyl	$C_{19}H_{17}Cl_2NO_4$	ESI+	[M+NH4]+	411	348	10	11	107	10	33
Clethodim	$C_{17}H_{26}ClNO_3S$	ESI+	[M+H]+	360	164	45	17	136	45	33
Clodinafoppropargyl	$C_{17}H_{13}ClFNO_4$	ESI+	[M+H]+	350	266	38	17	91	38	20
Clomazone	$C_{12}H_{14}ClNO_2$	ESI+	[M+H]+	240	125	10	29	89	10	39
Clopyralid	$C_6H_3Cl_2NO_2$	ESI+	[M+H]+	192	146	55	23	110	52	32
Cyazofamid	$C_{13}H_{13}ClN_4O_2S$	ESI+	[M+H]+	325	108	52	13	261	52	9
Cycloxydim	$C_{17}H_{27}NO_3S$	ESI+	[M+H]+	326	280	10	11	180	10	22
Cyhalofop-butyl	$C_{20}H_{20}FNO_4$	ESI+	[M+NH4]+	375	256	38	17	120	38	30
Cyromazine	$C_6H_{10}N_6$	ESI+	[M+H]+	167	85	17	17	125	17	15
Dementon-S-methyl sulfoxid	$C_6H_{15}O_4PS_2$	ESI +	[M+H]+	247	169	33	10	127	18	25
Demeton-S-methyl	$C_6H_{15}O_3PS_2$	ESI +	[M+H]+	231	89	21	5	61	20	25
Demeton-S-methyl sulfon	$C_6H_{15}O_5PS_2$	ESI +	[M+H]+	263	169	55	15	127	45	28
Dichlofenthion	$C_{10}H_{13}Cl_2O_3PS$	ESI+	[M+H]+	315	259	55	17	115	52	45
Dichlorprop (/Dichlorprop-P)	$C_9H_8Cl_2O_3$	ESI-	[M-H]-	233	161	52	17	125	52	26
Diethofencarb	$C_{14}H_{21}NO_4$	ESI +	[M+H]+	268	226	51	15	180	33	17
Dimethomorph	$C_{21}H_{22}ClNO_4$	ESI +	[M+H]+	388	301	45	20	165	23	30
Dinoterb	$C_{10}H_{12}N_2O_5$	ESI-	[M-H]-	239	207	31	23	177	31	25

Pesticide/Metabolite	Molecular formula	Ionisation, ESI +/-	Molecular ion	Precursor	Transition 1			Transition 2		
					Product	Cone voltage (V)	Collision energy (eV)	Product	Cone voltage (V)	Collision energy (eV)
DNOC	$C_7H_6N_2O_5$	ESI-	[M-H]-	197	137	10	17	109	10	20
Epoxiconazole	$C_{17}H_{13}ClFN_3O$	ESI+	[M+H]+	330	121	45	23	91	45	41
Ethoxyquin	$C_{14}H_{19}NO$	ESI+	[M+H]+	218	148	38	25	174	38	26
Fenamiphos	$C_{13}H_{22}NO_3PS$	ESI+	[M+H]+	304	217	31	23	202	31	33
Fenazaquin	$C_{20}H_{22}N_2O$	ESI+	[M+H]+	307	161	55	17	131	52	14
Fluazifop-p-butyl	$C_{19}H_{20}F_3NO_4$	ESI+	[M+H]+	384	282	38	17	91	38	32
Flumioxazin	$C_{19}H_{15}FN_2O_4$	ESI+	[M+NH4]+	372	355	38	33	299	17	30
Fluoxastrobin	$C_{21}H_{16}ClFN_4O_5$	ESI+	[M+H]+	459	427	45	17	188	45	37
Fluroxypyr	$C_7H_5Cl_2FN_2O_3$	ESI+	[M+H]+	255	181	17	23	209	17	15
Flusilazole	$C_{16}H_{15}F_2N_3Si$	ESI+	[M+H]+	316	165	51	20	247	20	17
Flutolanil	$C_{17}H_{16}F_3NO_2$	ESI +	[M+H]+	324	262	33	35	242	33	25
Hexaconazole	$C_{14}H_{17}Cl_2N_3O$	ESI+	[M+H]+	314	70	24	17	159	24	27
Hexythiazox	$C_{17}H_{21}ClN_2O_2S$	ESI +	[M+H]+	353	228	45	11	168	45	27
Imidacloprid	$C_9H_{10}ClN_5O_2$	ESI +	[M+H]+	256	208	21	15	175	20	20
Iodosulfuron-methyl	$C_{14}H_{13}IN_5NaO_6S$	ESI+	[M+H]+	530	163	21	13	390	21	14
Iprovalicarb	$C_{18}H_{28}N_2O_3$	ESI+	[M+H]+	321	119	45	17	91	45	48
Isoproturon	$C_{12}H_{18}N_2O$	ESI+	[M+H]+	207	72	38	23	165	17	13
Jodfenphos	$C_8H_8Cl_2IO_3PS$	ESI+	[M+H]+	413	287	21	27	143	17	23
Lufenuron	$C_{17}H_8Cl_2F_8N_2O_3$	ESI+	[M+H]+	511	158	33	21	141	33	41
Malaoxon	$C_{10}H_{19}O_7PS$	ESI +	[M+H]+	315	127	48	10	99	33	21
Maleic hydrazide	$C_4H_4N_2O_2$	ESI-	[M-H]-	111	83	55	17	55	23	17
MCPA	$C_9H_9ClO_3$	ESI-	[M-H]-	199	141	55	11	105	55	26
Mecoprop (/Mecoprop-P)	$C_{10}H_{11}ClO_3$	ESI-	[M-H]-	213	141	38	23	105	38	28
Mepanipyrim	$C_{14}H_{13}N_3$	ESI+	[M+H]+	224	106	17	23	77	17	38
Metalaxyl -M	$C_{15}H_{21}NO_4$	ESI+	[M+H]+	280	220	52	11	160	52	22
Methacrifos	$C_7H_{13}O_5PS$	ESI+	[M+NH4]+	258	209	17	11	125	21	25
Methiocarb sulfone	$C_{11}H_{15}NO_4S$	ESI+	[M+NH4]+	275	122	33	25	201	33	10
Methiocarb sulfoxide	$C_{11}H_{15}NO_3S$	ESI+	[M+H]+	242	185	33	10	122	33	30
Metribuzin	$C_8H_{14}N_4S$	ESI+	[M+H]+	215	187	52	23	84	21	20
Metsulfuron-methyl	$C_{14}H_{15}N_5O_6S$	ESI+	[M+H]+	382	167	52	17	135	52	32
Molinate	$C_9H_{17}NOS$	ESI+	[M+H]+	188	126	52	11	83	30	18
Monocrotophos	$C_7H_{14}NO_5P$	ESI +	[M+NH4]+	241	193	21	10	127	10	20
Monolinuron	$C_9H_{11}ClN_2O_2$	ESI+	[M+H]+	215	126	55	17	99	52	30
Nuarimol	$C_{17}H_{12}ClFN_2O$	ESI+	[M+H]+	315	252	55	23	139	52	34

Pesticide/Metabolite	Molecular formula	Ionisation, ESI +/-	Molecular ion	Precursor	Transition 1			Transition 2		
					Product	Cone voltage (V)	Collision energy (eV)	Product	Cone voltage (V)	Collision energy (eV)
Ofurace	$C_{14}H_{16}ClNO_3$	ESI+	[M+NH4]+	299	254	17	17	160	17	27
Omethoate	$C_5H_{12}NO_4PS$	ESI+	[M+H]+	214	183	10	11	143	10	17
Oxadixyl	$C_{14}H_{18}N_2O_4$	ESI+	[M+H]+	279	219	17	17	132	17	30
Oxycarboxin	$C_{12}H_{13}NO_4S$	ESI+	[M+H]+	268	175	52	17	147	52	22
Pendimethalin	$C_{13}H_{19}N_3O_4$	ESI +	[M+H]+	282	212	33	10	194	33	10
Phosmet	$C_{11}H_{12}NO_4PS_2$	ESI+	[M+NH4]+	335	160	17	17	133	17	45
Picolinafen	$C_{19}H_{12}F_4N_2O_2$	ESI+	[M+H]+	377	256	45	23	238	45	30
Pirimicarb	$C_{11}H_{18}N_4O_2$	ESI+	[M+H]+	239	72	25	16	182	25	14
Propamocarb	$C_9H_{20}N_2O_2$	ESI+	[M+H]+	189	102	24	17	74	24	27
Propargit	$C_{19}H_{26}O_4S$	ESI+	[M+NH4]+	268	231	24	11	175	24	15
Proquinazid	$C_{14}H_{17}IN_2O_2$	ESI +	[M+H]+	373	331	52	11	289	52	25
Prothioconazole	$C_{14}H_{15}Cl_2N_3OS$	ESI+	[M+H]+	344	189	38	17	125	38	36
Pymetrozine	$C_{10}H_{11}N_5O$	ESI +	[M+H]+	218	105	39	25	79	43	40
Pyraclostrobin	$C_{19}H_{18}ClN_3O_4$	ESI+	[M+H]+	388	194	24	11	163	24	25
Pyraflufen-ethyl	$C_{15}H_{13}Cl_2F_3N_2O_4$	ESI+	[M+H]+	413	340	38	11	289	38	27
Pyridaphenthion	$C_{14}H_{17}N_2O_4PS$	ESI +	[M+H]+	341	189	39	30	205	35	18
Pyridate	$C_{19}H_{23}ClN_2O_2S$	ESI+	[M+H]+	379	207	45	17	104	45	30
Pyrimethanil	$C_{12}H_{13}N_3$	ESI+	[M+H]+	200	107	30	25	82	33	27
Pyriproxyfen	$C_{20}H_{19}NO_3$	ESI +	[M+H]+	322	96	55	20	185	27	23
Resmethrin	$C_{22}H_{26}O_3$	ESI +	[M+H]+	339	137	55	15	143	35	23
Rimsulfuron	$C_{14}H_{17}N_5O_7S_2$	ESI +	[M+H]+	432	182	21	15	325	21	13
Spiroxamin	$C_{18}H_{35}NO_2$	ESI +	[M+H]+	298	144	51	20	100	35	30
Tebufenozide	$C_{22}H_{28}N_2O_2$	ESI +	[M+H]+	353	133	24	17	297	24	5
Tebufenpyrad	$C_{18}H_{24}ClN_3O$	ESI+	[M+H]+	334	147	55	23	117	55	30
Tetraconazole	$C_{13}H_{11}Cl_2F_4N_3O$	ESI+	[M+H]+	372	159	45	25	70	30	23
Thifensulfuron-methyl	$C_{12}H_{13}N_5O_6S_2$	ESI-	[M-H]-	386	139	31	25	220	31	5
Thiodicarb	$C_{10}H_{18}N_4O_4S_3$	ESI +	[M+H]+	355	88	27	15	108	27	15
Tri-allate	$C_{10}H_{16}Cl_3NOS$	ESI +	[M+H]+	306	145	24	23	86	24	15
Triasulfuron	$C_{14}H_{16}ClN_5O_5S$	ESI +	[M+H]+	402	167	52	17	141	52	22
Tribenuron-methyl	$C_{15}H_{17}N_5O_6S$	ESI +	[M+H]+	396	155	52	17	181	52	22
Tridemorph	$C_{19}H_{39}NO$	ESI +	[M+H]+	298	130	10	23	98	10	25
Triflumuron	$C_{15}H_{10}ClF_3N_2O_3$	ESI +	[M+H]+	359	156	21	25	139	20	30
Triforine	$C_{10}H_{14}Cl_6N_4O_2$	ESI+	[M+H]+	435	390	17	5	215	17	25
Trinexapac-ethyl	$C_{13}H_{16}O_5$	ESI +	[M+H]+	253	207	52	11	69	52	21

Appendix 2. Repeatability, reproducibility, recovery and limit of detection.

The tables are repeatability, reproducibility and LOD for compounds ionised by ESI- and ESI+, respectively. Values outside the acceptance criteria is marked in italic.

ESI-		**Wheat**			
Concentration, mg/kg		0.02	0.04	0.20	LOD
2-naphtoxy acetic acid	RSD$_r$, %	27%	19%	2%	
	RSD$_R$, %	27%	19%	14%	
	Recov.,%	97%	87%	72%	0.016
2,4-D	RSD$_r$, %			12%	
	RSD$_R$, %			12%	
	Recov.,%			72%	0.050
4-chlorophenoxyacetic acid	RSD$_r$, %	20%	14%	6%	
	RSD$_R$, %	20%	21%	*25%*	
	Recov.,%	111%	105%	70%	0.014
Bentazone	RSD$_r$, %	21%	15%	3%	
	RSD$_R$, %	24%	19%	6%	
	Recov.,%	75%	94%	72%	0.011
Bromoxynil	RSD$_r$, %		17%	*22%*	
	RSD$_R$, %		18%	*22%*	
	Recov.,%	79%	116%	63%	0.025
Dichlorprop	RSD$_r$, %	11%	25%	6%	
	RSD$_R$, %	13%	25%	18%	
	Recov.,%	106%	111%	67%	0.008
Dinoterb	RSD$_r$, %	19%	11%	7%	
	RSD$_R$, %	19%	18%	13%	
	Recov.,%	83%	82%	62%	0.009
DNOC	RSD$_r$, %	14%	17%	8%	
	RSD$_R$, %	14%	22%	*21%*	
	Recov.,%	80%	81%	*66%*	0.006
MCPA	RSD$_r$, %	20%	24%	4%	
	RSD$_R$, %	24%	24%	11%	
	Recov.,%	*148%*	*122%*	79%	0.021
Mecoprop	RSD$_r$, %		11%	14%	
	RSD$_R$, %		11%	14%	
	Recov.,%	106%	96%	73%	0.012
Thifensulfuron-methyl	RSD$_r$, %	17%	26%	10%	
	RSD$_R$, %	17%	26%	*22%*	
	Recov.,%	*125%*	110%	89%	0.013

ESI+		**Wheat**			
Concentration, mg/kg		0.02	0.04	0.20	LOD
Acetamiprid	RSD$_r$, %			18%	
	RSD$_R$, %			19%	
	Recov.,%			90%	0.105
Azimsulfuron	RSD$_r$, %			*21%*	
	RSD$_R$, %			*21%*	
	Recov.,%			*67%*	0.085
Bitertanol	RSD$_r$, %			18%	
	RSD$_R$, %			18%	
	Recov.,%			104%	0.112
Bupirimate	RSD$_r$, %		26%	10%	
	RSD$_R$, %		26%	16%	
	Recov.,%		103%	100%	0.032
Buprofenzin	RSD$_r$, %		21%	14%	
	RSD$_R$, %		26%	17%	
	Recov.,%		98%	94%	0.030
Clethodim	RSD$_r$, %			20%	
	RSD$_R$, %			20%	
	Recov.,%			72%	0.089
Clomazone	RSD$_r$, %	3%	25%	19%	
	RSD$_R$, %	25%	25%	19%	
	Recov.,%	102%	98%	101%	0.015
Demeton-S-methyl	RSD$_r$, %	3%		*35%*	
	RSD$_R$, %	17%		*35%*	
	Recov.,%	78%	74%	*81%*	0.008
Demeton-S-methyl sulfon	RSD$_r$, %		11%	17%	
	RSD$_R$, %		*28%*	17%	
	Recov.,%		91%	98%	0.030
Demeton-S-methyl sulfoxid	RSD$_r$, %	18%	11%	10%	
	RSD$_R$, %	28%	24%	19%	
	Recov.,%	107%	*127%*	94%	0.018
Dimethomorph	RSD$_r$, %	21%	21%	*28%*	
	RSD$_R$, %	27%	24%	*28%*	
	Recov.,%	95%	107%	92%	0.016
Ethoxyquin	RSD$_r$, %		17%	19%	
	RSD$_R$, %		17%	19%	

ESI+		**Wheat**			
Concentration, mg/kg		0.02	0.04	0.20	LOD
Fenazaquin	RSD$_r$, %	21%	22%	9%	
	RSD$_R$, %	23%	22%	21%	
	Recov.,%	103%	*81%*	*104%*	0.014
Fluoxastrobin	RSD$_r$, %		17%	12%	
	RSD$_R$, %		18%	*26%*	
	Recov.,%		94%	90%	0.021
Fluzilafop-p-buthyl	RSD$_r$, %	23%	13%	13%	
	RSD$_R$, %	24%	26%	13%	
	Recov.,%	108%	113%	77%	0.015
Iodosulfuron-methyl	RSD$_r$, %		26%	11%	
	RSD$_R$, %		26%	11%	
	Recov.,%		*128%*	87%	0.040
Iprovalicarb	RSD$_r$, %		20%	11%	
	RSD$_R$, %		23%	11%	
	Recov.,%		66%	84%	0.019
Isoproturon	RSD$_r$, %		20%	15%	
	RSD$_R$, %		22%	18%	
	Recov.,%		*95%*	*90%*	0.025
Malaoxon	RSD$_r$, %	25%	24%	15%	
	RSD$_R$, %	25%	24%	20%	
	Recov.,%	109%	103%	98%	0.017
Methacrifos	RSD$_r$, %		26%	5%	
	RSD$_R$, %		26%	18%	
	Recov.,%		*146%*	107%	0.045
Methalaxyl-M	RSD$_r$, %	17%	11%	17%	
	RSD$_R$, %	21%	*15%*	19%	
	Recov.,%	115%	105%	78%	0.015
Methiocarb sulfon	RSD$_r$, %	18%	26%	*25%*	
	RSD$_R$, %	24%	26%	*25%*	
	Recov.,%	101%	119%	96%	0.015
Methiocarb sulfoxid	RSD$_r$, %			6%	
	RSD$_R$, %			18%	
	Recov.,%			83%	0.091
Metsulfuron-methyl	RSD$_r$, %	23%	*37%*	13%	
	RSD$_R$, %	30%	*37%*	19%	
	Recov.,%	88%	*115%*	89%	0.016
Monocrotophos	RSD$_r$, %		2%	5%	
	RSD$_R$, %		26%	15%	
	Recov.,%		116%	100%	0.037

ESI+			**Wheat**		
Concentration, mg/kg		0.02	0.04	0.20	LOD
Monolinuron	RSD$_r$, %		20%	10%	
	RSD$_R$, %		24%	19%	
	Recov.,%		*89%*	*105%*	0.026
Ofurace	RSD$_r$, %			17%	
	RSD$_R$, %			19%	
	Recov.,%			89%	0.099
Omethoate	RSD$_r$, %	18%	4%	16%	
	RSD$_R$, %	26%	*49%*	16%	
	Recov.,%	100%	90%	101%	0.099
Oxycarboxim	RSD$_r$, %	24%	20%	16%	
	RSD$_R$, %	27%	20%	18%	
	Recov.,%	90%	101%	88%	0.015
Pendimethalin	RSD$_r$, %			19%	
	RSD$_R$, %			19%	
	Recov.,%			118%	0.135
Pirimicarb	RSD$_r$, %	18%	12%	7%	
	RSD$_R$, %	25%	24%	19%	
	Recov.,%	97%	89%	105%	0.013
Propamocarb	RSD$_r$, %	13%	26%	18%	
	RSD$_R$, %	17%	26%	*22%*	
	Recov.,%	115%	112%	85%	0.012
Pymetrozin	RSD$_r$, %	14%	9%	10%	
	RSD$_R$, %	17%	26%	*22%*	
	Recov.,%	113%	82%	100%	0.011
Pyraclostrobin	RSD$_r$, %	12%	25%	11%	
	RSD$_R$, %	23%	25%	20%	
	Recov.,%	88%	93%	86%	0.012
Pyridaben	RSD$_r$, %			1%	
	RSD$_R$, %			21%	
	Recov.,%		*83%*	*98%*	0.125
Pyridaphenthion	RSD$_r$, %	21%	*32%*	6%	
	RSD$_R$, %	29%	*32%*	16%	
	Recov.,%	80%	83%	74%	0.014
Pyridate	RSD$_r$, %	26%	26%	6%	
	RSD$_R$, %	26%	26%	9%	
	Recov.,%	90%	*84%*	*57%*	0.014
Pyrimethanil	RSD$_r$, %			12%	
	RSD$_R$, %			18%	
	Recov.,%			103%	0.112

ESI+			**Wheat**		
Concentration, mg/kg		0.02	0.04	0.20	LOD
Spiroxamin	RSD$_r$, %	17%	18%	17%	
	RSD$_R$, %	30%	18%	20%	
	Recov.,%	85%	90%	78%	0.015
Tebufenpyrad	RSD$_r$, %		22%	7%	
	RSD$_R$, %		22%	18%	
	Recov.,%		104%	94%	0.027