

## REASONED OPINION

### Reasoned opinion on the setting of import tolerances for acetochlor in soya beans and cotton seeds<sup>1</sup>

European Food Safety Authority<sup>2</sup>

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#### ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, Spain, the evaluating Member State, received an application from Monsanto Europe NV to set import tolerances for the active substance acetochlor in soya bean and cotton seed, imported from the USA at the level of 0.6 mg/kg. This proposal included a change in the residue definition for the European MRL to acetochlor and its metabolites containing the ethyl methyl aniline (EMA) moiety and the hydroxyethyl methyl aniline (HEMA) moiety calculated as the stoichiometric equivalents of acetochlor. Spain drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA. According to EFSA, an appropriate residue definition for risk assessment and MRLs on soya bean and cotton seed cannot be proposed.

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#### KEY WORDS

acetochlor, soya bean, cotton seed, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, chloroacetanilide, 2(1-hydroxyethyl)-6-methylaniline, 2-ethyl-6-methylaniline

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## SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, Spain, hereafter referred to as the evaluating Member State (EMS), received an application from Monsanto Europe NV to set import tolerances at the level of 0.6 mg/kg for the active substance acetochlor in soya bean and cotton seed imported from the USA. This proposal included a change in the residue definition set for acetochlor at European level. Spain drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA on 29 February 2012. EFSA identified some data gaps, which prevented EFSA from concluding on the consumer risk assessment. On 10 June 2014, the EMS provided a revised evaluation report, including an assessment of the reply from the applicant on these gaps.

EFSA bases its assessment on the evaluation report submitted by the EMS (Spain, 2014), the Draft Assessment Report (DAR) (and its addenda) prepared under Council Directive 91/414/EEC Spain, 2005, 2007, 2010, 2011), the Commission Review Report on acetochlor (European Commission, 2011b), the conclusion on the peer review of the pesticide risk assessment of the active substance acetochlor (EFSA, 2011), as well as the conclusions from the previous EFSA reasoned opinion on acetochlor carried out according to article 12 of Regulation (EC) No 396/2005.

The toxicological profile of acetochlor was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.0036 mg/kg bw per day and an acute reference dose (ARfD) of 1.5 mg/kg bw applicable to acetochlor and some specifically listed transformation products.

In the framework of the peer review, the metabolism of acetochlor in primary crops was investigated in the cereal group only (maize) and the residue definition for enforcement was proposed as “*all compounds forming EMA and HEMA on hydrolysis expressed as acetochlor*”. In addition, the *N*-oxamic acid (68) metabolite was included in the residue definition for risk assessment. The residue definition for enforcement placed in the legislation Regulation (EC) No 396/2005 is limited to acetochlor.

Further metabolism studies on the pulses/oilseeds crop group (soya bean and cotton) were submitted in the framework of this MRL application. Several plant metabolites above 0.01 mg/kg in beans of soya bean remained unidentified and it was therefore not possible to conclude on their toxicological profile. Since concerns on the genotoxic and carcinogenic properties of an identified metabolite could not be excluded on the basis of the available data, EFSA concludes that appropriate residue definitions for monitoring and risk assessment cannot be proposed for the pulses/oilseeds crop group, whilst all components present in beans of soya bean above 0.01 mg/kg have not been fully identified.

Residues trials on soya bean and cotton conducted in the USA according to the US GAPs were submitted. Tentative MRLs were derived according to the residue definition for enforcement proposed in the conclusion of the peer review taking into account all components forming EMA and HEMA on hydrolysis. Note the peer review only considered metabolism in the cereals crop group. Since the residue definitions applicability to the pulses/oilseeds crop group could not be concluded, EFSA does not recommend the setting of import tolerances for soya bean and cotton seed.

Studies investigating the nature and magnitude of acetochlor residues in processed commodities were assessed in the framework of this application for MRL modification. Residues from acetochlor that form EMA and HEMA on hydrolysis were lower in soya and cotton seed oil than in beans and seeds. Concentration of these residues was found in soya bean meal but not cotton seed meal.

Since the proposed use of acetochlor is on imported crops, investigations of residues in rotational crops are not required.

Provisionally, livestock dietary burden calculations were conducted based on acetochlor residues forming EMA and HEMA on hydrolysis. Estimated intakes were below the trigger value of 0.1 mg/kg (dry matter) for all relevant species, and therefore the transfer of acetochlor residues to livestock has not been reconsidered.

Whilst it is not possible to conclude what would be appropriate, applicable toxicological reference values for the unidentified components that are present in beans of soya bean and seed of cotton seed, a valid consumer risk assessment could not be performed.

Thus EFSA does not propose any amendments to the existing MRLs as reported in the summary table.

**Summary table**

Code number <sup>(a)</sup>	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
<b>Enforcement residue definition: acetochlor</b>				
0401070	Soya bean	0.01*	No proposal	The submitted residue and toxicology data are not sufficient to propose residue definitions for the pulses/oilseeds crop group and therefore, to derive MRL proposals.
0401090	Cotton seed	0.01*		

(a): According to Annex I of Regulation (EC) No 396/2005.

(\*): Indicates that the MRL is set at the limit of analytical quantification.

## TABLE OF CONTENTS

Abstract .....	1
Summary .....	2
Table of contents .....	4
Background .....	5
Terms of reference.....	5
The active substance and its use pattern.....	6
Assessment .....	7
1. Method of analysis.....	7
1.1. Methods for enforcement of residues in food of plant origin .....	7
1.2. Methods for enforcement of residues in food of animal origin .....	8
2. Mammalian toxicology.....	8
3. Residues.....	9
3.1. Nature and magnitude of residues in plant.....	9
3.1.1. Primary crops.....	9
3.1.2. Rotational crops.....	14
3.2. Nature and magnitude of residues in livestock .....	14
3.2.1. Dietary burden of livestock .....	14
4. Consumer risk assessment .....	15
Conclusions and recommendations .....	15
References .....	17
Appendices .....	19
Appendix A. Good Agricultural Practice (GAPs) .....	19
Appendix B. List of metabolites and related structural formula.....	20
Appendix C. Abbreviations .....	25

## BACKGROUND

Regulation (EC) No 396/2005<sup>3</sup> establishes the rules governing the setting of pesticide MRLs at European Union level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC<sup>4</sup>, repealed by Regulation (EC) No 1107/2009<sup>5</sup>, shall submit to a Member State, when appropriate, an application to set an import tolerance in accordance with the provisions of Article 7 of that Regulation.

Spain, hereafter referred to as the evaluating Member State (EMS), received from the company Monsanto Europe NV<sup>6</sup> an application to set import tolerances for the active substance acetochlor in soya bean and cotton seed. This application was notified to the European Commission and EFSA and was subsequently evaluated by the EMS in accordance with Article 8 of the Regulation. After completion, the evaluation report was submitted to the European Commission who forwarded the application, the evaluation report and the supporting dossier to EFSA on 29 February 2012.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2012-00364 and the following subject:

*Acetochlor - Application to modify the existing MRLs in soya bean and cotton seed.*

The EMS proposed to raise the existing MRLs of acetochlor in soya bean and cotton seed from the current default LOQ value of 0.01 mg/kg to 0.6 mg/kg, this proposal included a change in the residue definition for enforcement. EFSA identified some data gaps, which prevented EFSA from concluding on the consumer risk assessment. On 10 June 2014 the EMS provided their reply with additional information in a revised evaluation report, which was taken into consideration by EFSA for the finalisation of this reasoned opinion.

EFSA proceeded with the assessment of the application and the evaluation report as required by Article 10 of the Regulation.

## TERMS OF REFERENCE

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

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<sup>3</sup> Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.03.2005, p. 1-16.

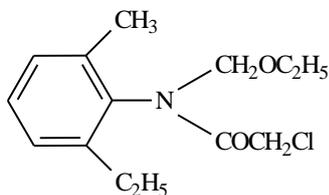
<sup>4</sup> Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1-32.

<sup>5</sup> Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

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## THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Acetochlor is the ISO common name for 2-chloro-*N*-ethoxymethyl-6'-ethylacet-*o*-toluidide (IUPAC). The chemical structure of the compound is reported below.



Molecular weight: 269.77 g/mol

Note, a systematic name used in the Federal Regulation documentation of the United States of America (USA) for acetochlor is 2-chloro-2'-methyl-6-ethyl-*N*-ethoxymethylacetanilide.

Acetochlor is a racemic mixture of two thermally stable rotational isomers (rotamers) on the nitrogen atom in the structure. Acetochlor is a selective herbicide belonging to the chloroacetanilide class. It is absorbed mainly by the shoots and secondarily by the roots of germinating plants and may act by inhibition of synthesis of very long chain fatty acids.

Acetochlor was evaluated in the framework of Directive 91/414/EEC with Spain designated as rapporteur Member State (RMS). The representative uses evaluated in the peer review were pre-sowing or early post-emergence application on maize. The Draft Assessment Report (DAR) and the Additional Report of acetochlor were peer reviewed by EFSA (EFSA, 2008, 2011). The active substance acetochlor was not approved in accordance with Regulation (EC) No 1107/2009 and the non-approval entered into force on 23 December 2011 by Commission Implementing Regulation (EU) No 1372/2011<sup>7</sup>

The EU MRLs for acetochlor are established in Annex III of Regulation (EC) No 396/2005, the enforcement residue definition in this regulation is acetochlor. Earlier EU MRLs that were contained in Annexe IIIA of Regulation (EC) No 396/2005 were reviewed by EFSA under Article 12 of Regulation (EC) No 396/2005 (EFSA, 2013). By Regulation (EU) 2015/603<sup>8</sup> all MRLs for acetochlor are set at the default LOQ of 0.01 mg/kg. Note these MRLs come into force on 7 December 2015.

No Codex maximum residue limits (CXLs) are established for acetochlor.

The pesticide tolerances for residues in the USA for acetochlor in soya bean seed (soybean seed, USA English) and cotton undelinted seed are established at 1.0 and 0.6 mg/kg<sup>9</sup> respectively, for an enforcement residue definition expressed as "*acetochlor, 2-chloro-2'-methyl-6-ethyl-N-ethoxymethylacetanilide, and its metabolites containing the ethyl methyl aniline (EMA) moiety and the hydroxyethyl methyl aniline (HEMA) moiety. Both parent and the named metabolites shall be determined as ethyl methyl aniline (EMA) and hydroxyethyl methyl aniline (HEMA), and calculated as the stoichiometric equivalents of acetochlor*". Even if expressed according to a different wording, this residue definition is similar to the residue definition proposed for acetochlor in the conclusion of the peer review of the active substance (EFSA, 2010) that just considered uses on maize.

<sup>7</sup> Commission Implementing Regulation (EU) No 1372/2011 of 21 December 2011 concerning the non-approval of the active substance acetochlor, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Decision 2008/934/EC. OJ L 341, 22.12.2011, p. 45-46.

<sup>8</sup> Commission Regulation (EU) 2015/603 of 13 April 2015 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for 2-naphthoxyacetic acid, acetochlor, chloropicrin, diflufenican, flurprimidol, flutolanil and spinosad in or on certain products

<sup>9</sup> US Code of Federal Regulations 40 CFR §180.470 acetochlor: tolerances for residues.

The details of GAPs in the application for acetochlor in the USA are given in Appendix A. As tolerances have been established in the USA, actual GAPs in the USA exist, but confirmation of these actual GAPs were not made available to EFSA.

## ASSESSMENT

EFSA bases its assessment on the evaluation report submitted by the EMS (Spain, 2014), the Draft Assessment Report (DAR) (and its addenda) prepared under Council Directive 91/414/EEC (Spain, 2005, 2007, 2010, 2011), the Commission Review Report on acetochlor (European Commission, 2011b), the conclusion on the peer review of the pesticide risk assessment of the active substance acetochlor (EFSA, 2011), as well as the conclusions from the previous EFSA reasoned opinion on acetochlor carried out according to article 12 of Regulation (EC) No 396/2005 (EFSA, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011<sup>10</sup> and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2000, 2010a, 2010b, 2011a; OECD, 2011).

### 1. METHOD OF ANALYSIS

#### 1.1. Methods for enforcement of residues in food of plant origin

During the peer review under Directive 91/414/EEC, an analytical method using GC-MS detection was evaluated and validated for the determination of parent acetochlor in plant matrices with an LOQ of 0.01 mg/kg in high water (apple), high oil (soybean), high acid (grape) and dry/starch (maize grain) content commodities. An Independent Laboratory Validation (ILV) was available and validated for dry and acid commodities. A confirmatory method using LC-MS/MS was also validated for the determination of parent acetochlor in dry commodities with an LOQ of 0.01 mg/kg (Spain, 2005).

The multi-residue QuEChERS method in combination with HPLC-MS/MS, as described by CEN (2008), is also available to analyse acetochlor in high water content and dry commodities. Nevertheless, the validation data reported are too limited to conclude on the validity of this analytical method (EURL, 2013).

Additionally, during the peer review under Directive 91/414/EEC, an analytical method using GC-MS was evaluated and validated for the determination of common moieties EMA and HEMA in plant matrices with an LOQ of 0.01 mg/kg for each moiety in dry/starch (maize grain) and high water content (maize forage) commodities. An ILV is also available and validated at the same LOQ (Spain, 2005, 2006). Moreover, an analytical method using HPLC-MS/MS was evaluated and validated for the determination of common moieties EMA and HEMA in plant matrices with an LOQ of 0.005 mg/kg for each moiety in high oil content matrices (cotton). However, ILV was not available (Spain, 2010).

Hence there are indications that acetochlor can be enforced in food of plant origin with an LOQ of 0.01 mg/kg in high water content, high oil content, acidic and dry commodities. Nevertheless, ILV in high water content commodities as well as confirmatory methods in acidic and high oil content commodities are missing.

There are also indications that compounds containing the common moieties EMA or HEMA can be enforced in food of plant origin with, for each moiety, an LOQ of 0.01 mg/kg in high water content and dry commodities and with a LOQ of 0.005 mg/kg in high oil content commodities. Nevertheless, confirmatory methods are missing as well as an ILV in high oil content commodities.

<sup>10</sup> Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.06.2011, p. 127-175.

## 1.2. Methods for enforcement of residues in food of animal origin

During the peer review under Directive 91/414/EEC, no analytical method was evaluated for the determination of acetochlor in food of animal origin. Hence, there is no evidence that residues of acetochlor can be enforced in food of animal origin.

## 2. MAMMALIAN TOXICOLOGY

The toxicological profile of the active substance acetochlor was assessed in the framework of the peer review under Directive 91/414/EEC (EFSA, 2011). The data were sufficient to derive toxicological reference values for acetochlor which are compiled in Table 2-1.

**Table 2-1:** Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
<b>Acetochlor</b>					
ADI	EFSA	2011	0.0036 mg/kg bw per day	78-week mouse	300 <sup>a</sup>
ARfD	EFSA	2011	1.50 mg/kg bw	Acute neurotoxicity rat	100
<b>Metabolites t-oxanilic acid (2), t-sulfinylacetic acid (3), t-sulfonic acid (7), s-sulfonic acid (13)</b> (provided they are present with an isomer ratio of 1:1) and <b>metabolite N-oxamic acid (68)</b>					
ADI	EFSA	2011	0.0036 mg/kg bw per day	(same as acetochlor)	300 <sup>a</sup>
ARfD	EFSA	2011	1.50 mg/kg bw	(same as acetochlor)	100

(a): Additional safety factor of 3 based on the use of a LOAEL.

During the peer review, it was agreed that the reference values of acetochlor would be applicable to the metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid (provided they are present with an isomer ratio of 1:1). Based on the available data, it was concluded that the toxicological reference values of acetochlor could apply to the metabolite N-oxamic acid.

As concerns the metabolite t-norchloro acetochlor, genotoxic and carcinogenic properties could not be excluded on the basis of the available data, no toxicological reference value could be derived.

In the context of the representative uses that had been considered on maize during the peer review, where the results of crop trials indicated that residues forming EMA and HEMA on hydrolysis would be below the limit of quantification, it was accepted that the reference values of acetochlor would be applicable to all compounds forming EMA and HEMA on hydrolysis in the context of setting a residue definition for risk assessment. This was reconfirmed in the reasoned opinion on acetochlor carried out according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2013). In this Article 12 opinion it was also concluded (in the context of residues being below the limit of quantification) that the reference values of acetochlor would be applicable to t-sulfinylacetic acid (that will form HEMA on hydrolysis). In the case of these uses for which import tolerances have been requested, it is considered inappropriate to apply the reference values of acetochlor to all compounds forming EMA and HEMA on hydrolysis (including t-sulfinylacetic acid identified in significant proportions in maize including grain and soya bean but not including seed), since positive residues of these moieties are measured in the supervised residues trials (see section 3.1.1.2).

The applicant was requested to address the toxicological relevance of all residues present in the pertinent oilseed crop metabolism studies in harvested seeds that may be present above 0.01 mg/kg. As part of their response they indicated that three metabolites (t-amide cysteine (56), s-cysteine conjugate and s-methylsulfone, identified in cotton leaves and stems, as well as in soybean forage and hay) potentially falling into this category, were rat metabolites. However when EFSA scrutinised the rat metabolism study reports that were available in the dossier provided for the peer review, it does not appear that they were present in sufficient amounts in rat, in order to be covered by the toxicological

reference values of acetochlor. For these three compounds and another 37 metabolites that the applicant considered might represent residues present in the pertinent oilseed crop metabolism studies in harvested beans above 0.01mg/kg, the applicant reported QSAR calculated LD<sub>50</sub> values. The applicant and EMS considered this sufficient information to conclude that the reference values of acetochlor could apply to these compounds.

Considering all together the data available for all metabolites and the limitations of QSAR approaches along with the limited acceptance of LD<sub>50</sub> results alone to address toxicological relevance, this was considered insufficient to extrapolate the toxicity profile of the parent and its reference values to any metabolites that are not included in Table 2-1, for situations where detectable metabolite residues are indicated.

### 3. RESIDUES

#### 3.1. Nature and magnitude of residues in plant

##### 3.1.1. Primary crops

##### 3.1.1.1. Nature of residues

In the framework of the peer review under Directive 91/414/EEC the metabolism of acetochlor in the primary crop was investigated in the cereal group only (maize) and was evaluated by the RMS Spain (Spain, 2010, 2011) and reviewed by EFSA (EFSA, 2011). These data were subsequently reconsidered in the EFSA Article 12 reasoned opinion on acetochlor (EFSA, 2013). Additional metabolism studies conducted on the pulses/oilseeds crop group (soya bean and cotton) were submitted in the framework of this MRL application and evaluated by the EMS Spain (Spain, 2014). The overview of the metabolism study designs is presented in Table 3-1.

**Table 3-1:** Summary of available metabolism studies in plants

Crop group	Crop	Label position	Application details				Remark
			Method	Rate (g/ha)	No	Sampling (DAT) <sup>(a)</sup>	
Cereals	Maize (glyphosate tolerant)	<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Pre-emergence	3360	1	95 (sweet corn), 111 (forage), 141 (grain)	Peer review (EFSA, 2011)
		<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Foliar BBCH 16-17	3360	1	54 (sweet corn), 70 (forage), 100 (grain)	
Pulses/oilseeds	Soya bean	<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Pre-seeding	3540	1	91 (forage), 122 (hay), 191 (seed)	Not peer reviewed
		<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Foliar BBCH 60-65	3670	1	7 (forage), 34 (hay) 101 (seed)	
	Cotton (glyphosate tolerant)	<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Pre-seeding	3630	1	205	
		<sup>14</sup> C-phenyl <sup>13</sup> C-acetamide	Foliar BBCH 60	3600	1	91	

(a): DAT: days after treatment

From the investigations carried out on maize where crops were treated with a mixture of the test substance and the safener furilazole, total radioactive residues (TRR) in sweet corn and mature grains were low (0.01 to 0.04 mg/kg). In contrast, significant TRRs were measured in forage and stover, the levels being higher upon post-emergence treatment (3.45 and 6.41 mg/kg) than after pre-emergence (0.67 and 1.84 mg/kg). Most of the radioactivity was extractable by solvents (*ca.* 60% in grain, 80% in other matrices). Chromatographic analyses showed the different plant extracts to be composed of a multiple number of individual fractions, confirming an extensive metabolism of acetochlor in maize

plants, though characterisation of the residues in sweet corn and mature maize grain was not possible. In the extracts of the other plant parts, more than 50 individual compounds were characterised, of which, more than 30 were identified, each accounting for less than 3% TRR, except the *t*-sulfonic acid (7) and the *N*-oxamic acid (68) metabolites that represented 3 to 6% of the TRR in the pre-emergence forage and stover samples, and the *s*-sulfinylacetic acid free and glucose conjugate and the *t*-sulfinyllactic acid (21) that accounted for 3% to 12% TRR in the post-emergence forage and stover samples.

Although very extensive metabolism was observed in both application patterns, with more than 10 common metabolites, the metabolite profiles appear to be slightly different. The oxanilic acid metabolites were predominant following pre-emergence application, as the result of the uptake of the main soil metabolites, whereas the sulfinyl acid metabolites resulting from the glutathione conjugation appear to be more prominent following post-emergence application.

Due to the metabolism pattern apparent following the application of acetochlor to maize, the peer review concluded that the residue definition for risk assessment should be “*all compounds forming EMA (34) plus HEMA (33) on hydrolysis and N-oxamic acid (68) expressed as acetochlor*”. Based on the pre-emergence investigations, a conversion factor of 2 was proposed as appropriate to be applied to all residues that may be quantified as EMA/HEMA following hydrolysis. This conversion factor was derived considering the total identified metabolites (34% TRR) and the total metabolites quantified as EMA/HEMA following hydrolysis (19% TRR). It is noted that this conversion factor is an overestimate as it includes all identified metabolites and not only EMA/HEMA metabolites and *N*-oxamic acid (68) as stated in the definition for risk assessment. This worst case approach was considered necessary, having regard to the toxicological profile of parent acetochlor (assessed as a potentially carcinogenic agent, (EFSA, 2011)).

The peer review concluded that the residue definition for monitoring should be “*all compounds forming EMA (34) plus HEMA (33) on hydrolysis expressed as acetochlor*”. It was concluded that there was no obvious individual marker compound that could be satisfactorily used as a monitoring definition. It has to be noted that this monitoring residue definition is not specific to acetochlor. Following hydrolysis, other chloroacetanilide herbicides (e.g. propisochlor, metolachlor and *S*-metolachlor) would also form the EMA (34) and HEMA (33) moieties. Moreover, although there are indications that these residues can be enforced in foods of plant origin with a combined LOQ of 0.04 mg/kg in high water content and dry commodities and a combined LOQ of 0.01 mg/kg in high oil content commodities, the available analytical method includes hydrolytic steps and might be considered less than ideal for enforcement.

From the investigations carried out on soya beans, total radioactive residues in bean seed were 0.175 to 0.192 mg/kg. Four resolved components (retention times 5.75, 9.25, 46.25 and 51.75 min) accounting for more than 0.01 mg/kg acetochlor equivalents (mg eq./kg) were not identified, whilst identification is required according to the agreed guidance (European Commission, 1997a). Identification is essential for the 51.75 min eluting peak accounting for 15.1% TRR and 0.029 mg eq./kg and is highly desirable for the other three components above 0.01mg/kg, so an acceptable consideration of their mammalian toxicology can be made (see section 2) in the context that there are indications that identified acetochlor metabolites (i.e. *t*-norchloro acetochlor) may have genotoxic and carcinogenic potential. Higher TRRs were measured in hay and forage, the levels being higher upon post-emergence treatment (57.7 and 11.4 mg eq./kg) than after pre-seeding (3.47 and 1.67 mg eq./kg). Most of the radioactivity was extractable by the solvent extraction methods employed (*ca* 82-95% in seed, 96% in other matrices). In the extracts of the other plant parts, chromatographic analysis showed the different extracts to be composed of a multiple number of individual fractions, confirming an extensive metabolism of acetochlor in soya plants. More than 31 individual compounds were characterised, of which, 25 were identified. In line with the results of metabolite identification in immature maize plants, soya bean forage and hay had *t*-sulfinyllactic acid (21) as a high proportion residue.

From the investigations carried out on cotton, total radioactive residues in seed were lower (0.103 to 0.133 mg eq./kg) compared to soya beans. As for soya, significant TRRs were measured in leaves and stems, the levels being higher upon post-emergence treatment (63.9 mg/kg) than after pre-seeding (5.7 mg/kg). Most of the radioactivity was extractable by solvents (*ca* 70% in seed, 92-97% in other matrices). Though characterisation of the residues in seed was not possible, as no individual extracted resolved component accounted for above 0.01mg eq./kg, this can be accepted according to agreed guidance. In the extracts of the other plant parts, chromatographic analysis showed the different plant extracts to be composed of a multiple number of individual fractions, confirming an extensive metabolism of acetochlor in cotton plants. More than 39 individual compounds were characterised, of which 22 were identified.

The structures of the identified metabolites are included in Appendix B. In total in the pulses/oilseeds metabolism studies, 40 different metabolites were identified. The applicant indicated that they considered it likely that the four unidentified components that were each individually above 0.01mg eq./kg in soya bean seed, were among the 40 identified compounds from other plant parts. However, it is also possible that they are simply among the many resolved but unidentified compounds. As discussed above, identification of the highest occurring of these four compounds is essential and is desirable for the other three, for an acceptable consideration of their mammalian toxicology to be made (see section 2). Whilst these four resolved soya bean seed residues remain unidentified, a robust consideration of their toxicology is not possible. **Consequently it is not possible to conclude on an appropriate residue definition for risk assessment for oilseed crops in relation the intended GAPs supported in this MRL application.**

The current residue definition set in Regulation (EC) No 396/2005 limited to acetochlor, differs from the residue definition for enforcement proposed in the peer review. For the uses supported in this import tolerance request, considering the results of the available primary crop metabolism studies, the active substance acetochlor is not expected to be present in the imported soya beans or cotton seed.

For the uses on soya bean and cotton seed, EFSA concludes that the metabolism of acetochlor has not been adequately addressed. An appropriate metabolism study on soya beans where all residues in harvested beans accounting for more than 0.01 mg/kg are identified is needed. Should this information become available an assessment of the toxicological profile of these metabolites would also be needed. These data gaps would have to be addressed to enable a credible consumer risk assessment to be carried out for any use that would result in detectable residues in the edible part of the plant.

In conclusion, the uses of acetochlor in the USA on soya beans and cotton are not adequately supported by the available primary crop metabolism studies. Consequently, it is unclear if the available toxicological reference values for acetochlor would cover the residues that are present in treated soya bean and cotton seed. Consequently the MRL proposals derived from the submitted residue trials (see point 3.1.1.2) cannot be supported by a reliable consumer risk assessment.

#### 3.1.1.2. Magnitude of residues

In support of the MRL application, the EMS selected residue trials conducted on soya bean and cotton in the USA during the growing season 2007 from 21 and 13 sites respectively and concluded to be appropriate to support the intended GAP. Trials were conducted with microencapsulated formulations containing the furilazole safener. Different applications patterns were investigated, including single post-emergence application or split pre-planting/post-emergence applications with a total dose rate of 3360 g/ha.

Samples were analysed with a method that hydrolysed acetochlor residues to EMA and HEMA and residue levels were expressed as acetochlor equivalents. It should be noted that out of the 40 identified metabolites in the cotton and soya bean metabolism studies, seven cannot form EMA and HEMA on hydrolysis (see Appendix B where compounds not forming EMA or HEMA are identified).

On soya bean and cotton, residue levels were higher in the trials conducted with the single post-emergence application at 3360 g/ha and therefore, tentative MRL proposals were derived from this agricultural practice. The EMS proposed to disregard some data identified as outliers according to Dixon Q-test. Since no information was provided to explain these atypical values, EFSA included these data in the calculations of possible MRLs for a not concluded uncertain residue definition.

For soya beans, residues were above the limit of quantification of 0.02 mg/kg at 20 of the 21 trial sites, with residues in the range 0.05 to 0.999 mg/kg, resulting in a calculated level of 1.5 mg/kg.

For cotton seed, residues were in the range of 0.010 to 0.365mg/kg, resulting in a calculated level of 0.7 mg/kg.

The length of time samples from the residue trials were store frozen prior to analysis and storage stability data under frozen conditions in high oil content matrices were not provided to confirm whether samples were stored under conditions for which integrity of the residues was demonstrated.

Overall, based on a not agreed residue definition for monitoring expressed as “*all compounds forming EMA and HEMA on hydrolysis expressed as acetochlor*”, the following MRLs might be proposed from the submitted residue trials conducted in the USA according to the US GAPs:

- Soya bean           1.5 mg/kg
- Cotton seed        0.7 mg/kg

However, since the MRLs currently in force in the USA on soya bean and cotton seed are 1 mg/kg and 0.6 mg/kg respectively, the setting of import tolerances above these US legal values might not be warranted.

Moreover, significant residues from acetochlor that form EMA and HEMA on hydrolysis were observed in the residue trials, up to 0.999 mg/kg in soya bean and up to 0.365 mg/kg in cotton seed. Therefore, the data gap identified in section 3.1.1.1 for an appropriate metabolism study on soya beans where all resolved components accounting for more than 0.01 mg/kg in harvested beans are identified and their toxicological profile assessed, would need to be filled, considering that genotoxic and carcinogenic properties could not be excluded on the basis of the available data for an identified metabolite. A credible consumer risk assessment cannot be carried out in absence of such information.

In conclusion, EFSA would not recommend the setting of import tolerances on soya bean and cotton seed as long as the data gaps identified here above have not been addressed. Depending on the evaluation of any information that might be provided to address these data gaps, different residue definitions for both enforcement and risk assessment than those adopted by the USA as exporting country might be considered appropriate.

**Table 3-1:** Overview of the available residues trials data

	Region (a)	Individual trial results (mg/kg)	Comments	Tentative MRL proposal (mg/kg)	HR (mg/kg) (c)	STMR (mg/kg) (b)
<b>Enforcement residue definition:</b> All compounds forming EMA (34) AND HEMA (33) on hydrolysis expressed as acetochlor.						
<b>Soya bean seed</b> (1× 3360 g/ha, at R1-R2 stage)	Outdoor USA	<0.02; 0.050; 0.081; 0.118; 0.123; 0.137; 0.148; 0.155; 0.172; 0.177; 0.202; 0.228; 0.232; 0.247; 0.272; 0.296; 0.313; 0.383; <u>0.540</u> ; <u>0.675</u> ; <u>0.999</u>	Residue levels significantly higher in the trials conducted with a single application at 3360 g/ha (U-Test, 5%). MRL proposal of 1.5 mg/kg derived from this dataset.	<b>1.5</b>	0.999	0.202
<b>Soya bean seed</b> (3× 1130 g/ha), 1 <sup>st</sup> : 45 days prior to sowing 2 <sup>nd</sup> : V3 stage 3 <sup>rd</sup> : at R1-R2 stage)	Outdoor USA	2x <0.02; 0.020; 0.042; 0.055; 0.058; 0.064; 0.072; 0.085; 0.097; 0.097; 0.104; 0.109; 0.116; 0.132; 0.136; 0.138; 0.213; 0.226; 0.234; <u>0.451</u>	MRL <sub>OECD</sub> : 1.2/1.5  Underlined values identified as outlier according to Dixon Test.	0.4	0.451	0.097
<b>Cotton seed</b> (1× 3360 g/ha), 15 days after majority of plants with 1 <sup>st</sup> flower open	Outdoor USA	0.010; 0.021; 0.045; 0.098; 0.101; 0.137; 0.142; 0.169; 0.256; 0.257; 0.293; 0.312; 0.365	Residue levels significantly higher in the trials conducted with a single application at 3360 g/ha, 15 days after majority plants with 1 <sup>st</sup> flower opened (H-Test, 5%). MRL proposal of 0.7 mg/kg derived from this dataset.	<b>0.7</b>	0.365	0.142
<b>Cotton seed</b> (1× 3360 g/ha), at 8 leaf stage	Outdoor USA	2x <0.005; 0.006; 0.008; 0.009; 0.017; 2x 0.019; 2x 0.029; 0.049; 0.085; <u>0.335</u>	MRL <sub>OECD</sub> : 0.64/0.7	0.40	0.335	0.019
<b>Cotton seed</b> (2× 1680 g/ha) 1 <sup>st</sup> : 30 days prior to sowing 2 <sup>nd</sup> : at 8 leaf stage	Outdoor USA	2x <0.005; 3x 0.005; 0.007; 2x 0.009; 2x 0.012; 0.015; 0.021; <u>0.063</u>	Underlined values identified as outlier according to Dixon Test.	0.08	0.063	0.009

(a): NEU, SEU, EU or Import (country code). In the case of indoor uses there is no necessity to differentiate between NEU and SEU.

(b): Median value of the individual trial results according to the enforcement residue definition.

(c): Highest value of the individual trial results according to the enforcement residue definition.

(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residues trial.

(\*): Indicates that the MRL is set at the limit of analytical quantification.

### 3.1.1.3. Effect of industrial processing and/or household preparation

Studies investigating the effect of processing on the magnitude of acetochlor residues in processed products of soya beans and cotton seeds in were assessed by the EMS in support of this MRL application (Spain, 2014).

Due to the data gaps identified in section 3.1.1.1, depending on the evaluation of any information that might be provided to address these data gaps, different residue definitions for both enforcement and risk assessment than those adopted by the USA as exporting country might be considered appropriate. Consequently a detailed evaluation of the available investigations on industrial processing is not presented in this reasoned opinion.

In general terms, residues from acetochlor that form EMA and HEMA on hydrolysis were lower in soya and cotton seed oil than in beans and seeds. Concentration of these residues was found in soya bean meal leading to a processing factor (PF) of 1.2, but not cotton seed meal (PF: 0.44). These PFs factors will be considered for the estimation of the dietary animal residue intakes (see point 3.2).

### 3.1.2. Rotational crops

The assessment of residues of acetochlor in rotational crops is not relevant for import tolerance applications.

## 3.2. Nature and magnitude of residues in livestock

The use of acetochlor resulted in significant residue levels in soya bean meal and residues below the limit of quantification in maize kernels, when determined as EMA and HEMA on hydrolysis in the analytical method. Soya bean meal and maize kernels are fed to livestock.

### 3.2.1. Dietary burden of livestock

The median and maximum dietary burden for livestock was calculated using the agreed European methodology (European Commission, 1996). The input values for the dietary burden calculations, summarised in Table 3-2, were selected according to the latest FAO recommendations (FAO, 2009) considering the livestock intake from soya bean cotton seed meal and maize. Residues in cotton meal were estimated to be 0.06 mg/kg, considering the median residue level of 0.142 mg/kg derived from the residue trials (see Table 2), and the processing factor (PF) of 0.44 (see section 3.1.13). For soya meal, residues were estimated to be 0.24 mg/kg, considering the median residue level 0.202 mg/kg derived from the residue trials and the PF of 1.2. For maize grain, a value of half the US EPA tolerance (0.05 mg/kg, US EPA, 2006) was used as a surrogate estimate for a median residue value for imported maize kernels.

**Table 3-2:** Input values for the dietary burden calculation

Commodity	Median dietary burden		Maximum dietary burden	
	Input (mg/kg)	Comment	Input (mg/kg)	Comment
<b>Provisional risk assessment residue definition:</b> all compounds forming EMA and HEMA on hydrolysis expressed as acetochlor				
Maize kernels	0.025	½ LOQ US EPA tolerance Corn, field, grain <sup>11</sup>	0.025	½ LOQ US EPA tolerance Corn, field, grain <sup>11</sup>
Cotton meal	0.06	Median residue × PF	0.06	Median residue × PF
Soya meal	0.24	Median residue × PF	0.24	Median residue × PF

PF= processing factor

<sup>11</sup> US Code of Federal Regulations 40 CFR §180.470 acetochlor: tolerances for residues

The results of the dietary burden calculations are summarised in the Table 3-3.

**Table 3-3:** Results of the **dietary** burden calculation

Animals	Median dietary burden (mg/kg bw per d)	Max. dietary burden (mg/kg bw per d)	Highest contributing commodity <sup>(a)</sup>	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
<b>Provisional risk assessment residue definition:</b> all compounds forming EMA and HEMA on hydrolysis expressed as acetochlor					
Dairy cattle	0.003	0.003	Soya meal	0.092	N
Beef cattle	0.004	0.004	Soya meal	0.092	N
Poultry	0.003	0.003	Maize grain	0.048	N
Pigs	0.003	0.003	Maize grain	0.067	N

(a): Related to the maximum dietary burden

The calculated dietary burden indicated that the trigger value of 0.1 mg/kg dry matter (DM) was not exceeded; therefore further considerations regarding residues in livestock and the setting of MRLs in commodities of animal origin are not necessary. This assessment should be considered tentative only, pending the conclusion on the residue definition applicable to the pulses/oilseeds crop group.

#### 4. Consumer risk assessment

Credible consumer risk assessments could not be performed, due to the fact that the nature of residues in harvested oilseeds were not adequately characterised in line with requirements set out in European guidance. Whilst the available primary crop metabolism studies on oilseeds have not adequately identified all the components of the residue in the way that is necessary, it is unclear if the available toxicological reference values for acetochlor would be applicable to the residues that are present in treated soya bean and cotton seed.

#### CONCLUSIONS AND RECOMMENDATIONS

The toxicological profile of acetochlor was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.0036 mg/kg bw per day and an acute reference dose (ARfD) of 1.5 mg/kg bw applicable to acetochlor and some specifically listed transformation products.

In the framework of the peer review, the metabolism of acetochlor in primary crops was investigated in the cereal group only (maize) and the residue definition for enforcement was proposed as “all compounds forming EMA and HEMA on hydrolysis expressed as acetochlor”. In addition, the N-oxamic acid (68) metabolite was included in the residue definition for risk assessment. The residue definition for enforcement placed in the legislation Regulation (EC) No 396/2005 is limited to acetochlor.

Further metabolism studies on the pulses/oilseeds crop group (soya bean and cotton) were submitted in the framework of this MRL application. Several plant metabolites above 0.01 mg/kg in beans of soya bean remained unidentified and it was therefore not possible to conclude on their toxicological profile. Since concerns on the genotoxic and carcinogenic properties of an identified metabolite could not be excluded on the basis of the available data, EFSA concludes that appropriate residue definitions for monitoring and risk assessment cannot be proposed for the pulses/oilseeds crop group, whilst all components present in beans of soya bean above 0.01 mg/kg have not been fully identified.

Residue trials on soya bean and cotton conducted in the USA according to the US GAPs were submitted. Tentative MRLs were derived according to the residue definition for enforcement proposed

in the conclusion of the peer review taking into account all components forming EMA and HEMA on hydrolysis. Note the peer review only considered metabolism in the cereals crop group. Since the residue definitions applicability to the pulses/oilseeds crop group could not be concluded, EFSA does not recommend the setting of import tolerances for soya bean and cotton seed.

Studies investigating the nature and magnitude of acetochlor residues in processed commodities were assessed in the framework of this application for MRL modification. Residues from acetochlor that form EMA and HEMA on hydrolysis were lower in soya and cotton seed oil than in beans and seeds. Concentration of these residues was found in soya bean meal but not cotton seed meal.

Since the proposed use of acetochlor is on imported crops, investigations of residues in rotational crops are not required.

Provisionally, livestock dietary burden calculations were conducted based on acetochlor residues forming EMA and HEMA on hydrolysis. Estimated intakes were below the trigger value of 0.1 mg/kg (dry matter) for all relevant species, and therefore the transfer of acetochlor residues to livestock has not been reconsidered.

Whilst it is not possible to conclude what would be appropriate, applicable toxicological reference values for the unidentified components that are present in beans of soya bean and seed of cotton seed, a valid consumer risk assessment could not be performed.

#### RECOMMENDATIONS

Code number <sup>(a)</sup>	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
<b>Enforcement residue definition: acetochlor</b>				
0401070	Soya bean	0.01*	No proposal	The submitted residue and toxicology data are not sufficient to propose residue definitions for the pulses/oilseeds crop group and therefore, to derive MRL proposals.
0401090	Cotton seed	0.01*		

(a): According to Annex I of Regulation (EC) No 396/2005.

(\*): Indicates that the MRL is set at the limit of analytical quantification.

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## APPENDICES

### A. GOOD AGRICULTURAL PRACTICE (GAPS)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remark (m)
				type (d-f)	conc. a.s. (i)	Method kind (f-h)	growth stage & season (j)	Num-ber (k)	interval min-max	g a.s./hL min max	water L/ha min-max	g a.s./ha min-max		
Soya bean	USA	F	Annual grasses, annual broadleaves	Encapsulated formulation	359	Spraying	Post-emergence, before R2 stage	1		1680-3360	100-200	3360	90	
		F	Annual grasses, annual broadleaves	Encapsulated formulation	359	Spraying	Pre planting (45 days) Post-emergence (stage V5-V6) Last application before R2	3		560-1120	100-200	1120	90	
Cotton	USA	F	Annual grasses, annual broadleaves	Encapsulated formulation	359	Spraying	Post-emergence (2-3 leaf stage) and Second before first bloom	2		840-1680	100-200	1680	90	
		F	Annual grasses, annual broadleaves	Encapsulated formulation	359	Spraying	Post-emergence, before first bloom	1		840-1680	100-200	1680	90	

#### Remarks:

- (a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
- (c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Technical Monograph No 2, 4<sup>th</sup> Ed., 1999 or other codes, e.g. OECD/CIPAC, should be used
- (f) All abbreviations used must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
- (i) g/kg or g/l
- (j) Growth stage at last treatment (Growth stages of mono- and dicotyledonous plants. BBCH Monograph, 2<sup>nd</sup> Ed., 2001), including where relevant, information on season at time of application
- (k) The minimum and maximum number of application possible under practical conditions of use must be provided
- (l) PHI - minimum pre-harvest interval
- (m) Remarks may include: Extent of use/restrictions (i.e. feeding, grazing)

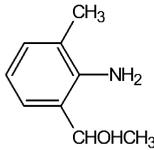
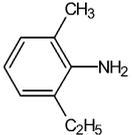
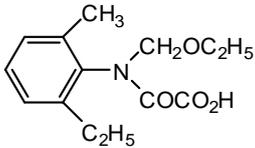
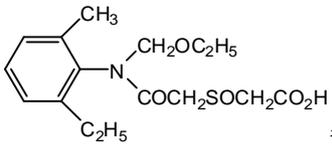
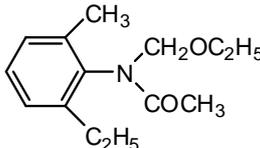
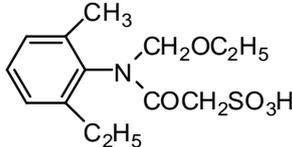
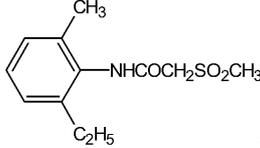
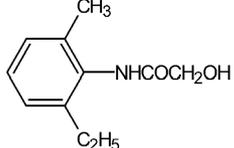
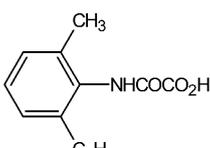
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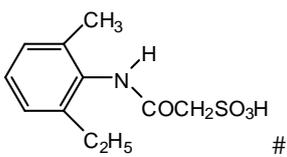
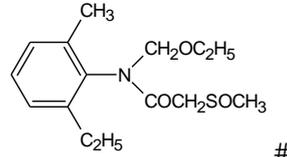
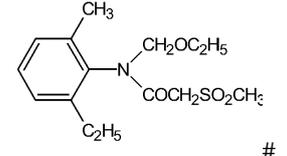
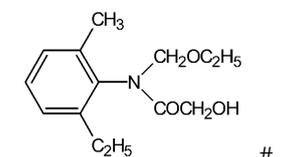
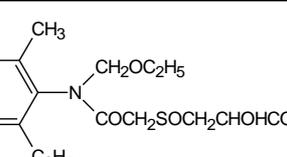
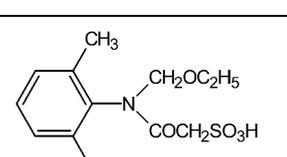
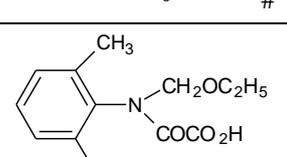
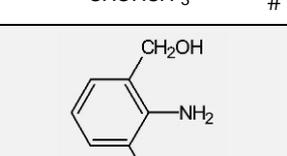
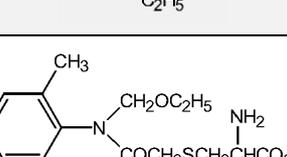
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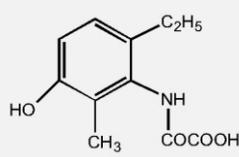
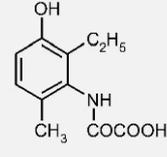
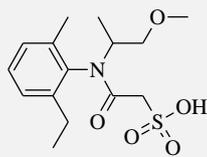
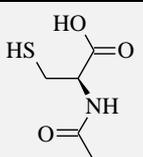
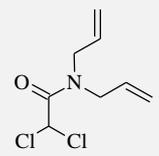
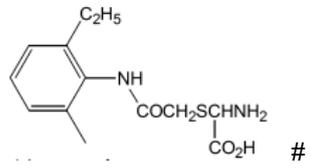
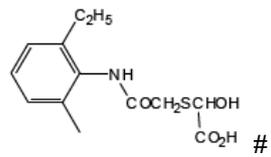
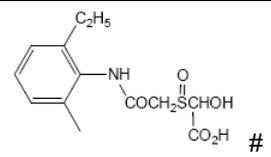
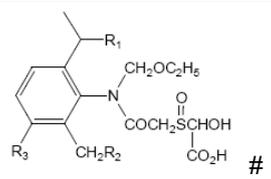
V6: 6<sup>th</sup> trifoliolate BBCH 17

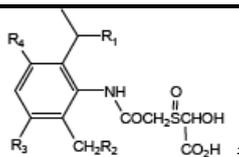
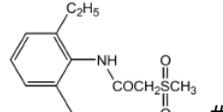
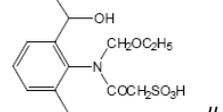
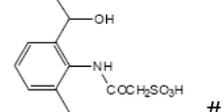
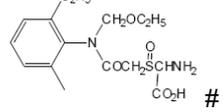
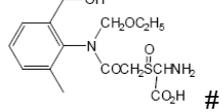
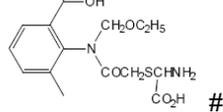
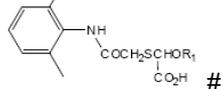
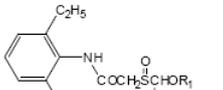
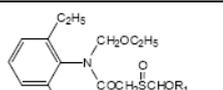
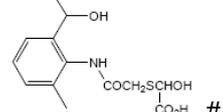
R2: full bloom BBCH 65

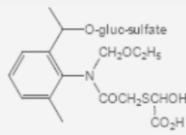
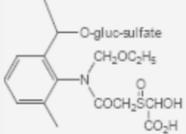
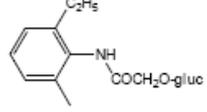
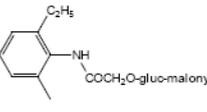
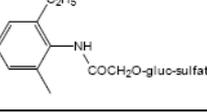
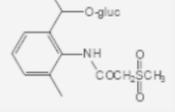
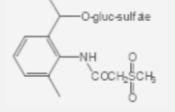
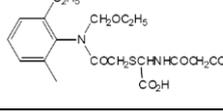
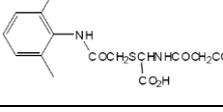
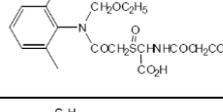
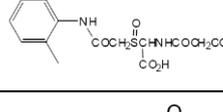
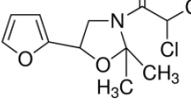
**B. LIST OF METABOLITES AND RELATED STRUCTURAL FORMULA**

Code/Trivial name	IUPAC name	Structure
HEMA (33) CP109703 hydroxyethyl methyl aniline	2-(1-hydroxyethyl)-6-methylaniline	
EMA (34) Compound 52 CP 68594 ethyl methyl aniline	2-ethyl-6-methylaniline	
t-oxanilic acid (2) R290130, compound 17, MON 52766, ICIA5796/17 t-OXA, AcOXA	[(ethoxymethyl)(2-ethyl-6-methylphenyl)amino](oxo)acetic acid	
t-sulfinylacetic acid (3) thioacetic acid sulphoxide, acetochlor thioacetate, Compound 48, MON 52709, ICIA5796/48 t-SSA, AcSAA	[(2-[(ethoxymethyl)(2-ethyl-6-methylphenyl)amino]-2-oxoethyl)sulfinyl]acetic acid	
t-norchloro acetochlor (6) des-chloro acetochlor, Compound 31 MON 52706, ICIA5796/31, CP101592 t-NCA	<i>N</i> -(ethoxymethyl)- <i>N</i> -(2-ethyl-6-methylphenyl)acetamide	
t-sulfonic acid (7) Compound 24, MON52754, ICIA5796/24 t-ESA AcESA	2-[(ethoxymethyl)(2-ethyl-6-methylphenyl)amino]-2-oxoethanesulfonic acid	
s-amide methyl sulfone (10) Compound 14 ICIA5676/14	2-methylsulfonyl- <i>N</i> -(2-ethyl-6-methylphenyl)acetamide	
s-hydroxy (11) Compound 6	2-hydroxy- <i>N</i> -(2-ethyl-6-methylphenyl)acetamide	
s-oxanilic acid (12) Compound 27 CP 91301	[2,6-dimethylphenylamino](oxo)acetic acid	

Code/Trivial name	IUPAC name	Structure
s-sulfonic acid (13) Compound 32 CP 92428 s-ESA EMAsESA	2-[(2-ethyl-6-methylphenyl)amino]-2-oxoethanesulfonic acid	 #
t-amide methyl sulfoxide (15) Compound 11	2-methylsulfinyl-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl) acetamide	 #
t-amide methyl sulfone (16) Compound 12	2-methylsulfonyl-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl)acetamide	 #
t-hydroxy acetochlor (17) Compound 20 CP 68365-3 t-HYD	N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)-2-hydroxyacetamide	 #
t-sulfinyllactic acid (21)	2-(2-carboxy-2-hydroxyethyl) sulfinyl 1-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl) acetamide	 #
Sulfonic acid 2 (24)	2-sulfonyl-N-ethoxymethyl-N-[2-(1-hydroxyethyl)-6-methylphenyl] acetamide	 #
hydroxyethyl-t-oxanilic acid (30)	N-ethoxymethyl-N-[2-(1-hydroxyethyl)-6-methylphenyl]oxamide	 #
HMEA (32) CP 105966	2-hydroxymethyl-6-ethylaniline	
t-amide cysteine (56) Compound 44 t-cysteine conjugate	2-cystein-S-yl-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl)acetamide	 #

Code/Trivial name	IUPAC name	Structure
N-oxamic acid (68) Compound 57 1 of 2 components of PJ2,	[(6-ethyl-3-hydroxy-2-methylphenyl)amino](oxo)acetic acid	
Metabolite 69 (69) Compound 55 ICIA5676/55	[(2-ethyl-3-hydroxy-6-methylphenyl)amino](oxo)acetic acid	
MeESA	2-[(2-ethyl-6-methylphenyl)(2-methoxy-1-methylethyl)amino]-2-oxoethanesulfonic acid	
tert-mercapturic acid	tert-mercapturic acid	
dichlormid	N,N-diallyl-2,2-dichloracetamide	
s-cysteine conjugate		
s-thiolactic acid		
s-sulfinyllactic acid		
hydroxyethyl t-sulfinyllactic acid		 R <sub>1</sub> = OH, R <sub>2</sub> = H, R <sub>3</sub> = H

Code/Trivial name	IUPAC name	Structure
hydroxyethyl s-sulfinyllactic acid and 5-hydroxy s-sulfinyllactic acid		 <p>R<sub>1</sub> = OH, R<sub>2</sub> = H, R<sub>3</sub> = H, R<sub>4</sub> = H R<sub>1</sub> = H, R<sub>2</sub> = H, R<sub>3</sub> = OH, R<sub>4</sub> = H</p>
s-methylsulfone		
hydroxyethyl t-sulfonic acid		
hydroxyethyl s-sulfonic acid		
t-cysteine sulfoxide		
hydroxyethyl t-cysteine sulfoxide		
hydroxyethyl t-cysteine		
s-thiolactic acid glucose and malonyl conjugates		 <p>R<sub>1</sub> = glucose, R<sub>1</sub> = malonyl</p>
s-sulfinyllactic acid glucose and malonyl conjugates		 <p>R<sub>1</sub> = glucose, R<sub>1</sub> = malonyl</p>
t-sulfinyllactic acid glucose and malonyl conjugates		 <p>R<sub>1</sub> = glucose, R<sub>1</sub> = malonyl</p>
hydroxyethyl s-thiolactic acid		

Code/Trivial name	IUPAC name	Structure
Hydroxyethyl t-thiolactic acid glucosylsulfate conjugate		
Hydroxyethyl s-thiolactic acid glucosylsulfate conjugate		
s-Hydroxyacetochlor glucose conjugate		 #
s-Hydroxyacetochlor glucose malonyl conjugate		 #
s-Hydroxyacetochlor glucose sulfate conjugate		 #
Hydroxyethyl s-methylsulfone glucose conjugate		
Hydroxyethyl s-methylsulfone glucosylsulfate conjugate		
t-Malonylcysteine		 #
s-Malonylcysteine		 #
t-Malonylcysteine sulfoxide		 #
s-Malonylcysteine sulfoxide		 #
furilazole	( <i>RS</i> )-3-dichloroacetyl-5-(2-furanyl)-2,2-dimethyl-1,3-oxazolidine	

#: Metabolites hydrolysed to EMA or HEMA with a pertinent analysis method  
 Metabolites not forming EMA or HEMA under hydrolysis are greyed.

### C. ABBREVIATIONS

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CEN	European Committee for Standardisation (Comité Européen de Normalisation)
CF	conversion factor for enforcement to risk assessment residue definition
cGAP	critical GAP
CIPAC	Collaborative International Pesticide Analytical Council
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DALA	days after last application
DAR	Draft Assessment Report
DAT	days after treatment
DM	dry matter
EC	European Community
EFSA	European Food Safety Authority
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
EU	European Union
EURLs	EU Reference Laboratories (former CRLs)
FAO	Food and Agriculture Organisation of the United Nations
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (former GIFAP)
ha	hectare
hL	hectolitre
HPLC	high performance liquid chromatography
HR	highest residue
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
L	litre
LOAEL	lowest observed adverse effect level
LOQ	limit of quantification
MRL	maximum residue level
MS	mass spectrometry
MS/MS	tandem mass spectrometry

NEU	northern European Union
OECD	Organisation for Economic Co-operation and Development
PF	processing factor
PHI	pre-harvest interval
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (method)
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SEU	Southern European Union
STMR	supervised trials median residue
TRR	total radioactive residue