Mesotrione

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 6 Supplement

RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

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

Table of Contents

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

This document supports the application for renewal of the regulatory approval of mesotrione under Commission Implementing Regulation (EU) 844/2012 of 18 September 2012. This document reviews the metabolism and residues data, including additional data and risk assessments, for mesotrione.

Mesotrione was included in Annex I of Council Directive 91/414/EEC (Commission Directive 2003/68/EC of 11 July 2003). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011.

In accordance with Commission Implementing Regulation (EU) 844/2012, this document summarises new information which are relevant for the renewal of the approval of mesotrione under Regulation (EC) 1107/2009. Where appropriate this document refers to the Commission Implementing Regulation (EU) No. 540/2011 for mesotrione and to the Review Report for mesotrione (SANCO/1416/2001 – Final, 14 April 2003), and in particular the endpoints provided in Appendices I and II thereof.

This document covers data and risk assessments which were not part of the original dossier and which are necessary to reflect changes:

- In requirements under Commission Regulation (EU) No 283/2013, and the associated Annex, which repeals Commission Regulation (EU) No 544/2011 which, under Regulation (EC) 1107/2009, replaced the requirements of Annex II to Directive 91/414/EEC

- In scientific and technical knowledge since the approval or last renewal of the approval

- To representative uses

Where the conclusions of the EU review had specific areas of concern on mesotrione, new data and/or reviews and/or risk assessments have been provided. Where additional and/or new data on mesotrione are provided, a justification has been included. Also a justification has been given if new data are required but none were provided.

Details of the literature search undertaken can be found in M-CA Section 9. If a relevant scientifically peer-reviewed open literature reference has been identified for mesotrione or its major metabolites, it has been discussed within the relevant data point.

A major proposal in this document is the request for a change of definition of Residue of crops for both enforcement and risk assessment (see Point CA 6.7.1). To support this proposal a number of additional studies have been submitted. These include the metabolism studies on peanuts and herbicide tolerant soya beans and the residue studies on sweet corn, poppy seed, linseed, oilseed rape and HT soya beans. This has been made clear at the start of each section. Maize is the representative crop in this submission and for this reason is the only crop to be included for dietary burden and risk assessment calculations.

CA 6.1 Storage stability of Residues

Stability of residues during storage of samples

The stability of mesotrione and its metabolite MNBA (4-methylsulfonyl-2-nitro benzoic acid) was investigated in maize grain, maize forage, maize fodder, soybean seed, and radish root.

Commodity	Author/s	Issue Year	Report Number
Maize, radish, soybean	Wiebe LA	1997	RR 97-042B INT

Resulting from the original evaluation of the results from this interim study report, mesotrione and MNBA were considered to be stable under freezer storage at -18°C ± 5°C in maize grain, maize fodder, and maize forage for at least 17 months, in radish root for at least 15 months and in soybean seed for at least 14 months.

All data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.7, December 1999**).

The final report of this study comprising an extension of the storage period is now available and presented in the following summary.

Report:	KCA 6.1/01. Wiebe, L.A. and Peyton C.S. (1999), ZA1296: Stability of ZA1296 and the Metabolite MNBA in Frozen Crops (Final Report), Report Number RR 97-042B FIN, Zeneca Inc., Western Research Center, Richmond, CA, USA. Syngenta File No: ZA1296/0125

Guidelines

EPA Pesticide Assessment Guideline Subdivision O, Section 171-4(e), superseded by OPPTS 860.1380 (compliant with the requirements of EU Directive 91/414/EEC)

GLP

The study was carried out according to the principles of good laboratory practice.

EXECUTIVE SUMMARY

Samples of maize grain, maize forage, maize fodder, radish root, and soybean seed were each fortified at 0.1 mg/kg with either mesotrione or MNBA. Duplicate samples were stored under frozen conditions (-18°C ± 5°C) and analysed at intervals over 40 to 44 months (7-8 sampling points). Both mesotrione and MNBA fractions were each quantified as 2-amino-4-methylsulfonyl benzoic acid (AMBA) by HPLC fluorescence detection. The limit of quantification for mesotrione and MNBA was 0.01 mg/kg.

Residues of mesotrione and MNBA were found to be stable in maize grain and maize fodder for at least 42 months, in maize forage for at least 31 months, in radish root for at least 44 months, and in soybean seed for at least 40 months when stored in the freezer.

Materials:

Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-1.

Table 6.1-1: Purity of analytical standards

Analyte	Standard Reference No.	Purity (wt. %)
ZA1296	ASW 1581A ASW 01662-01R	99.5 99.7
MNBA	ASW 1580A ASW 01714-01A	99 99.6

Analyte	Standard Reference No.	Purity (wt. %)
AMBA	ASW 1664-01R	99
	ASW 1664R	99
	ASW 01725-01A	99

Test Commodities

Test commodities were maize grain, maize forage, maize fodder, radish root, and soybean seed. Samples were either control samples from magnitude-of-the-residue studies carried out for Zeneca Ag Products or were purchased fresh from the market.

Test Facilities

This study was performed at Zeneca Ag Products, Western Research Center, 1200 South 47 Street, Richmond, CA 94804-4610, USA.

Study Design and Methods:

Fortification and Storage of Samples

Samples of maize grain, maize forage, maize fodder, radish root and soybean seed were each fortified at 0.1 mg/kg with either mesotrione or MNBA. Duplicate samples were stored under frozen conditions (-18°C ± 5°C) and analysed at intervals over 40 to 44 months (7-8 sampling points).

Analytical Method

Analysis of the samples was performed according to the methods TMR0643B and TMR0882B.

Commodity	Author/s	Issue Year	Report Number
Crops	Alferness, PL	1996	TMR0643B
Crops	Alferness PL	1999	TMR0882B

The methods include extraction of the samples with acetonitrile:water mixture (1:1 v:v), followed by either partitioning with ethyl acetate and solid-phase extraction cleanup or evaporation of acetonitrile. After separation via reversed-phase HPLC, the elution volumes of mesotrione and MNBA were collected. MNBA was reduced to AMBA using $SnCl_2$ in HCl. Mesotrione was oxidised to MNBA with hydrogen peroxide, followed by reduction to AMBA as before. Both mesotrione and MNBA fractions were each quantified as AMBA by HPLC fluorescence detection. The limit of quantification for mesotrione and MNBA was 0.01 mg/kg.

All data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.7, December 1999**).

Results and Discussion:

Method Validation

Procedural recoveries and blanks were determined using freshly fortified samples at each interval. Maize grain, maize forage, maize fodder, radish root, and soybean seed samples were fortified with mesotrione and MNBA at 0.1 mg/kg. Mean recoveries and %RSD are summarised in Table 6.1-2.

Table 6.1-2: Summary of procedural recoveries

Crop/ Commodity	mesotrione		MNBA	
	Mean Recovery (%)	RSD (%)	Mean Recovery (%)	RSD (%)
Maize grain	91	12	90	9
Maize Forage	77	5	85	17
Maize Fodder	72	21	87	14
Radish Root	90	11	92	10
Soybean Seed	88	9	98	10

Storage Stability of Residues

No residues above the limit of quantification of 0.01 mg/kg for each analyte were found in the control samples.

The recoveries of mesotrione and MNBA after storage at -18°C ± 5°C are respectively summarised in the Table 6.1-3 and Table 6.1-4 below. Unless otherwise indicated, the results presented are an average of duplicate samples and are not corrected for freshly fortified recoveries.

Table 6.1-3: Freezer storage stability for mesotrione at 0.1 mg/kg in maize grain, maize forage, maize fodder, radish root, and soybean seed

Month of storage	Maize grain (% recovery)	Maize forage (% recovery)	Maize fodder (% recovery)	Radish root (% recovery)	Soybean seed (% recovery)
0	72	79	53*	86	89
0.5			58		
1	89	70	61	79	
2					80
3		75	77		78
4	86				
5				94	
6					79
7			86	80	
8	81	75			
13				87	
14					102
15				77	
17	86		78		
18		74			
29					129
30			110		
31	109	81			97
32				104	
40					91*
42	86	65*	73*		
44				85	

*single value reported; duplicate sample lost during sample cleanup

Table 6.1-4: Freezer storage stability for MNBA at 0.1 mg/kg in maize grain, maize forage, maize fodder, radish root, and soybean seed

Month of storage	Maize grain (% recovery)	Maize forage (% recovery)	Maize fodder (% recovery)	Radish root (% recovery)	Soybean seed (% recovery)
0	79	78	76	95	92
0.5			87		
1	88	89	85	83	
2					81
3		86	92		84
4	86				
5				89	
6					101
7			100	90	
8	80	84			
13				91*	
14					114
15				80	
17	103		107		
18		105			
29	89		87		94
30			81		
31		85			
32				81	
40					92
42	100	85*	91		
44				93	

*single value reported; duplicate sample lost during sample cleanup

Conclusions:

Results of this study indicate that residues of mesotrione and MNBA are stable in maize grain and maize fodder for at least 42 months, in maize forage for at least 31 months, in radish root for at least 44 months, and in soybean seed for at least 40 months when stored in the freezer.

In this study, commodities with high water content (maize forage, maize fodder), high oil content (soybean seed), high protein content (soybean) and high starch content (radish root and maize grain) were investigated. Sufficient data are available to extrapolate to all other crop commodities according to EU guidelines (EU guideline Document 7032/VI/95 rev. 5) with the exception of high acid crop types. The representative uses of mesotrione supported in this submission are not on high acid crop types and therefore no further in information is required.

A residue definition for animal products has not been proposed **(see Section CA 6.7.1**), since the uses of mesotrione will not lead to significant residues in any edible animal tissue or milk. Thus, no stability data in commodities of animal origin are required.

Stability of residues in sample extracts

Procedural recoveries obtained during residue analysis demonstrate the stability of residues of mesotrione and MNBA in sample extracts.

CA 6.2 Metabolism, Distribution and Expression of Residues

CA 6.2.1 Metabolism, distribution and expression of residues in plants

Metabolism, distribution and expression of residues in maize

The metabolism of mesotrione has been studied in maize using ^{14}C-mesotrione labelled in each crucial substructure ([cyclohexane-2-^{14}C]- and [phenyl-U-^{14}C]-mesotrione).

All data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.1.1, December 1999**).

Commodity	Author/s	Issue Year	Report Number
Corn	Wei Y and Dohn D.R	1997	ZA1296/0405
Corn	Tarr J.B and van Neste L	1997	ZA1296/0404

EXECUTIVE SUMMARY

Two metabolism studies in maize (*Zea mays*) were carried out using mesotrione [^{14}C] radiolabelled at both crucial substructures ([cyclohexane-2-^{14}C] mesotrione and [phenyl-U-^{14}C] mesotrione). Separate plots for pre-emergence and post-emergence application were established. [^{14}C] mesotrione was applied pre-emergence after planting the seeds at a rate of 280 g a.s./ha (RR 96-007B) and 307 g a.s./ha (RR 96-026B) and post-emergence 28 days after planting at a rate of 161 g a.s./ha (RR 96-026B) and 164 g a.s./ha (RR 96-007B). Plant samples of forage (55 days after planting) and of grain and straw from mature crops (125 days after post-emergence treatment) were taken.

Radioactivity was measured by liquid scintillation counting (LSC). Samples were extracted and fractionated. Chemical and enzymatic hydrolysis was carried out. Compounds were analysed by co-chromatography with reference compounds using normal and reversed Thin Layer Chromatography (TLC) and reversed-phase HPLC.

Residue profiles were essentially the same after pre- or post-emergence application. Total radioactive residues (TRR) in grain were low (≤0.014 mg/kg). Single extractable radioactive residues in water/acetonitrile extracts of grain were <0.01 mg/kg and not further analysed. In forage samples (post-emergence), mesotrione was present at trace levels (<0.01 mg/kg), 4-hydroxy mesotrione was found up to 0.016 mg/kg and MNBA and AMBA accounted for 3.3% and 13.1% of TRR, respectively (RR 96-007B). Also evidence for the fragmentation of the cyclohexane ring and incorporation of the radiolabelled carbon into natural products was found. This was underpinned by the results obtained from analysis of fodder samples (RR 96-026B). Key metabolites identified in fodder (post-emergence, RR 96-007B) were 4-hydroxy mesotrione (0.007 mg/kg), MNBA (0.019 mg/kg) and AMBA (0.301 mg/kg). AMBA was found primarily in a variety of conjugated forms. Attempts to release conjugated AMBA residues were investigated using fodder samples and the results demonstrated that acid or base hydrolysis did not successfully free AMBA. Additionally, a variety of enzymes (porcine carboxylic acid esterase, papain and pancreation) were tested for their ability to release free AMBA from fodder extracts. None of these enzyme preparations were effective.

Based on the results, the following pathway was proposed. Mesotrione was cleaved into MNBA which was subsequently reduced to AMBA. Conjugates of AMBA were formed. Mesotrione was also hydroxylated to 4-hydroxy mesotrione. Furthermore, mesotrione became part of the carbon pool and was incorporated into plant constituents.

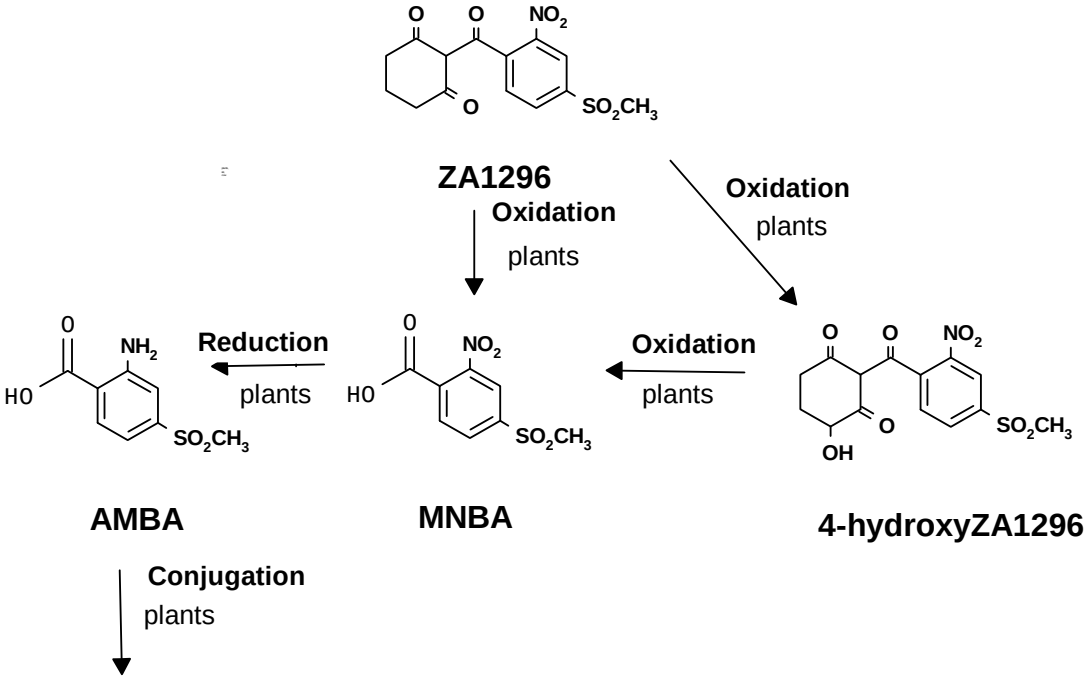
Proposed metabolic pathway for mesotrione in maize

The proposed metabolic pathway for mesotrione in maize involves oxidation followed by cleavage of the cyclohexane ring, which is further broken down to smaller fragments which are incorporated into sugars and proteins.

4-hydroxy mesotrione and MNBA were minor residues in forage and fodder and were present at a maximum of 6.6% of the TRR (up to 0.016 mg/kg). The major residue in forage and fodder was AMBA which was present at a maximum of 28.2% of the TRR (up to 0.301 mg/kg), found primarily in a variety of conjugated forms.

The proposed metabolic pathway is given in Figure 6.2.1-1.

Figure 6.2.1-1: Proposed metabolic pathway for mesotrione in maize



Conclusions:

The results obtained from experiments with [cyclohexane-2-^{14}C] mesotrione and [Phenyl-U-^{14}C] mesotrione on maize indicated that mesotrione was metabolised to 4-hydroxy-mesotrione and MNBA which was further reduced to AMBA which formed complex conjugates. The method and timing (pre- or post-emergence) of the application of mesotrione had little effect on the nature of the residues.

Additional plant metabolism studies

Metabolism studies of mesotrione in peanuts and herbicide tolerant (HT) soybean have also been conducted. These studies were not available during the first EU evaluation of mesotrione and to support the new proposed residue definition full summaries are presented here.

Metabolism, distribution and expression of residues in peanuts

Report:	KCA 6.2.1/01. Brumback, D. (2003), [Cyclohexane-2-^{14}C] Mesotrione: Nature of the Residue in Peanuts, Report Number 1287-01; Syngenta Crop Protection, Inc., Greensboro, NC 27419, USA. Syngenta File Number ZA1296/1350

Guidelines

EPA Residue Chemistry Test Guideline OPPTS 860.1300, Nature of the Residue in Plants (August 1996).

GLP

The study was carried out according to the principles of good laboratory practice.

EXECUTIVE SUMMARY

This study was designed to provide information on the magnitude and nature of residues following pre-emergence applications of mesotrione in peanuts (*Arachis hypogaea var.* NCV 11). Mesotrione, labelled in C-2 of the cyclohexane ring ([cyclohexane-2-^{14}C]-mesotrione) was used. Peanuts were planted in silt loam soil in three outdoor subplots. ^{14}C-Mesotrione was solubilised in acetonitrile and diluted with aqueous Callisto 4SC blank formulation. Two application rates of [cyclohexane-2-^{14}C]-mesotrione were used during the study, in addition to a control. [Cyclohexane-2-^{14}C]-mesotrione was applied to the soil surface after planting the seeds (pre-emergence) using a back-pack sprayer at rates of 327 g a.s./ha and 836 g a.s./ha. The radioactive residues in samples of peanut foliage harvested 90 days after planting (50% mature) and mature peanut hay, hulls and nutmeat, harvested 154 days after treatment, were quantified and characterised.

Auxiliary in vitro experiments with peanut cell culture and excised peanut shoots were performed to generate metabolites for identification. Peanut cells were dosed at 50 mg/L [cyclohexane-2-^{14}C]-mesotrione diluted in dimethyl sulfoxide (DMSO) and harvested 7 and 14 days after dosing. Peanut shoots were dosed at 100 mg/L and harvested after 2 days.

A subsample of each plant commodity type was homogenised in the presence of dry ice and the radioactive residue determined by combustion/LSC. Peanut samples that contained a radioactive residue greater than 0.01 mg/kg were analysed further.

Radioactivity was measured by LSC. Samples were extracted using a number of solvents of varying polarities and fractionated. Further treatment included chemical and enzymatic hydrolysis and methylation and were carried out as appropriate. Extractable radioactivity was analysed by co-chromatography with reference compounds using normal and reverse-phase thin layer chromatography (TLC) and reverse-phase HPLC. Additional separation was performed by anion exchange chromatography where necessary. For metabolite identification, mass spectrometry and NMR were also used for the metabolites isolated from the in vitro experiments.

After treatment with [cyclohexane-2-^{14}C]-mesotrione at 327 g a.s./ha and 836 g a.s./ha, the total radioactive residues (TRRs) were 0.006 mg/kg and 0.020 mg/kg in 50% mature foliage, 0.004 and 0.011 mg/kg in peanut hay, 0.005 mg/kg and 0.015 mg/kg in hulls and 0.007 mg/kg and 0.022 mg/kg in nutmeat, respectively. No further analysis was performed on the samples treated at the lower application rate due to the very low TRRs obtained.

Characterization of extracts from 50% mature foliage, hay and hull fractions treated at 836 g a.s./ha of [cyclohexane-2-^{14}C]-mesotrione showed similar complex mixtures of components with one significant peak. This component was also generated by the in vitro metabolism of [cyclohexane-^{14}C]-mesotrione in peanut cell cultures. It was identified as 4-hydroxy mesotrione and

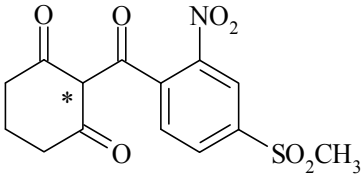
co-chromatographed with the significant peak in peanut foliage extracts. The peanut oil fraction was shown to be composed primarily of ^{14}C-labelled neutral lipids resulting from metabolism of mesotrione to single carbon units that entered the carbon pool.

In conclusion the results indicated that mesotrione was metabolised to 4-hydroxy-mesotrione and to single carbon units that were subsequently further incorporated into the lipid biopathway.

MATERIALS AND METHODS

Materials

Test Materials

Structure/Label	[Cyclohexane-2-^{14}C]-mesotrione
	 ($* = ^{14}C$ position)
Common name	Mesotrione
Syngenta code	ZA1296
CAS Number	104206-82-8
Batch number	CL-L-84
Specific Activity	1.48 MBq/mg
Radiochemical Purity	97.8% by TLC

Test System

Peanut (*Arachis hypogaea*), variety NCV 11 were used for the field phase and variety Jumbo Virginia 5123 was used for the *in vitro* experiments.

Test Soil

A silt loam soil was used in this study.

Test Facilities

The biological phase was performed at Syngenta Crop Protection, Inc., Southern Regional Technical Center, Leland, MS 38756, USA.

The analytical phase was performed at Vero Beach Research Center (VBRC), Syngenta Crop Protection, Inc., Vero Beach, FL 32967, USA and Syngenta Crop Protection, Inc., Greensboro, NC 27419, USA.

Study Design and Methods

Field Phase

The field phase was conducted in Leland, MS, USA. Peanuts (variety NCV 11) were planted in rows approximately 1 m apart in three separate outdoor subplots, one for each treatment group and a control plot. The temperature ranged from 19°C to 31°C with a daily average of 22°C. The cumulative

precipitation was 658 mm. ^{14}C-Mesotrione was solubilised in acetonitrile and diluted with aqueous Callisto 4SC blank formulation. Pre-emergence applications were made by spraying [cyclohexane-2-^{14}C]-mesotrione onto the test plots one day after planting with a hand held spray boom. Two application rates were used; 327 g a.s./ha and 836 g a.s./ha, in addition to a control.

Table 6.2.1-1: Mesotrione application details

Target application rate	280 g a.s./ha	840 g a.s./ha
Achieved application rate	327 g a.s./ha	836 g a.s./ha
Number of applications	1	1
Formulation	Acetonitrile and aqueous Callisto 4SC blank formulation	Acetonitrile and aqueous Callisto 4SC blank formulation
Amount Mesotrione applied	237.3 mg (2.055 x 10^{10} dpm, or approx.9.259 mCi or approx. 342.6 MBq)	703.3 mg (6.09 x 10^{10} dpm or approx. 27.441 mCi or approx. 1015.3MBq)
Plot size	Approx. 4.16 m^2 (approx. 1.52 x 2.74 m)	Approx 4.16 m^2 (approx. 1.52 x 2.74 m)
Spray volume	Approx. 200 mL	Approx. 210 mL
Method of application	Hand held spray boom	Hand held spray boom
Application	1 day after planting	1 day after planting
Environmental conditions	Outdoor plot	Outdoor plot

Auxiliary *In vitro* Experiments

Peanut cells cultures were obtained from sterile peanut shoots (variety Jumbo Virginia 5123). After 7 days of subculturing in media at 25°C, shaken at 100 rpm, peanut cells were treated with 50 mg/L of [cyclohexane-^{14}C]-mesotrione diluted in DMSO. Peanut cells were harvested 7 and 14 days after treatment and stored frozen until analysis. Additionally, peanut plants were germinated in growth media under greenhouse conditions, harvested at the first true leaf stage of development and excised. Excised shoots were treated with 100 mg/L of [cyclohexane-^{14}C]-mesotrione and harvested after 2 days.

Test Samples

Soil core samples were collected prior to application, post-application, at 50% mature harvest and at the final harvest. A total of 8 samples were collected for each application rate of [cyclohexane-2-^{14}C]-mesotrione and a total of four samples were taken for the control. All samples were stored frozen until analysis.

Peanut foliage was harvested 90 days after application (50% maturity). Mature peanuts and peanut hay were harvested 154 days after application. After sampling, mature peanuts were separated into hulls and nutmeat. All samples were stored frozen until analysis.

Sample Preparation

Plant samples were homogenised with solid carbon dioxide using a Wiley or Rotoplex mill. Soil cores homogenised without solid carbon dioxide. Following homogenisation, the samples were analysed by combustion/LSC of sub-samples, to determine the level of radioactive residue present. Radioactivity in liquid samples was determined directly by LSC.

Extraction and Fractionation of Residues

Plant samples having radioactive residues greater than or equal to 0.010 mg/kg were extracted. The radioactive residues in the peanut foliage, hay and hulls were extracted with a mixture of water and

acetonitrile (8:2). Due to the high oil content, nutmeat was sequentially extracted with hexane, hexane:ethyl acetate and twice with acetonitrile:water (8:2) and the filtrates/extracts combined. All extracts were radioassayed by LSC. The pellets or filtercakes were extracted using acetonitrile:water (8:2), air dried, combusted, and radioassayed.

Aliquots of the extracts were partitioned between aqueous and organic phases, i.e. hexane or methanol and chloroform, using separating funnels. Both phases were radioassayed.

An aqueous buffer mixture of 0.1 M sodium acetate buffer and 0.1 M acetic acid (1:1) was added to selected subsample extracts. Following addition of cellulase and amyloglucosidase enzymes to the extracts, the samples were incubated for approximately 16 hours at 37 to 47°C.

The nutmeat extracts were acidified to pH 1 with 12 N hydrochloric acid after microwave treatment and partitioning between water and hexane.

When required, samples were methylated using diazomethane. Samples were concentrated to dryness and an ethereal solution of diazomethane was added. After 2 hours, the reaction mixture was dried under nitrogen and subsequently dissolved in acetonitrile.

Soil core samples were extracted sequentially using acetonitrile:water (80:20), ethyl acetate, acetonitrile:0.5 N hydrochloric acid and 0.5 N sodium hydroxide. The PESs were air-dried and combusted to determine the unextracted (bound) residues.

Chromatography

Components in extracts were separated using 2-dimensional normal phase TLC on silica gel plates with different solvent systems, mostly ethyl acetate:n-propanol:water:acetic acid (64:22:12:2 v/v/v/v) and methyl ethyl ketone:acetonitrile:acetic acid:water (80:16:4:6 v/v/v/v). Reversed-phase HPLC coupled to a UV detector, radioisotope flow monitor and a fraction collector was also used. Additional separation was performed by anion exchange chromatography where necessary.

Components in extracts were identified using co-chromatography with a number of proposed metabolites; mesotrione, ^{14}C-mesotrione, 4-hydroxy-mesotrione. In addition a number of radiolabelled triglyceride standards were also used (1-stearoyl-20[1-^{14}C]archidonyl-sn-glycerol, trimyristin[myristic-1-^{14}C], triolein[carboxyl-^{14}C], tripalmitin[palmitic-1-^{14}C], and trilinolenin[linolenic-1-^{14}C]) to investigate the possibility that mesotrione can be metabolised into smaller moieties that enter the carbon pool for lipid biosynthesis.. Additional confirmation and identification was undertaken using tandem mass spectrometry and ^{1}H-NMR for the metabolites isolated from the in vitro experiments.

RESULTS AND DISCUSSION:

Characterisation of residues

Overview

In samples where total radioactive residues (TRRs) >0.01 mg/kg were determined, characterisation using a series of extraction and fractionation techniques was performed. The results from the extraction of samples are summarised in Table 6.2.1-2 to Table 6.2.1-4.

Samples of peanuts treated with [cyclohexane-2-^{14}C]-mesotrione at the lower dose rate of 327 g a.s./ha resulted in very low TRRs; 0.006 ppm in peanut foliage (50% mature), 0.004 ppm in peanut hay, 0.005 ppm in peanut hulls and 0.007 ppm in nutmeat. No further analysis or processing of commodities from this application rate was therefore performed.

Plants treated with a higher application rate of 836 g a.s./ha of [cyclohexane-2-^{14}C]-mesotrione showed evidence of initial phytotoxicity when compared to the control plants and plants treated at the lower application rate. The stunted plants recovered but reached maturity later than the other plants used in the study.

For plants treated at the higher application rate the following TRRs were observed; 0.020 mg/kg in peanut foliage (50% mature), 0.011 mg/kg in peanut hay, 0.015 mg/kg in peanut hulls and 0.022 mg/kg in nutmeat. Extraction of the peanut foliage, hay and hull samples with acetonitrile:water solubilised 38.9% TRR (0.008 mg/kg) from 50% mature foliage, 28.2% TRR (0.003 mg/kg) from hay and 19.9% TRR (0.003 mg/kg) from the hulls. Extraction of nutmeat with acetonitrile:water and then with non polar solvents solubilised a total of 56.1% TRR. Following extraction 65.9% TRR for 50% mature foliage samples, 71.6% for mature hay samples, 84.5% TRR for hulls and 50.8% TRR for nutmeat samples remained unextracted.

Two auxiliary *in vitro* experiments with excised peanut plants and peanut cell cultures, were performed to better understand the transformation pathway of mesotrione in peanuts. The excised extracts showed one major metabolite that was identified as 4-hydroxy-mesotrione. This metabolite co-chromatographed with the major peak identified in peanut foliage extracts.

Residues in Soil

Analysis of the soil core samples confirmed that the mean estimates for the pre-emergence application rates to the test plots (327 and 836 g a.s./ha) were comparable to the calculated treatment application rates of 280 and 840 g a.s./ha.

Residues in 50% Mature Peanut Foliage

The TRR in peanut foliage was low (0.020 mg/kg) following pre-emergence treatment with [cyclohexane-2-^{14}C]-mesotrione, at an application rate of 836 g a.s./ha. Following extraction with neutral solvent, 38.9% TRR was solubilised and 65.9% TRR remained in the PES. The soluble residues present in the peanut foliage samples were characterised, using anion exchange chromatography, as a mixture of early eluting neutral/basic components and later eluting acidic components consisting of multiple peaks. The TRR for both the neutral/basic components and acidic components was 0.003 mg/kg (11.7% TRR and 17.3% TRR, respectively). Further characterisation using C18 SPE and HPLC was carried out. Individual components in these neutral/basic and acid fractions were <0.001 mg/kg (<5% TRR).

The residues detected are summarised in Table 6.2.1-2 for [cyclohexane-2-^{14}C]-mesotrione treated peanut foliage.

Table 6.2.1-2: Summary of radioactive residues in peanut foliage samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Crop and Commodity:		Peanut foliage	
Application Rate:		836 g a.s./ha	
Total Radioactive Residue:		0.020 mg/kg	
Initial extraction (%TRR):		0.008 mg/kg, (38.9%)	
Origin of component	**Component**	**mg/kg**	**%TRR**
Anion exchange fractionation of extractable components	**Neutral/base components**	0.003	11.7
	Acidic components[1]	0.003	17.3
	Organic wash	<0.001	1.2
Unextractable (PES)		0.013	65.9
Total (characterised)[2]		0.006	30.2

Crop and Commodity:		Peanut foliage	
Application Rate:		836 g a.s./ha	
Total Radioactive Residue:		0.020 mg/kg	
Initial extraction (%TRR):		0.008 mg/kg, (38.9%)	
Origin of component	**Component**	**mg/kg**	**%TRR**
Losses/gains on fractionation[3]		<0.001	3.9
Total		0.020	100

- Not applicable
1 Three separate regions 5.6, 3.5 and 8.2% TRR
2 Sum of anion exchange fractions
3 Sum of anion exchange fractions and PES compared to radioactive residues measured by combustion. Individual components in these neutral/basic and acid fractions were <0.001 mg/kg (<5% TRR)

Residues in Mature Peanut Hay

The TRR in peanut hay was low (0.011 mg/kg) following pre-emergence treatment with [cyclohexane-2-^{14}C]-mesotrione, at an application rate of 836 g a.s./ha. Following extraction with neutral solvent, 28.2% TRR was solubilised and 71.3% TRR remained in the PES. The soluble residues present in the peanut hay samples were characterised, using anion exchange chromatography, as a mixture of early eluting neutral/basic components and later eluting acidic components consisting of multiple peaks. The TRRs were 0.001 mg/kg (6.7% TRR) for the neutral/basic components and 0.002 mg/kg (16.0% TRR) for the acidic components. Partitioning of the neutral/base and acidic components was performed, followed by reverse-phase HPLC. The significant peak identified in the acid components was characterized as 4-hydroxy mesotrione (1.4% TRR).

The residues detected are summarised in Table 6.2.1-3 for the [cyclohexane-2-14C]-mesotrione treated peanut hay.

Table 6.2.1-3: Summary of radioactive residues in peanut hay samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Crop and Commodity:		Peanut hay	
Application Rate:		836 g a.s./ha	
Total Radioactive Residue:		0.011 mg/kg	
Initial extraction (%TRR):		0.003 mg/kg, (28.2%)	
Origin of component	**Component**	**mg/kg**	**%TRR**
Anion exchange fractionation of extractable components	**Neutral/base components**	0.001	6.7
	Acidic components[1]	0.002	16.0
	Organic wash	<0.001	1.4
Unextractable (PES)		0.008	71.6
Total (characterised)[2]		0.003	24.1
Losses/gains on fractionation[3]		<0.001	4.3
Total		0.011	100

- Not applicable
1 Two separate regions 7.9 and 8.1% TRR. Contained a component characterised as 4-hydroxy mesotrione (1.4% TRR)
2 Sum of anion exchange fractions
3 Sum of anion exchange fractions and PES compared to radioactive residues measured by combustion.

Residues in Mature Peanut Hulls and Nutmeat

The TRRs in both peanut hulls and nutmeat were low (0.015 and 0.022 mg/kg, respectively) following pre-emergence treatment with [cyclohexane-2-^{14}C]-mesotrione, at an application rate of 836 g a.s./ha.

In the peanut hulls, following extraction with neutral solvent, 19.9% TRR was solubilised and 84.5% TRR remained in the PES. The soluble residues were identified, using anion exchange chromatography, as a mixture of early eluting neutral/basic components and later eluting acidic components consisting of multiple peaks (none greater than 5% TRR, 0.001 mg/kg). The TRRs were <0.001 mg/kg (4.4% TRR) for the neutral/basic components and 0.003 mg/kg (12.6% TRR) for the acidic components. Partitioning of the neutral/base and acidic components was performed, followed by reverse-phase HPLC. A significant peak identified in the acid components was characterized as 4-hydroxy mesotrione (0.5%TRR).

Extraction of nutmeat was performed using two different techniques. The first technique involved extraction with acetonitrile:water mixture (80:20) followed by ethyl acetate which solubilised 9.2% TRR and 34.3% TRR, respectively. Partitioning of the acetonitrile:water fraction was performed, followed by reverse-phase HPLC. The second technique was used to increase the extractability from the sample and involved further sequential extractions using a range of solvents. Non polar solvents extracted 51.4% TRR (0.011 mg/kg) and neutral solvents extracted 4.7% TRR (0.001 mg/kg). The non-extractable residue concentration was low (50.8% TRR, 0.011 mg/kg).

The non-polar soluble fractions from nutmeat were separated via amino solid phase extractions into neutral lipids (37.8% TRR), fatty acids (5.7% TRR) and phospholipid (4.1% TRR) fractions. This indicated that the ^{14}C radioactivity found in the peanut oil fraction was incorporated into neutral lipids and when base hydrolyzed the ^{14}C was shown to be a component of the fatty acid chains (by HPLC comparison with base hydrolysed ^{14}C-triacylglyceride reference chemicals). Thus through metabolism, the ^{14}C radiolabel from the mesotrione used in the study had become part of the carbon pool used for lipid biosynthesis.

The residues detected in peanut hulls and nutmeat are summarised in Table 6.2.1-4.

Table 6.2.1-4: Summary of radioactive residues in peanut hulls and nutmeat samples following treatment with [cyclohexane-2-14C]-mesotrione

Crop and Commodity:		Peanut hulls		Peanut nutmeat	
Application Rate:		836 g a.s./ha			
Total Radioactive Residue:		0.015 mg/kg		0.022mg/kg	
Aqueous acetonitrile extract (%TRR):		0.003 mg/kg, (19.9%)		0.001 mg/kg, (4.7%)	
Non polar (hexane, ethyl acetate) solubles		-		0.011 mg/kg, (51.4%)	
Origin of component	**Component**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Anion exchange fractionation of aqueous acetonitrile extract[2]	**Neutral/base components**	<0.001	4.4	-	-
	Acidic components[1]	0.003	12.6	-	-
	Organic wash	<0.001	1.8	-	-
Anion exchange fractionation of non-polar solubles	**Lipids[3]**	-	-	0.008	37.8
	Fatty acids[3]	-	-	0.001	5.7
	Phospholipids[3]	-	-	0.001	4.1
Unextractable (PES)		0.013	84.5	0.011	50.8
Total (characterised)[4]		0.003	18.8	0.011	52.3
Losses/gains on fractionation[5]		<0.001	-3.3	<0.001	-3.1
Total		0.015	100	0.011	100

- Not applicable
1 Three separate regions 3.7, 4.3 and 4.6% TRR. Contained a component characterised as 4-hydroxy mesotrione (1.4% TRR)
2 Aqueous acetonitrile extract for hulls. Equivalent not analysed for nutmeat due to low levels
3 From the non polar solubles for nutmeat
4 Sum of anion exchange fractions for hulls and aqueous acetonitrile extract, lipids, fatty acids and phospholipids for nutmeat
5 Sum of anion exchange fractions and PES compared to radioactive residues measured by combustion for hulls and aqueous acetonitrile extract, lipids, fatty acids, phospholipids and PES for nutmeat

Storage Stability

For both application rates of mesotrione the initial radiocomponent profiles of extractable residues in peanut foliage, hay and hull samples, were obtained within 180 days of harvest. Further analysis was performed within approximately 8 months of initial profiling. Comparison of the initial and final radiocomponent profiles obtained showed that no significant change in the profiles for any of the commodities had occurred during the interim period of storage.

Proposed metabolic pathway for mesotrione in peanuts

The proposed metabolic pathway of [cyclohexane-^{14}C] mesotrione in peanuts proceeds via two pathways. Firstly by degradation of the cyclohexane dione ring to CO_2 and secondly by the oxidation of the cyclohexane dione ring to form 4-hydroxy-mesotrione which leads to multiple metabolites.

The proposed metabolic pathway for mesotrione in peanuts is given in Figure 6.2.1-2 after the second study summary.

CONCLUSIONS:

Following separate pre-emergence applications of [cyclohexane-2-^{14}C]-mesotrione to peanuts at nominal rates of 327 g a.s./ha and 836 g a.s./ha, samples of 50% mature foliage (taken 90 days after planting) and mature commodities of peanut hay, hulls and nutmeat (taken 154 days after treatment) were harvested.

Samples of peanuts treated with [cyclohexane-2-^{14}C]-mesotrione at the lower dose rate of 327 g a.s./ha resulted in very low TRRs; 0.006 mg/kg in peanut foliage (50% mature), 0.004 mg/kg in peanut hay,

0.005 mg/kg in peanut hulls and 0.007 mg/kg in nutmeat. No further analysis or processing of commodities from this application rate was therefore performed.

The plants which had been treated at the higher application rate of 836 g a.s./ha showed evidence of phyotoxicity and matured later than the plants treated at 327 g a.s./ha.

The TRRs for commodities harvested from plants treated at 836 g a.s./ha were 0.020 mg/kg (50% mature foliage), 0.011 mg/kg (hay) and 0.015 mg/kg (hulls) and 0.022 mg/kg (nutmeat).

All plant samples that contained radioactive residues greater than or equal to 0.010 mg/kg were extracted. The samples were separated into aqueous and organic fractions and profiled by reverse-phase HPLC. Additional separation was performed by anion exchange chromatography where necessary.

Extractabilities for samples treated at 836 g a.s./ha were 38.9% TRR for 50% mature foliage, 28.2% TRR for mature hay, 19.9% TRR for mature hulls and a total of 56.1% TRR for nutmeat. Corresponding PES values were 0.013 mg/kg (65.9% TRR), 0.008 mg/kg (71.6% TRR), 0.013 mg/kg (84.5% TRR) and 0.011 mg/kg (50.8% TRR), respectively.

Characterization of extracts from 50% mature foliage, hay and hull fractions showed similar complex mixture of components with one significant peak. This component was identified as 4-hydroxy mesotrione. The peanut oil fraction was shown to be composed primarily 14C-labelled neutral lipids resulting from metabolism of mesotrione to single carbon units that entered the carbon pool.

In conclusion the results obtained from experiments with [cyclohexane-2-^{14}C] mesotrione indicated that mesotrione was metabolised to 4-hydroxy-mesotrione and to single carbon units that were incorporated into the lipid biopathway.

Report:	KCA 6.2.1/02. Brown, K. (2003), [Phenyl-U-^{14}C] Mesotrione: Nature of the Residue in Peanuts, Report Number: 1286-01; Syngenta Crop Protection, Inc., Greensboro, NC 27419, USA. Syngenta File Number: ZA1296/1349

Guidelines

EPA Residue Chemistry Test Guideline OPPTS 860.1300, Nature of the Residue in Plants (August 1996).

GLP

The study was carried out according to the principles of good laboratory practice.

EXECUTIVE SUMMARY

This study was designed to provide information on the magnitude and nature of residues following pre-emergence applications of mesotrione in peanuts (*Arachis hypogaea var.* NCV 11). Mesotrione, uniformly labelled in the phenyl ring: ([phenyl-U-^{14}C]-mesotrione) was used. Peanuts were planted in silt loam soil in three outdoor subplots. ^{14}C-Mesotrione was solubilised in acetonitrile and diluted with aqueous Callisto 4SC blank formulation. Two application rates of [phenyl-U-^{14}C]-mesotrione were used during the study, in addition to a control. [Phenyl-U-^{14}C]-mesotrione was applied to the soil surface after planting the seeds (pre-emergence) using a back-pack sprayer at target application rates of 280 g a.s./ha 840 g a.s./ha. Actual rates achieved were 305 and 796 g a.s./ha. The radioactive residues in samples of peanut foliage harvested 90 days after planting (50% mature) and mature peanut hay, hulls and nutmeat, harvested 153 days after treatment, were quantified and characterised.

A subsample of each commodity type was homogenised in the presence of dry ice and the radioactive residue determined by combustion/LSC. All samples were found to have a radioactive residue greater than 0.01 mg/kg and were therefore analysed further.

Radioactivity was measured by LSC. Samples were extracted using a number of solvents of varying polarities and fractionated. Further treatment comprised chemical and enzymatic hydrolysis, derivatisation and aminolysis and were carried out as appropriate. Extractable radioactivity was analysed by co-chromatography with reference compounds using normal and reverse-phase thin layer chromatography (TLC) and reverse-phase HPLC. Additionally separation was conducted with ion exchange chromatography.

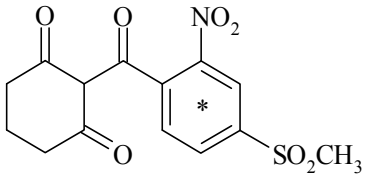
After treatment with [phenyl-U-^{14}C]-mesotrione at 305 g a.s./ha and 796 g a.s./ha, the total radioactive residues (TRRs) were 0.028 and 0.064 mg/kg in 50% mature foliage, 0.012 and 0.028 mg/kg in peanut hay, 0.011 and 0.025 mg/kg in hulls and 0.013 and 0.037 mg/kg in nutmeat, respectively. The extractable residues identified were MNBA (4-methylsulfonyl-2-nitro benzoic acid), AMBA (2-amino-4-methylsulfonyl benzoic acid), and MBA (4-methylsulfonyl benzoic acid) with corresponding TRRs of 0.6-10.9%, 0.5- 15.0%, 0.6-6.7%. 4-Hydroxy mesotrione was also found in samples of nutmeat treated at 305 mg/kg (6.9% TRR) after further extraction of the post-extracted solids (PES). Some evidence indicated that MNBA or AMBA may have been incorporated into acylglycerides.

The metabolic pathway of phenyl-mesotrione in peanuts following a pre-emergence application proceeds via cleavage of the parent molecule to yield MNBA. MNBA is reduced to its amino analogue, AMBA, which is converted to numerous conjugates or can be further degraded to MBA. Mesotrione is also hydroxylated in the cyclohexanedione ring to give 4-hydroxy-mesotrione.

MATERIALS AND METHODS

Materials

Test Materials:

Structure/Label	**[Phenyl-U-^{14}C]-mesotrione**
	 (* = ^{14}C position)
Common name	Mesotrione
Syngenta code	ZA1296
CAS Number	104206-82-8
Batch Number	CL-L-82
Specific Activity	1.5 MBq/mg (40.5 µCi/mg)
Radiochemical Purity	98.5%

Test System

Peanut (*Arachis hypogaea*), variety NCV 11.

Test Soil

A silt loam soil was used in this study.

Test Facilities

The biological phase was performed at Syngenta Crop Protection, Inc., Southern Regional Technical Center, Leland, MS 38756, USA.

The analytical phase was performed at Vero Beach Research Center (VBRC), Syngenta Crop Protection, Inc., Vero Beach, FL 32967, USA and Syngenta Crop Protection, Inc., Greensboro, NC 27419, USA.

Study Design and Methods

Field Phase

The field phase was carried out in Leland, MS, USA. Peanuts were planted in rows 1 m apart in three separate outdoor subplots, one for each treatment group and a control plot. The temperature ranged from 19°C to 31°C with a daily average of 22°C. The cumulative precipitation was 658 mm. ^{14}C-Mesotrione was solubilised in acetonitrile and diluted with aqueous Callisto 4SC blank formulation. Pre-emergence applications were made by spraying [phenyl-U-^{14}C]-mesotrione onto the test plots one day after planting with a back-pack sprayer. Two application rates were used; 305 g a.s./ha and 796 g a.s./ha, in addition to a control. Details are shown in Table 6.2.1-5.

Table 6.2.1-5: Mesotrione application details

Target application rate	280 g a.s./ha	840 g a.s./ha
Achieved application rate	305 g a.s./ha	796 g a.s./ha
Number of applications	1	1
Formulation	Acetonitrile and aqueous Callisto 4SC blank formulation	Acetonitrile and aqueous Callisto 4SC blank formulation
Amount Mesotrione applied	237.3 mg (2.14 x 10^{10} dpm, or approx.9.61 mCi or approx. 356 MBq)	703.2 mg (6.33 x 10^{10} dpm or approx. 28.5 mCi or approx. 1055 MBq)
Plot size	Approx. 4.16 m^2 (approx. 1.52 x 2.74 m)	Approx 4.16 m^2 (approx. 1.52 x 2.74 m)
Spray volume	Approx. 200 mL	Approx. 210 mL
Method of application	Backpack sprayer	Backpack sprayer
Application	1 day after planting	1 day after planting
Environmental conditions	Outdoor plot	Outdoor plot

Test Samples

Soil core samples were collected prior to application, post-application, at 50% mature harvest and at the final harvest. A total of 8 samples were collected for each application rate of [Phenyl-U-^{14}C]-mesotrione and a total of four samples were taken for the control. All samples were stored frozen until analysis.

Peanut foliage was harvested 90 days after application (50% maturity). Mature peanuts and peanut hay were harvested 153 days after application. After sampling, mature peanuts were separated into hulls and nutmeat. Samples were stored frozen at -20°C.

Sample Preparation

Plant samples were homogenised with solid carbon dioxide using a Wiley or Rotoplex mill. Soil cores were air dried and homogenised without dry ice. Following homogenisation the samples were analysed by combustion/LSC of sub-samples, to determine the level of radioactive residue present. Radioactivity in liquid samples was determined directly by LSC.

Extraction and Fractionation of Residues

Plant samples having radioactive residues greater than or equal to 0.010 mg/kg were extracted. The radioactive residues in the peanut foliage, hay and hulls were extracted four times with a mixture of water and acetonitrile (8:2) and the filtrates/extracts combined. Nutmeat was extracted twice with hexane and twice with acetonitrile:water (8:2) and the filtrates/extracts combined. All extracts were radioassayed by LSC. The post-extraction solids were air dried, combusted, and radioassayed.

Aliquots of the extracts were partitioned between aqueous and organic phases, i.e., hexane, dichloromethane or chloroform, using separating funnels. Both phases were radioassayed.

Cellulase and amyloglucosidase enzymes were added to sodium acetate buffered subsamples of aqueous and hexane fractions (pH 4.6). Esterase, lipase, and/or pancreatin were added to TRIS-hydrochloric acid buffered subsamples of aqueous and hexane fractions (pH 7.8-8). Samples were incubated for approximately 24 hours at 42 or 47°C.

Aqueous and hexane fractions and post-extracted solids (PES) were hydrolysed with 6N hydrochloric acid under reflux for approximately 4 or 24 hours followed by XAD-7 separation and/or dichloromethane partitioning.

Hexane fractions were hydrolysed with 1N potassium hydroxide in water under reflux for approximately 6 or 24 hours. The hydrolysates were adjusted to pH 2 with either formic acid or hydrochloric acid and then partitioned with dichloromethane.

When required, samples were methylated using diazomethane. Samples were concentrated to dryness and an ethereal solution of diazomethane was added. After 2 hours, the reaction mixture was dried and subsequently dissolved in methanol.

Aminolysis using diethylamine was attempted; diethylamine was added to the hexane fraction produced from nutmeat samples of the 796 g a.s./ha [phenyl-U-^{14}C]-mesotrione application trials. The mixture was heated at approximately 52°C for approximately 6 hours and then concentrated under a stream of nitrogen.

PES were refluxed over night with water to extract various complex sugars. Following filtration, the liquid filtrate containing polysaccharides was retained and the solids were refluxed over night with 10% sodium hydroxide solution. Following filtration, the filtered solid was considered to contain celluloses. The remaining filtrate was adjusted to pH 1 with hydrochloric acid leading to precipitation of lignin. The solution was filtered once more to remove the lignin and the filtrate was partitioned with dichloromethane.

Soil core samples were extracted using acetonitrile:water (8:2). Further extractions were performed using ethyl acetate, acetonitrile:0.5 N hydrochloric acid and 0.5N sodium hydroxide. The PES were air-dried and combusted to determine the unextracted (bound) residues.

Solid/Liquid partitions

Appropriate plant extracts were applied to specific bond-elut columns in order to clean-up samples or separate different fractions.

A C_{18} column was used to separate chlorophylls and also to prepare samples for chromatography. The columns were typically pre-conditioned with organic solvents and then eluted with either methanol or acetonitrile.

NH_2 bond-elut columns were used to separate different components in nutmeat hexane fractions. Columns were pre-conditioned with hexane and then eluted with a variety of solvents in order to release the different fractions from the columns. Lipids, fatty acids, phospholipids, acylglyderiols etc. could be removed in this manner.

Chromatography

Components were separated using 2-dimensional normal phase TLC on silica gel plates with different solvent systems, mostly ethyl acetate:n-propanol:water:acetic acid (64:22:12:2 v/v/v/v) and methyl ethyl ketone:acetonitrile:acetic acid:water (80:16:4:6 v/v/v/v).

Reversed-phase HPLC coupled to UV detector, radioisotope flow monitor and a fraction collector was also used. Additional separation was performed by ion exchange chromatography where necessary.

Components were identified using co-chromatography with a number of proposed metabolites; mesotrione, ^{14}C-mesotrione, 4-hydroxy-mesotrione, ^{14}C-4-hydroxy-mesotrione, MNBA, ^{14}C -MNBA, AMBA, ^{14}C –AMBA and MBA.

RESULTS AND DISCUSSION:

Characterisation of residues

Overview

In samples where total radioactive residues (TRRs) were >0.01 mg/kg were determined, characterisation using a series of extraction and fractionation techniques was performed. The results from the extraction of samples are summarised in Table 6.2.1-6 to Table 6.2.1-8.

Plants treated with a higher application rate of 796 g a.s./ha of [phenyl-U-^{14}C]-mesotrione showed evidence of initial phytotoxicity when compared to the control plants and plants treated at the lower application rate. The stunted plants did recover, however they reached maturity later than the other plants used in the study.

For all peanut commodities, the total radioactive residues were low regardless of the application rate used. After treatment at 305g a.s./ha, TRRs of 0.028 ppm in peanut foliage (50% mature), 0.012 ppm in peanut hay, 0.011 ppm in peanut hulls and 0.013 ppm in nutmeat were observed. For plants treated at 796 g a.s./ha, 0.064 mg/kg TRR (50% mature foliage), 0.028 mg/kg TRR (peanut hay), 0.025 mg/kg (peanut hulls) and 0.037 mg/kg TRR (peanut nutmeat) were determined.

Extractabilities of the peanut foliage, hay, hull, and nutmeat samples treated at 305 g a.s./ha were 42.2%, 31.5%, 23.0%, and 40.0%, corresponding to post-extracted solids of 48.7% TRR (0.014 ppm), 62.8% TRR (0.008 ppm), 60.1% TRR (0.007 ppm), and 60.7% TRR (0.008 ppm), respectively. Extractabilities of the peanut foliage, hay, hull, and nutmeat samples treated with 796 g a.s./ha were 40.5%, 34.2%, 19.6%, and 35.9%, corresponding to post-extracted solids of 59.6% TRR (0.038 ppm), 67.7% TRR (0.019 ppm), 68.5% TRR (0.017 ppm), and 61.5% TRR (0.023 ppm), respectively.

MNBA, AMBA, MBA, and 4-hydroxy mesotrione were identified in the extracts. MNBA exhibited the highest concentration in the initial sample extract, ranging from 0.6 %to 10.9% TRR, AMBA ranged from 0.5 to 15.0% TRR and MBA from 0.6 to 6.7% TRR. Hydroxy-mesotrione was found in nutmeat (6.9% TRR) after further extraction of the post-extracted solids with sodium hydroxide.

Hexane fractions from nutmeat were further treated using 1N KOH, 6N HCl, diethylamine, and the enzymes cellulase, glucosidase, pancreatin, esterase, and lipase. The results led to the proposal that the hexane fraction consisted of a mixture of acylglycerides that have incorporated MNBA or AMBA.

Residues in Soil

Analysis of the soil core samples confirmed that the mean estimates for the pre-emergence application rates to the test plots (305 and 796 g a.s./ha) were comparable to the calculated treatment application rates of 280 and 840 g a.s./ha.

Residues in 50% Mature Peanut Foliage

The TRR in peanut foliage was low (0.028 mg/kg) following pre-emergence treatment with [phenyl-U-^{14}C]-mesotrione, at an application rate of 305 g a.s./ha. The TRR in 50% mature foliage treated at 796 g a.s./ha was 0.064 mg/kg. Initial solvent extractabilities of the foliage were 42.2% (0.012 mg/kg) and 40.5% (0.026 mg/kg) from the 305 g and 796 g a.s./ha treatments respectively. This corresponded to post-extraction solids (PES) of 48.7% (0.014 mg/kg) and 59.6% (0.038 mg/kg), respectively. Residues of MNBA and AMBA were detected in 50% mature foliage samples treated at both application rates, with higher quantities being detected in the 305 g a.s./ha samples. The extracts were partitioned into aqueous and organic fractions and chromatographed. In the aqueous fractions the levels of MNBA were highest in the initial extract (0.003 mg/kg, 10.9% and 0.007 mg/kg, 10.7% TRR). AMBA was also present in the initial sample extracts at 0.001 mg/kg (2.1% TRR) and <0.001 mg/kg (0.5% TRR). The organic fractions at each application rate were hydrolysed with a 6 N hydrochloric acid:acetonitrile solution. AMBA was found at 0.001 mg/kg (4.9% TRR) and 0.003 mg/kg (4.3% TRR). Further treatment of the PES with sodium hydroxide resulted in <0.001 mg/kg (1.4% TRR) of MNBA and 0.003 mg/kg (9.7% TRR) of AMBA being extracted from the lower application rate samples. MBA and AMBA were both extracted from peanut foliage samples treated at the higher application rate at <0.001 (0.6% TRR) and 0.02 mg/kg (2.3% TRR) respectively.

The residues detected are summarised in Table 6.2.1-6 for ^{14}C-phenyl labelled mesotrione treated peanut foliage.

Table 6.2.1-6: Summary of radioactive residues in peanut foliage samples following treatment with [phenyl-U-^{14}C]-mesotrione

Crop and Commodity:		**Peanut foliage**			
Application Rate:		305 g a.s./ha		796 g a.s./ha	
Total Radioactive Residue (%TRR):		0.028 mg/kg (100%)		0.064 mg/kg (100%)	
Extractable residues (%TRR)[1]		0.012 (42.2%)		0.026 (40.5%)	
Aqueous following partition (%TRR):		0.007 mg/kg (23.6%)		0.012 mg/kg, (19.2%)	
Origin of component	**Component (code or structure)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of aqueous partition	MNBA	0.003	10.9	0.007	10.7
	AMBA	0.001	2.1	<0.001	0.5
	Unknown 1	0.001	4.5	0.003	4.4
	Unknown 2	0.001	1.9	-	-
	Unknown 3	-	-	-	-
	Unknown 4	-	-	-	-

Crop and Commodity:		**Peanut foliage**			
Application Rate:		305 g a.s./ha		796 g a.s./ha	
Total Radioactive Residue (%TRR):		0.028 mg/kg (100%)		0.064 mg/kg (100%)	
Extractable residues (%TRR)[1]		0.012 (42.2%)		0.026 (40.5%)	
Aqueous following partition (%TRR):		0.007 mg/kg (23.6%)		0.012 mg/kg, (19.2%)	
Origin of component	**Component (code or structure)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
	Others	[1]	-	[2]	
Organic following partition(%TRR):		0.004	15.8	0.010	15.6
Organic after 6N HCl hydrolysis		0.003	12.3	0.009	14.1
Chromatography of hydrolysed residue	AMBA	0.001	4.9	0.003	4.3
Unextractable (PES)		0.014	48.7	0.038	59.6
PES further treated with NaOH	MNBA	<0.001	1.4	-	-
	MBA	-	-	<0.001	0.6
	AMBA	0.003	9.7	0.002	2.3
	4-Hydroxy mesotrione	-	-	-	-
Total (characterised)[2]		0.008	29.0	0.012	18.4
Gains/losses on fractionation and processing[3]		0.003	11.9	0.004	5.6
Total		0.028	100	0.064	100

1 Extract was separated into aqueous and organic fraction,
- Not applicable
[1] At least 7 components ranging from 0.2% to 1.4% TRR
[2] At least 8 components ranging from 0.1% to 1.2% TRR
2 Sum of MNBA, AMBA and MBA
3 Sum of organic and aqueous partition of extracted residues and PES subtracted from radioactive residues measured by combustion

Residues in Mature Peanut Hay

The TRR in peanut hay was low (0.012 mg/kg) following pre-emergence treatment with [phenyl-U-^{14}C]-mesotrione, at an application rate of 305 g a.s./ha. The TRR in peanut hay for plants treated at a higher application rate of 796 g a.s./ha of [phenyl-U-^{14}C]-mesotrione was 0.028 mg/kg. Initial extractabilities of the peanut hay were 31.5% (0.004 mg/kg) and 34.2% (0.010 mg/kg) from the 305g and 796g a.s./ha treatments respectively corresponding to initial post-extraction solids of 62.8% (0.008 mg/kg) and 67.7% (0.019mg/kg), respectively. The extracts were partitioned into aqueous and organic fractions and chromatographed. Residues of MNBA were detected in peanut hay samples treated at both application rates. In the aqueous fractions the levels of MNBA were 0.001 mg/kg (4.0% TRR) and 0.002 mg/kg (5.8% TRR). AMBA and MBA were only detected in the 796 g a.s./ha treated hay samples at low levels (<0.001 mg/kg, 1.1% TRR). Following hydrolysis of the organic fractions with a 6 N hydrochloric acid:acetonitrile solution, AMBA was present at <0.001 mg/kg for both application rates (representing 2.2% TRR and 1.5% TRR, respectively). Further treatment of the PES with sodium hydroxide resulted in approximately 0.001 mg/kg MNBA, MBA and AMBA being extracted which corresponds to 1.1%, 3.2% and 4.7% TRR for the lower application rate and 0.6%, 1.7% and 2.0% for the higher application rate.

The residues detected are summarised in Table 6.2.1-7 for the ^{14}C-phenyl labelled mesotrione treated peanut hay.

Table 6.2.1-7: Summary of radioactive residues in peanut hay samples following treatment with [phenyl-U-^{14}C]-mesotrione

Crop and Commodity:		**Peanut hay**			
Application Rate:		305 g a.s./ha		796 g a.s./ha	
Total Radioactive Residue:		0.012 mg/kg		0.028 mg/kg	
Extractable residues (%TRR)[1]		0.004 mg/kg, (31.5%)		0.010 mg/kg, (34.2%)	
Aqueous following partition (%TRR):		0.002 mg/kg, (16.0%)		0.007 mg/kg, (24.8%)	
Origin of component	**Component (code or structure)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of aqueous partition	MNBA	0.001	4.0	0.002	5.8
	AMBA	-	-	<0.001	1.1
	MBA	-	-	<0.001	1.1
	Unknown 1	0.001	4.0	0.002	7.6
	Unknown 2	<0.001	1.0	0.001	3.4
	Unknown 3	-	-	-	-
	Unknown 4	-	-	0.001	3.3
	Others	[1]	-	-	-
Organic following partition(%TRR):		0.002	13.3	0.003	8.8
Organic after 6N HCl hydrolysis		0.001	10.3	0.002	6.7
Chromatography of hydrolysed residue	AMBA	<0.001	2.2	<0.001	1.5
Unextractable (PES)		0.008	62.8	0.019	67.7
PES further treated using NaOH	MNBA	<0.001	1.1	<0.001	0.6
	MBA	<0.001	3.2	0.001	1.7
	AMBA	<0.001	4.7	0.001	2.0
	4-Hydroxy mesotrione	-	-	-	-
Total (characterised)[2]		0.002	15.2	0.004	13.8
Gains/losses on fractionation and processing[3]		<0.001	7.9	<0.001	-1.3
Total		0.012	100	0.028	100

1 Extract was separated into aqueous and organic fraction,
- Not applicable
[1] At least 5 components ranging from 0.3% to 0.7% TRR
2 Sum of MNBA, AMBA and MBA
3 Sum of organic and aqueous partition of extracted residues and PES subtracted from radioactive residues measured by combustion

Residues in Mature Peanut Hulls and Nutmeat

The TRRs in hulls and nutmeat were low (0.011 and 0.013 mg/kg) following pre-emergence treatment with [phenyl-U-^{14}C]-mesotrione, at an application rate of 305 g a.s./ha. The TRRs in hulls and nutmeat for plants treated with a higher application rate of 796 g a.s./ha of [phenyl-U-14C]-mesotrione were 0.025 and 0.037 mg/kg, respectively.

Extractabilities of the hulls were 23.0% (0.003 mg/kg) and 19.6% (0.005 mg/kg) from the 305 g and 796 g a.s./ha treatments respectively. This lead to initial post-extraction solids of 60.1% (0.007 mg/kg) and 68.5% (0.017 mg/kg), respectively. Low levels of MNBA and AMBA residues were detected in hull samples treated at both application rates. The extracts were partitioned into aqueous and organic fractions and chromatographed. In the aqueous fractions the levels of MNBA were <0.001 mg/kg (2.4% and 1.7% TRR, respectively). MNBA was also detected in samples treated at 305 g a.s./ha following further treatment of the PES with sodium hydroxide (<0.001 mg/kg, 1.2% TRR) and slightly higher levels were

detected from samples treated at 796 g a.s./ha (0.002 mg/kg, 7.9% TRR). In addition, AMBA was detected at <0.001 mg/kg (1.6% and 1.4% TRR, respectively). MBA was only detected in hull samples treated at 305 g a.s./ha following further treatment of the PES with sodium hydroxide (0.001 mg/kg, 6.7% TRR). The aqueous fraction obtained from partition was also treated with acid (6N HCl) in an attempt to further characterise unknown 1 (*peak 1*). Unknown 1 was reduced along with the amount of MNBA but two other unknown components were generated.

Extractabilities of the peanut nutmeat were 40.0% (0.005 mg/kg) and 35.9% (0.013 mg/kg) from the 305g and 796g a.s./ha treatments respectively, which corresponded to initial post-extraction solids of 60.7% (0.008 mg/kg) and 61.5% (0.023 mg/kg), respectively. In treated at 305 g a.s./ha, MBA and AMBA residues were detected at 0.001 and 0.002 mg/kg, respectively (6.7 and 15% TRR) after further treatment of the PES with sodium hydroxide. 4-Hydroxy mesotrione was also found at 0.001 mg/kg (6.9% TRR). Low levels of MNBA and AMBA were detected at <0.001 mg/kg (2.4% and 1.4% TRR respectively) in samples treated at 796 g a.s./ha.

Hexane fractions from peanut nutmeat were further treated using 1N potassium hydroxide, 6N hydrochloric acid, diethylamine, and the enzymes cellulase, glucosidase, pancreatin, esterase, and lipase. The results led to the conclusion that the hexane fraction consisted of a mixture of acylglycerides that have incorporated MNBA or AMBA.

The residues detected in peanut hulls and nutmeat are summarised in Table 6.2.1-8.

Table 6.2.1-8: Summary of radioactive residues in peanut hulls and nutmeat samples following treatment with [phenyl-U-^{14}C]-mesotrione

Crop and Commodity:		**Peanut hull/nutmeat**			
Application Rate:		305 g a.s./ha		796 g a.s./ha	
Total Radioactive Residue:		0.011/0.013 mg/kg		0.025/0.037 mg/kg	
Extractable residues (%TRR)		0.003 mg/kg, (23.0%)[1]/ 0.005 mg/kg, (40.0%)		0.005 mg/kg, (19.6%)[1]/ 0.013 mg/kg, (35.9%)	
Aqueous following partition hull extract(%TRR):		0.002 mg/kg, (15.5%)		0.005 mg/kg, (18.2%)	
Aqueous acetonitrile fraction from nutmeat extract[2]		<0.001 mg/kg, (3.8%)		0.001 mg/kg, (3.9%)	
Hexane fraction from nutmeat extract[3]		0.005 mg/kg, (36.2%)		0.013 mg/kg, (35.9%)	
Origin of component	**Component (code or structure)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of aqueous partition for hulls	MNBA	<0.001	2.4	<0.001	1.7
	Unknown 1	<0.001	5.4	0.002	6.7
	Unknown 2	<0.001	3.0		
	Unknown 3	-	-	<0.001	1.7
	Unknown 4	-	-	-	-
	Others	[1]		[2]	
Organic following partition of hull extract (%TRR):		<0.001	5.3	<0.001	2.2
Unextractable (PES)		0.007/ 0.008	60.1/ 60.7	0.017/ 0.023	68.5/ 61.5
PES were further treated using NaOH	MNBA	<0.001	1.2	0.002 <0.001	7.9 2.4
	MBA	0.001	6.7	-	-
	AMBA	<0.001/ 0.002	1.6/ 15.0	<0.001/ <0.001	1.4/ 1.4
	4-Hydroxy mesotrione	0.001	6.9	-	-
Total (characterised)[4]		<0.001/ 0.004	5.2/ 28.6	0.003/ 0.001	11.0/ 3.8
Gains/losses on fractionation and processing[5]		0.002/<0.001	19.1/-0.6	0.003/<0.001	11.1/-1.3
Total		0.0110.013	100	0.011/0.037	100

1 Extract was separated into aqueous and organic fraction
2 Low residues in the aqueous fraction and its concentrated matrices prevented TLC and HPLC analyses of samples
- Not applicable
[1] At least 3 components ranging from 0.2% to 1.2% TRR
[2] At least 4 components ranging from 0.2% to 1.4% TRR
3 The hexane fraction was further characterised by treatment with base, partition, treatment with acid and further partition or with a mixture of enzymes which afforded several unknowns none greater than 0.002 mg/kg
4 Sum of MNBA, AMBA and MBA for 305 g a.i. /ha hulls and sum of 4-hydroxy mesotrione, AMBA and MBA for 305 g a.s. /ha nutmeat and sum of MNBA and AMBA for 796 g a.s. /ha hulls and nutmeat
5 Sum of organic and aqueous partition of extracted residues and PES for hulls and sum of hexane and aqueous acetonitrile fractions from the extracted residues and PES for nutmeat subtracted from radioactive residues measured by combustion

Storage Stability

For both application rates of [phenyl-U-^{14}C]-mesotrione, the initial radiocomponent profiles of extractable residues in peanut foliage, hay and hull samples, were obtained within 6 months of harvest. Further analysis was performed within approximately 13 months of initial profiling. Comparison of the initial and final radiocomponent profiles obtained showed that no significant change in the profiles for any of the commodities had occurred during the interim period of storage under both refrigerator and freezer conditions.

CONCLUSIONS:

Following separate pre-emergence applications of [phenyl-U-^{14}C]-mesotrione to peanuts at nominal rates of 305 g a.s./ha and 796 g a.s./ha, samples of 50% mature foliage (taken 90 days after planting) and mature commodities of peanut hay, hulls and nutmeat (taken 153 days after treatment) were harvested.

The plants which had been treated at the higher application rate of 796 g a.s./ha showed evidence of phyotoxicity and matured later than the plants treated at 305 g a.s./ha.

The total radioactive residues in peanuts treated at both application rates were low with the highest residues being found in the 50% mature foliage. The TRRs for commodities harvested from plants treated at 305 g a.s./ha were 0.028 mg/kg (50% mature foliage), 0.012 mg/kg (hay) and 0.011 mg/kg (hulls) and 0.025 mg/kg (nutmeat). In plants treated at the higher application rate of 796 g a.s./ha the TRRs were found to be 0.064 mg/kg (50% mature foliage), 0.028 mg/kg (hay) and 0.013 mg/kg (hulls) and 0.037 mg/kg (nutmeat).

All plant samples contained radioactive residues greater than or equal to 0.010 mg/kg and were therefore extracted. The samples were separated into aqueous and organic fractions and profiled by HPLC.

Initial solvent extractabilities for samples treated at 305 g a.s./ha were 42.2% (0.012 mg/kg), 31.5% (0.004 mg/kg), 23.0% (0.003 mg/kg) and 40.0% (0.005 mg/kg), respectively for 50% mature foliage, mature hay, hulls and nutmeat. Corresponding PES values were 0.014 mg/kg (48.7% TRR), 0.008 mg/kg (62.8% TRR), 0.007 mg/kg (60.1% TRR) and 0.008 mg/kg (60.7% TRR), respectively. For samples treated at 796 g a.s./ha extractabilities for 50% mature foliage, mature hay, hulls and nutmeat were 40.5% (0.026 mg/kg), 34.2% (0.010 mg/kg), 19.6% (0.005 mg/kg) and 35.9% (0.013 mg/kg), respectively. Corresponding PES values were 0.038 mg/kg (59.6% TRR), 0.019 mg/kg (67.7% TRR), 0.017 mg/kg (68.5% TRR) and 0.023 mg/kg (61.5% TRR) for 50% mature foliage, mature hay, hulls and nutmeat, respectively.

Metabolites characterized in samples treated at both application rates included MNBA, AMBA and MBA. Residue values for MNBA ranged from 0.6% to 10.9% TRR. Values for AMBA ranged from 0.5% TRR to 15.0% TRR. Values for MBA ranged from 0.6 % TRR to 6.7% TRR. 4-Hydroxy mesotrione was only found in mature nutmeat PES which had been treated with the lower application rate of 305 g a.s./ha and accounted for 6.9% TRR.

Hexane fractions from mature nutmeat were treated with a variety of methods. Treatments with 1N potassium hydroxide, 6N hydrochloric acid, diethylamine, cellulase, glucosidase, pancreatin, esterase and lipase resulted with only a minor change in the HPLC profile. It is proposed that the mature nutmeat is comprised of a mixture of acylglycerides that probably have incorporated MNBA or AMBA.

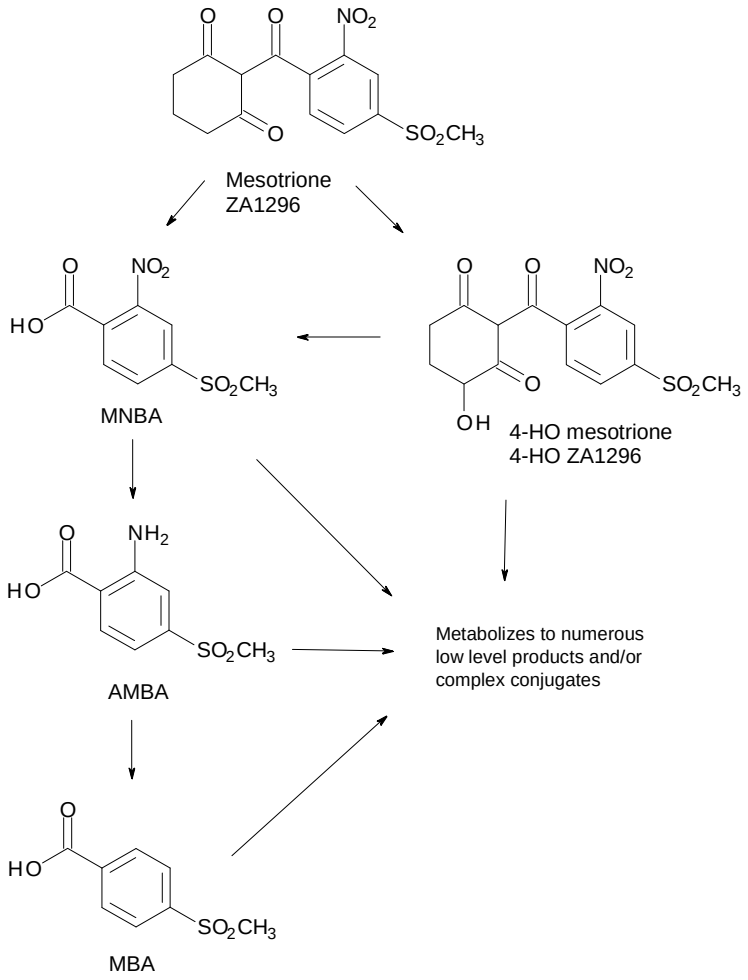
The metabolic pathway of phenyl ^{14}C-labelled mesotrione in peanuts following a pre-emergence application proceeds via cleavage of the parent molecule to yield MNBA. MNBA is reduced to its amino analogue, AMBA, which is converted to numerous conjugates or can be further degraded to MBA. Mesotrione is also hydroxylated in the cyclohexanedione ring to give 4-hydroxy-mesotrione.

Proposed metabolic pathway for Mesotrione in peanuts

The metabolic pathway of mesotrione in peanuts following a pre-emergence application proceeds via cleavage of the parent molecule to yield MNBA. MNBA is reduced to its amino analogue, AMBA which is converted to numerous conjugates or can be further degraded to MBA. Mesotrione is also hydroxylated in the cyclohexanedione ring to give 4-hydroxy mesotrione. The major metabolites MNBA, AMBA, MBA and 4-hydroxy mesotrione are all present in low quantities.

The proposed metabolic pathway is given in Figure 6.2.1-2.

Figure 6.2.1-2: Proposed metabolic pathway for mesotrione from (^{14}C-phenyl label) and (^{14}C-cyclohexane label) in peanuts



Metabolism, distribution and expression of residues in HT soy bean

This study is included to support the new proposed residue definition in crops. (See section 6.7.1)

Report:	KCA 6.2.1/03. Dohn, D., Chu, J. (2012), ^{14}C-Mesotrione – Nature of the Residue in Herbicide Tolerant (HT) Soybeans. Report Number 1943W, Syngenta Crop Protection, Inc., Greensboro, NC 27419, USA. Syngenta File Number ZA1296_50531

Guidelines

Residue Chemistry Test Guidelines, OPPTS 860.1300, Nature of the Residue – Plants

OECD Guidelines for the Testing of Chemicals, Test No. 501: Metabolism in Crops, adopted 8 January 2007

Japanese Ministry of Agriculture, Forestry and Fisheries Guideline on the Application for Agricultural Chemicals Registration (12 Nohsan No. 8147, November 24, 2000)

GLP

The study was carried out according to the principles of good laboratory practice.

Executive Summary

This study was designed to provide information on the magnitude and nature of residues following pre- and/or post-emergence applications of mesotrione in genetically modified herbicide tolerant (HT) soybeans (*Glycine max var.* Jack). Two radiolabelled forms of mesotrione were used: uniformly labelled in the phenyl ring: ([phenyl-U-^{14}C]-mesotrione) and labelled in C-2 of the cyclohexane ring ([cyclohexane-2-^{14}C]-mesotrione). HT soybean seeds were grown under greenhouse conditions, in containers filled with a sandy loam soil. ^{14}C-Mesotrione was solubilised in 0.01 M potassium phosphate buffer (pH 7.0) and diluted with aqueous Callisto 4SC blank formulation. The two radio labelled forms of mesotrione (^{14}C-U-phenyl and 2-^{14}C-cyclohexane) were applied separately using three separate treatment regimes in this study, in addition to a control.

The first application was a single pre-emergence treatment at a nominal rate of 225 g a.s./ha. The second was a combined pre-emergence treatment at nominally 225 g a.s./ha followed by a post-emergence treatment at 125 g a.s./ha (350 g a.s./ha in total). The third was a single post-emergence treatment at a nominal 225 g a.s./ha. ^{14}C-Mesotrione was applied to the plots as a suspension concentrate using a plastic hand held sprayer. The radioactive residues in samples of soybean forage, hay and beans, were quantified and characterised.

A subsample of each plant commodity type was homogenised in the presence of solid carbon dioxide and the radioactive residue determined by combustion/LSC. Soybean samples that contained a radioactive residue greater than 0.01 mg/kg were analysed further.

The total radioactive residues (TRR) for each soybean commodity are summarised in the Table below:

Table 6.2.1-9: Total radioactive residues in soybean RACs

Soybean RAC	Application Stage	PHI (days)	Total Radioactive Residue (mg/kg) Phenyl label	Total Radioactive Residue (mg/kg) Cyclohexane label
Forage	Pre-emergence	28	0.212	0.077
	Pre-/post emergence	28	0.162	0.055
	Post-emergence	22	0.499	0.260
Hay	Pre-emergence	42	0.142	0.076
	Pre-/post emergence	42 (1st app.) 9 (2nd app.)	2.015	1.632
	Post-emergence	40	0.370	0.082
Seed	Pre-emergence	123	0.063	0.039
	Pre-/post emergence	123 (1st app.) 90 (2nd app.)	0.104	0.093
	Post-emergence	110 (phenyl) 118 (cyclo)	0.052	0.015

RAC = Raw agricultural commodity
* = TRRs for this study have been calculated by adding the ^{14}C-residues and the post-extracted ^{14}C- residues
- = Not applicable

Radioactivity was measured by LSC. Samples were extracted multiple times using a number of solvents of varying polarities, fractionated and analysed using HPLC. The identities of the metabolites were confirmed using normal-phase thin layer chromatography (TLC) and LS-MS.

The extractable residues identified were MNBA, AMBA, 4/5-hydroxy mesotrione, parent mesotrione together with unknown polar components and are summarised in the Table below.

Table 6.2.1-10: TRR (mg/kg) of key ^{14}C-residues in cyclo and phenyl radiolabelled soybean RACs following mesotrione application(s)

RAC	Application Stage	TRR mg/kg Cyclo (Phenyl)	Mesotrione	MNBA	AMBA	4-OH/5-OH Mesotrione	Polar Component[A]	Initial PES[B]
Soybean Seed	Pre-Emergence	0.039 (0.063)	0.002 (0.006)	- (0.001)	- (0)	0.001 (0.003)	0.007 (0.004)	0.020 (0.035)
	Pre/Post-Emergence	0.093 (0.104)	0.003 (0.003[C])	- (0.005[C])	- (0.002)	0.003 (0.007[C])	0.029[D] (0.010[E])	0.039 (0.052)
	Post-Emergence	0.015 (0.052)	- (0.002)	- (0)	- (0)	- (0.004)	- (0.008)	0.008 (0.030)
Soybean forage	Pre-Emergence	0.077 (0.212)	0.013 (0.030)	- (0.052)	- (0.003)	0.011 (0.017)	0.009 (0.005)	0.034 (0.087)
	Pre/Post-Emergence	0.055 (0.162)	0.010 (0.021[C])	- (0.039[C])	- (0.001)	0.007 (0.011[C])	0.005 (0.006)	0.025 (0.074)
	Post-Emergence	0.260 (0.499)	0.022 (0.028)	- (0.065)	- (0.004)	0.050 (0.073)	0.034 (0.008)	0.097 (0.245)
Soybean hay	Pre-Emergence	0.076 (0.142)	0.005 (0.009)	- (0.015)	- (0)	0.012 (0.013)	0.012 (0.006)	0.037 (0.074)
	Pre/Post-Emergence	1.632 (2.015)	0.134[C] (0.178[C])	- (0.410[C])	- (0.055[C])	0.407[C] (0.331[C])	0.243[F] (0.026)	0.357 (0.68)
	Post-Emergence	0.082 (0.370)	0.006 (0.023)	- (0.042)	- (0)	0.016 (0.054)	0.012 (0.006)	0.033 (0.195)

A Polar component unretained on reverse phase HPLC (Rt of approximately 2-3 min).
B Initial value measured by combustion analysis.
C Confirmed by normal phase TLC.
D Further characterized by additional experiments as multiple components each < 0.007 mg/kg (< 6.5% TRR).
E Initial characterisation value of 0.01 mg/kg, but further characterisation demonstrated the value to be actually lower, 0.006-0.007 mg/kg
F Further characterized by additional experiments as multiple components, each < 0.087 mg/kg (< 5.3% TRR).

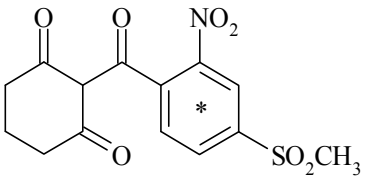
The radioactive residues from the initial post-extraction solids (PES) were further characterised using a range of techniques including buffer sonication, enzyme and/or acid hydrolysis. Harsher extraction techniques were also used as appropriate for lignin, hemicellulose and cellulose.

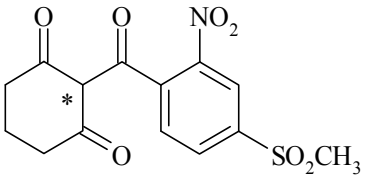
The results indicated that mesotrione in soybeans was metabolised to 4/5-hydroxy mesotrione and two discrete metabolites lacking the cyclohexanedione ring, MNBA and AMBA. Mesotrione and its metabolites undergo further metabolism to small molecular fragments which are incorporated into natural products and to very polar components.

Materials and Methods

Materials

Test Materials:

Structure/Label	[Phenyl-U-^{14}C]-mesotrione
	 (* = ^{14}C position)
Common name	Mesotrione
Syngenta code	ZA1296
CAS Number	104206-82-8
Batch number	RDR-VI-15
Specific activity	58.2 µCi/mg (2.1534 MBq/mg)
Average radiochemical purity	98.6% by HPLC and TLC (first application) 99.1% by HPLC and 98.7% by TLC (second application)

Structure/Label	[Cyclohexane-2-^{14}C] mesotrione
	 (* = ^{14}C position)
Common name	Mesotrione
Syngenta code	ZA1296
CAS Number	104206-82-8
Batch number	RDR-III-96
Specific Activity	53.7 µCi/mg (1.9869 MBq/mg)
Average radiochemical purity	98.1% by HPLC and 99.1% by TLC (first application) 98.9% by HPLC and 97.7% by TLC (second application)

Test System

Genetically modified (HR) soybean (Glycine max), maturity group MG-III, event SYTH04R, USDA notification: 09-063-104n, variety Jack.

Test Soil

A loamy sand soil was used in this study.

Test Facilities

The study was conducted on behalf of Syngenta Crop Protection, Inc.

The field phase was performed at Landis International Inc., 3185 Madison Highway, Valdosta, GA 31601, USA.

The analytical phase was performed at PTRL West Inc, 625-B Alfred Nobel Drive, Hercules, CA 94547, USA.

Characterisation of the soil used to grow the soybeans was performed by Agvise Laboratories Inc, Post Office Box 510, Hwy 15, Northwood, ND 58267, USA.

Study Design and Methods

Field Phase

The field phase was conducted in Valdosta, GA, USA. Genetically modified (HR) soybean seeds (variety Jack) were grown, under greenhouse conditions, in wooden containers filled with a loamy sand test soil. The seeds were planted in five rows per plot. In the first greenhouse, a total of three plots were prepared, one for each treatment group. In the second greenhouse, a single plot was prepared for the control. Both greenhouses were temperature and light controlled. The mean air temperature ranged from 22°C to 31°C in the test greenhouse and 22°C to 37°C in the control greenhouse. Plants were watered as and when required, the total volume of water used per plot during the study was approximately 533 mm.

^{14}C-Mesotrione was solubilised in 0.01 M potassium phosphate buffer (pH 7.0) and diluted with aqueous Callisto 4SC blank formulation. Both radio labelled forms of mesotrione were separately applied for each of the treatment regimes (a single pre-emergence treatment, a combined pre-/post emergence treatment and a single post-emergence treatment) using a plastic hand held sprayer.

Full details of the application regime are presented in Table 6.2.1-11.

Table 6.2.1-11: Mesotrione application details

	Pre-emergence	Pre-/post emergence	Post-emergence
Target application rate	225 g a.s./ha	350 g a.s./ha	225 g a.s./ha
Achieved application rate phenyl label	217.7 g a.s./ha	345.5 g a.s./ha (217.7 + 127.8 g a.s./ha)	224.2 g a.s./ha
Achieved application rate cyclohexane label	225.8 g a.s./ha	356 g a.s./ha (225.8 + 130.2 g a.s./ha)	229.6 g a.s./ha
Number of applications	1	2	1
Formulation	0.01 M potassium phosphate buffer (pH 7.0) and aqueous Callisto 4SC blank formulation	0.01 M potassium phosphate buffer (pH 7.0) and aqueous Callisto 4SC blank formulation	0.01 M potassium phosphate buffer (pH 7.0) and aqueous Callisto 4SC blank formulation
Amount Mesotrione applied phenyl label	3.63 x 10^9 dpm, or approx.1.63 mCi or approx. 60.5 MBq)	5.753 x 10^9 dpm, or approx.2.59 mCi or approx. 95.9 MBq	1.87 x 10^9 dpm, or approx.0.844 mCi or approx. 31.2 MBq
Amount Mesotrione applied cyclohexane label	3.468 x 10^9 dpm, or approx.1.56 mCi or approx. 57.8 MBq	5.495 x 10^9 dpm, or approx.2.47 mCi or approx. 91.6 MBq	1.77 x 10^9 dpm, or approx.0.798 mCi or approx. 29.5 MBq
Plot size	Approx. 1.24 m^2 (approx. 152.4 x 81.3 cm)	Approx. 1.24 m^2 (approx. 152.4 x 81.3 cm)	Approx. 0.62 m^2 (approx. 76.2 x 81.3 cm)

	Pre-emergence	Pre-/post emergence	Post-emergence
Spray volume	Approx. 240-245 mL	First application: approx. 240-245 mL Second application 255-264.5 mL	Approx. 225-232 mL
Method of application	Plastic hand held sprayer	Plastic hand held sprayer	Plastic hand held sprayer
Application	1 day after planting	First application: 1 day after planting Second application: 33 days after planting	12 days after planting
Environmental conditions	Greenhouse	Greenhouse	Greenhouse

Test Samples

Soybean forage was harvested at growth stage R1, 28 days after the application of the pre-emergence and the combined pre-/post emergence regimes with ^{14}C-mesotrione. Soybean forage for the post-emergence regime was also harvested at growth stage R1, 22 days after application.

Soybean hay was harvested at growth stage R2, 42 days after the application of ^{14}C-mesotrione for the pre-emergence treatment regime and after the first application for the combined treatment regime (9 days after the second application for the combined regime). Soybean hay for the post-emergence regime was harvested 40 days after application.

Mature soybean seeds were harvested 123 days after the application of ^{14}C-mesotrione for the pre-emergence treatment regime and after the first application for the combined regime (90 days after the second application for the combined regime). Seeds for the post-emergence regime were harvested 110 days after application of the phenyl ^{14}C-mesotrione and 118 days for the cyclohexane ^{14}C-mesotrione. In order to meet with GMO regulations, following harvest, the soybean seeds were rendered non-viable at the field site by crushing and freezing. All samples were stored frozen until analysis.

Sample Preparation

Soybean forage and hay samples were homogenised with solid carbon dioxide (dry ice) using a cutter/mixer. Soybean seed samples were homogenised with solid carbon dioxide using a blender or coffee mill. Following homogenisation, the solid carbon dioxide in each sample was left to sublime overnight in a freezer. All samples were stored frozen until analysis.

The homogenised samples were analysed by combustion/LSC of sub-samples, to determine the level of radioactive residue present. Radioactivity in liquid samples was determined directly by LSC.

Extraction and Fractionation of Residues

Plant samples having radioactive residues greater than or equal to 0.010 mg/kg were extracted. The radioactive residues in the soybean foliage and hay samples were extracted twice with a mixture of acetonitrile and water (1:1 v/v). Following a further extraction with acetonitrile, the extracts were combined and analysed using reverse-phase HPLC. Due to the high lipid content, the soybean seed samples were sequentially extracted with acetone:hexane (1:4 v/v), acetonitrile:water (1:1 v/v) and acetonitrile.

The post extraction solids (PES) were allowed to air dry following the extraction procedures. Sub-samples of the PES were subjected to combustion analysis to quantify the unextracted radiocarbon and to determine if further PES analysis was required. Further characterisation of the PES samples, using mild and/or harsh treatment, was attempted. Buffer sonication, treatment with Viscozyme and Driselase

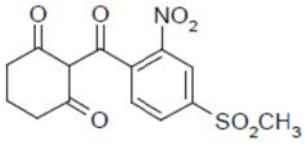
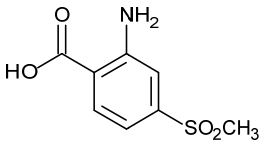
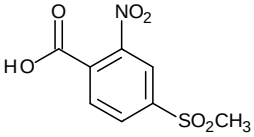
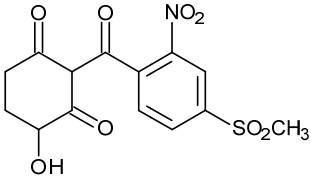
hydrolytic enzymes, hydrolysis with 1N hydrochloric acid at room temperature and/or 60°C was performed on PES that contained residues ≥10% of the TRR or ≥0.05 mg/kg. The resulting aqueous hydrolysates were further characterised using ethyl acetate partitioning were possible. Analysis was performed using TLC and/or HPLC. PES remaining after these treatments and with residues > 10% of the TRR or > 0.05 mg/kg were characterised further using harsher methods (for lignin, hemi-celluloses and/or cellulose). The aqueous hydrolysates however were not suitable for further characterisation.

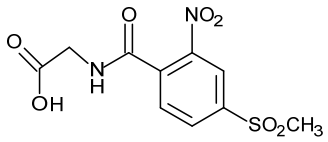
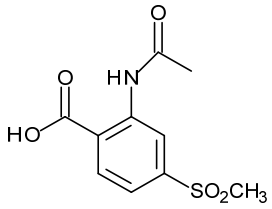
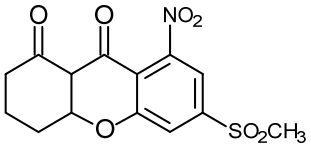
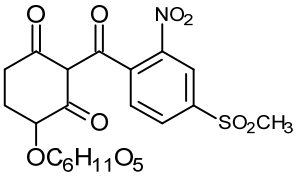
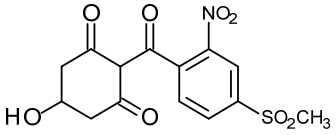
Chromatography

Reverse-phase HPLC coupled to a UV detector, radioisotope flow monitor and a fraction collector was the primary analytical method used for purity checking and soybean sample analyses. Thin layer chromatography was used as a second method to verify metabolites. One and two-dimensional normal phase TLC was performed using silica gel plates with different solvent systems, including ethyl acetate:methanol:water:acetic acid (83:10:5:2 v/v/v/v) and chloroform:ethyl acetate:methanol:formic acid (15:15:15:1 v/v/v/v). Additional separation was performed by reverse-phase anion exchange chromatography where necessary.

Analytes were identified using co-chromatography with a number of proposed metabolites; mesotrione, AMBA, MNBA, MBA, 4-hydroxy mesotrione, R285039, N-acetyl AMBA, R388754, 4-hydroxy mesotrione glucoside and 5-hydroxy mesotrione. The structures of the proposed metabolites and reference materials are presented in Table 6.2.1-12. Additional confirmation and identification was undertaken using mass spectrometry.

Table 6.2.1-12: Structures of mesotrione test and reference substances

Syngenta Code(s) [CAS #, if known]	**Structure**
Mesotrione [104206-82-8]	
AMBA [393085-45-5]	
MNBA [110964-79-9]	
MBA [4052-30-6]	
4-Hydroxy mesotrione [N/A]	

Syngenta Code(s) [CAS #, if known]	Structure
R285039 [N/A]	
N-Acetyl AMBA [N/A]	
R388754 [N/A]	
4-Hydroxy mesotrione glucoside [N/A]	
5-Hydroxy mesotrione [N/A]	

Results and Discussion:

Characterisation of residues

Overview

Following the single pre-emergence application at 225 g a.s./ha, a small amount of phytotoxicity was observed in the test plants following both radiolabelled treatment. The plants recovered and this did not have any effects on the outcome of the study. The plants from the remaining treatment groups did not show any signs of phytotoxicity during the study.

The total radioactive residues (TRR) and initial extractabilities for each soybean commodity treated with [phenyl-U-^{14}C]-mesotrione are summarised in Table 6.2.1-13 and the corresponding data for [cyclohexane-2-^{14}C]-mesotrione are summarised in Table 6.2.1-14.

Due to extensive metabolism of mesotrione, the PES obtained for each of the soybean commodities were significant and ranged from 21.9% to 57.7%. Enzyme hydrolysis was therefore performed on all PES, with the exception of soybean seed produced after a single post-emergent treatment with cyclohexane labelled material.

Table 6.2.1-13: Summary of total radioactive residues in soybean RACs following treatment with [phenyl-U-^{14}C]-mesotrione

Soybean RAC	Application Stage	Initial Extraction mg/kg	Post Extraction Solids (PES) mg/kg	Acetone/Hexane Extraction mg/kg	TRR mg/kg*
Forage	Pre-emergence	0.125 (59.0% TRR)	0.087 (41.0% TRR)	-	0.212
	Pre-/post emergence	0.088 (54.3% TRR)	0.074 (45.7% TRR)	-	0.162
	Post-emergence	0.254 (50.9% TRR)	0.245 (49.1% TRR)	-	0.499
Hay	Pre-emergence	0.068 (47.9% TRR)	0.074 (52.1% TRR)	-	0.142
	Pre-/post emergence	1.335 (66.3% TRR)	0.680 (33.7% TRR)	-	2.015
	Post-emergence	0.175 (47.3% TRR)	0.195 (52.7% TRR)	-	0.370
Seed	Pre-emergence	0.022 (34.9% TRR)	0.035 (55.6% TRR)	0.006 (9.5% TRR)	0.063
	Pre-/post emergence	0.044 (42.3% TRR)	0.052 (50.0% TRR)	0.008 (7.7% TRR)	0.104
	Post-emergence	0.017 (32.7% TRR)	0.030 (57.7% TRR)	0.005 (9.6% TRR)	0.052

RAC = Raw agricultural commodity - = Not applicable
* = TRRs for this study have been calculated by adding the extracted ^{14}C-residues and the post-extracted ^{14}C- residues

Table 6.2.1-14: Summary of total radioactive residues in soybean RACs following treatment with [cyclohexane-2-14C]-mesotrione

Soybean RAC	Application Stage	Initial Extraction (mg/kg)	Post Extraction Solids (PES) (mg/kg)	Acetone/Hexane Extraction (mg/kg)	TRR (mg/kg)*
Forage	Pre-emergence	0.043 (55.8% TRR)	0.034 (44.2% TRR)	-	0.077
	Pre-/post emergence	0.030 (54.5% TRR)	0.025 (45.5% TRR)	-	0.055
	Post-emergence	0.163 (62.7% TRR)	0.097 (37.3% TRR)	-	0.260
Hay	Pre-emergence	0.039 (51.3% TRR)	0.037 (48.7% TRR)	-	0.076
	Pre-/post emergence	1.275 (78.1% TRR)	0.357 (21.9% TRR)	-	1.632
	Post-emergence	0.049 (59.8% TRR)	0.033 (40.2% TRR)	-	0.082
Seed	Pre-emergence	0.012 (30.8% TRR)	0.020 (51.3% TRR)	0.007 (17.9% TRR)	0.039
	Pre-/post emergence	0.042 (45.2% TRR)	0.039 (41.9% TRR)	0.012 (12.9% TRR)	0.093
	Post-emergence	0.005 (33.3% TRR)	0.008 (53.3% TRR)	0.002 (13.3% TRR)	0.015

RAC = Raw agricultural commodity - = Not applicable
* = TRRs for this study have been calculated by adding the extracted ^{14}C-residues and the post-extracted ^{14}C- residues

For the soybean forage samples, enzyme hydrolysis solubilised a further 7.5% TRR (0.016 mg/kg) from the pre-emergence application for phenyl labelled plants and 16.9% TRR (0.013 mg/kg) for the corresponding cyclohexane labelled plants. From the combined pre-/post emergence application, 8.0% and 16.4%TRR (0.013 and 0.009 mg/kg) was solubilised from the phenyl labelled and cyclohexane labelled plants, respectively. Enzymes solubilised 7.0% and 11.2% TRR (0.03 mg/kg and 0.029 mg/kg) from the post-emergence application with phenyl and cyclohexane labels, respectively.

For the soybean hay samples, enzyme hydrolysis, followed by extraction and hydrolysis with 1N hydrochloric acid and lignin digestion solubilised a further 15.5 and 18.4% TRR (0.022 and 0.014 mg/kg) from the pre-emergence application (phenyl and cyclo), 27.0 and 16.8% TRR (0.544 and 0.274 mg/kg) from the combined pre-/post emergence application (phenyl and cyclo) and 13.2 and 9.8% TRR (0.049 and 0.008 mg/kg) from the post-emergence application (phenyl and cyclo).

For the soybean seed samples, the TRRs obtained from the combined sodium acetate and enzyme hydrolysis extracts were 31.7 and 43.6% TRR (0.020 and 0.017 mg/kg) from the pre-emergence application (phenyl and cyclo. respectively), 25.0 and 35.5% TRR (0.026 and 0.017 mg/kg) from the combined pre-/post emergence application (phenyl and cyclo) and 34.6 and 35.5% TRR (0.018 and 0.018 mg/kg) from the post-emergence application.

MNBA, AMBA, 4/5-hydroxy mesotrione, parent mesotrione and an unknown polar component were identified in each soybean commodity treated with phenyl label material whilst 4/5-hydroxy mesotrione, parent mesotrione and an unknown polar component were identified in each soybean commodity following treatment with [cyclohexane-2-^{14}C] mesotrione.

Residues in Soybean Forage

Phenyl label plants

The TRRs in soybean forage treated with [phenyl-U-^{14}C]-mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.212 mg/kg, 0.162 mg/kg and 0.499 mg/kg, respectively.

Initial solvent extractabilities of the soybean forage were 59.0% (0.125 mg/kg), 54.3% (0.088 mg/kg) and 50.9% (0.254 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to post-extraction solids (PES) of 41.0% (0.087 mg/kg), 45.7% (0.074 mg/kg) and 49.1% (0.245 mg/kg), respectively. The extracted residues where characterised by chromatography (Table CA 6.2.1/05-5). For all application rates, the PES was digested in sodium acetate buffer using Viscozyme and Driselase enzymes. This released a further 0.016 mg/kg (7.5% TRR), 0.013 mg/kg (8.0%) and 0.035 mg/kg (7.0%) of residues from the pre-emergence, combined and post-emergence application rates, respectively. The enzyme solubilised radioactivity from the single post-emergence application rate was partitioned with ethyl acetate which recovered 0.008 mg/kg (1.6% TRR) of residue.

Following enzyme hydrolysis, further characterisation was performed on the PES for each application rate. The PES for the single pre-emergence and the combined pre-/post emergence application rates were extracted and hydrolysed 2x using 1N HCl. A total of 0.009 mg/kg of residue (4.3% of TRR) for the pre-emergence and 0.008 mg/kg (5.0% of TRR) of residue for the combined pre-/post emergence application rates were extracted. Extraction and hydrolysis with 1N HCl released a further 0.024 mg/kg (4.8% TRR) of residue. Lignin extraction of this material released 0.110 mg/kg (22.0% of TRR). Mild base extraction with 0.1M KOH followed by hemicellulose extraction with a stronger 24% KOH solution released an additional 0.014 mg/kg (2.8% of TRR) in total. A final cellulose digestion with 72% H_2SO_4 released 0.016 mg/kg (3.2% of TRR) of residue. The remaining PES accounted for 8.0% TRR (0.040 mg/kg)

A summary of radioactive residues from [phenyl-U-^{14}C]-mesotrione treated soybean forage is detailed in Table 6.2.1-15 . A summary of the characterisation and identification of residues present in soybean forage PES for [phenyl-U-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-16.

Residues of MNBA, AMBA, 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in forage samples treated at all application rates. MNBA was the most abundant residue present in the single pre-emergence and combined pre-/post emergence samples and accounted for 24.5% TRR (0.052 mg/kg) and 24.1% TRR (0.039 mg/kg), respectively. 4/5-Hydroxy mesotrione was the most abundant residue in the post-emergence forage sample at 14.6% TRR (0.073 mg/kg) where as MNBA accounted for 13.0% TRR (0.065 mg/kg). AMBA was detected at low levels in all samples and ranged from 0.001 to 0.004 mg/kg. 4/5-Hydroxy mesotrione residues of 0.017 mg/kg (8.0%) and 0.011 mg/kg (6.8%) were detected in the pre-emergence and combined samples respectively. Parent mesotrione residues were detected at 0.030 mg/kg (14.2%), 0.021 mg/kg (13.0%) and 0.028 mg/kg (5.6%), from the pre-emergence, combined and post-emergence treatments, respectively. Residues of unknown polar

components were detected in samples from each treatment regime at 0.005 mg/kg (2.4%), 0.006 mg/kg (3.7%) and 0.008 mg/kg (1.6%), respectively.

Table 6.2.1-15: Summary of radioactive residues in soybean forage samples following treatment with [phenyl-U-^{14}C]-mesotrione

Crop and Commodity:		**Soybean forage**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		217.7 g a.s./ha		345.5 g a.s./ha*		224.2 g a.s./ha	
Total Radioactive Residue (mg/kg):		0.212 mg/kg		0.162 mg/kg		0.499 mg/kg	
Initial extraction applied to chromatography (mg/kg):		0.125		0.088		0.254	
%TRR:		59.0		54.3		50.9	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction (acetonitrile:water combined supernatants)	MNBA	0.052	24.5	0.039a	24.1	0.065	13.0
	AMBA	0.003	1.4	0.001	0.6	0.004	0.8
	4/5-Hydroxy mesotrione	0.017	8.0	0.011a	6.8	0.073	14.6
	Mesotrione	0.030	14.2	0.021a	13.0	0.028	5.6
	Polar unknowns	0.005	2.4	0.006	3.7	0.008	1.6
	Unassigned peaks (each ≥0.01 mg/kg but <10% TRR)	-	-	-	-	0.032	6.4
	Non-defined (each <0.01 mg/kg)	0.018	8.5	0.010	6.2	0.044	8.8
	Total characterised	0.125	59.0	0.088	54.3	0.254	50.9
	PES	0.087	41.0	0.074	45.7	0.245	49.1
Total		0.212	100	0.162	100	0.499	100

* = Forage harvested prior to second application
a = Confirmed by TLC
- = Not applicable

Table 6.2.1-16: Summary of characterisation and identification of radioactive residues in soybean forage PES samples following treatment with [phenyl-U-14C]-mesotrione

Application Stage	**Pre-Emergence**		**Pre/Post-Emergence**		**Post-Emergence**	
TRR, mg/kg	0.212		0.162		0.499	
Origin of component	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps	0.087	41.0	0.074	45.7	0.245	49.1
Viscozyme + Driselase	0.016	7.5	0.013	8.0	0.035	7.0
Organic Fraction	NA	NA	NA	NA	0.008	1.6
Aqueous Fraction	NA	NA	NA	NA	0.027	5.4
1N HCl Extraction	0.005	2.4	0.004	2.5	0.011	2.2
Organic Fraction	NA	NA	NA	NA	0.005	1.0
Aqueous Fraction	NA	NA	NA	NA	0.006	1.2
1N HCl Hydrolysis	0.004	1.9	0.004	2.5	0.013	2.6
Organic Fraction	NA	NA	NA	NA	0.007	1.4
Aqueous Fraction	NA	NA	NA	NA	0.006	1.2
Lignin Extraction	NA	NA	NA	NA	0.110	22.0

Application Stage	Pre-Emergence		Pre/Post-Emergence		Post-Emergence	
0.1M KOH Extraction	NA	NA	NA	NA	0.007	1.4
24% KOH Extraction	NA	NA	NA	NA	0.014	2.8
72% H_2SO_4 Extraction	NA	NA	NA	NA	0.016	3.2
Total PES Characterization	0.025	11.8	0.021	13.0	0.206	41.3
Final PES (combustion)	0.062[C]	29.2	0.053[C]	32.7	0.040	8.0
Total PES	0.087	41.0	0.074	45.7	0.245	49.1

Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]
C = Calculated by subtraction. NA = not applicable

Cyclohexane label plants

The TRRs in soybean forage treated with [cyclohexane-2-^{14}C] mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.077 mg/kg, 0.055 mg/kg and 0.260 mg/kg, respectively.

Initial solvent extractabilities of the soybean forage were 55.8% (0.043 mg/kg), 54.5% (0.030 mg/kg) and 62.7% (0.163 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to PES of 44.2% (0.034 mg/kg), 45.5% (0.025 mg/kg) and 37.3% (0.097 mg/kg), respectively. The extracted residues where characterised by chromatography (Table 6.2.1-15). For all application rates, the PES was digested in sodium acetate buffer using Viscozyme and Driselase enzymes. This released a further 0.013 mg/kg (16.9% TRR), 0.009 mg/kg (16.4%) and 0.029 mg/kg (11.2%) of residues from the pre-emergence, combined and post-emergence application rates, respectively. The enzyme solubilised radioactivity from the single post-emergence application rate was partitioned with ethyl acetate which only recovered 0.002 mg/kg (0.8% of TRR) of residue.

Following enzyme hydrolysis, further characterisation was performed on the PES for the single post-emergence application rate. Extraction and hydrolysis with 1N HCl released a further 0.013 mg/kg (5.0% of TRR) of residue. Lignin extraction released 0.022 mg/kg (8.5% of TRR). Extraction with 0.1M KOH followed by hemicellulose extraction with 24% KOH solution released an additional 0.008 mg/kg (3.1% of TRR) in total. A final cellulose digestion with 72% H_2SO_4 released 0.021 mg/kg (8.1% of TRR) of residue. The remaining PES accounted for 1.6% TRR (0.004 mg/kg).

A summary of radioactive residues from [cyclohexane-2-^{14}C]-mesotrione treated soybean forage is detailed in Table 6.2.1-17. A summary of the characterisation and identification of residues present in soybean forage PES for [cyclohexane-U-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-18.

Residues of 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in forage samples treated at all application rates, with higher quantities being detected in the single post-emergence samples. 4/5-Hydroxy mesotrione residues of 0.011 mg/kg (14.3%), 0.007 mg/kg (12.7%) and 0.050 mg/kg (19.2%) were detected in the pre-emergence, combined and post-emergence treatments, respectively. Parent mesotrione residues were detected in pre-emergence, combined and post-emergence samples at 0.013 mg/kg (16.9%), 0.010 mg/kg (18.2%) and 0.022 mg/kg (8.5%), respectively. Residues of unknown polar components were detected in samples from each treatment regime at 0.009 mg/kg (11.7%), 0.005 mg/kg (9.1%) and 0.034 mg/kg (13.1%), respectively.

Table 6.2.1-17: Summary of radioactive residues in soybean forage samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Crop and Commodity:		**Soybean forage**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		225.8 g a.s./ha		356 g a.s./ha		229.6 g a.s./ha	
Total Radioactive (mg/kg):		0.077 mg/kg		0.055 mg/kg*		0.260 mg/kg	
Initial extraction applied to chromatography (mg/kg):		0.043		0.030		0.163	
%TRR:		55.8		54.5		62.7	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction (acetonitrile:water combined supernatants)	4/5-Hydroxy mesotrione	0.011	14.3	0.007	12.7	0.050	19.2
	Mesotrione	0.013	16.9	0.010	18.2	0.022	8.5
	Polar unknowns	0.009	11.7	0.005	9.1	0.034a	13.1
	Non-defined (each <0.01 mg/kg)	0.010	13.0	0.08	14.5	0.057	21.9
	Total characterised	0.043	55.8	0.030	54.5	0.163	62.7
	PES	0.034	44.2	0.025	45.5	0.097	37.3
Total		**0.077**	**100**	**0.055**	**100**	**0.260**	**100**

* = Forage harvested prior to second application - = Not applicable
a = A similar polar component was also found in cyclohexane hay samples and upon exhaustive characterization of the hay cyclohexane pre-/post-emergent polar peak was found to be multi-component each <5.3% TRR

Table 6.2.1-18: Summary of characterisation and identification of radioactive residues in soybean forage PES samples following treatment with [cyclohexane-2-14C]-mesotrione

Application Stage	**Pre-Emergence**		**Pre/Post-Emergence**		**Post-Emergence**	
TRR, mg/kg	0.077		0.055		0.260	
Origin of component	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps	0.034	44.2	0.025	45.5	0.097	37.3
Viscozyme + Driselase	0.013	16.9	0.009	16.4	0.029	11.2
Organic Fraction	NA	NA	NA	NA	0.002	0.8
Aqueous Fraction	NA	NA	NA	NA	0.027	10.4
1N HCl Extraction	NA	NA	NA	NA	0.007	2.7
1N HCl Hydrolysis	NA	NA	NA	NA	0.006	2.3
Lignin Extraction	NA	NA	NA	NA	0.022	8.5
0.1M KOH Extraction	NA	NA	NA	NA	0.003	1.2
24% KOH Extraction	NA	NA	NA	NA	0.005	1.9
72% H_2SO_4 Extraction	NA	NA	NA	NA	0.021	8.1
Total PES Characterization	0.013	16.9	0.009	16.4	0.093	35.8
Final PES (combustion)	0.021^C	27.3	0.016^C	29.1	0.004^C	1.6
Total PES	**0.034**	**44.2**	**0.025**	**45.5**	**0.097**	**37.3**

Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]
C = Calculated by subtraction. NA = not applicable

Residues in Soybean Hay

Phenyl label plants

The TRRs in soybean hay treated with [phenyl-U-^{14}C]-mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.142 mg/kg, 2.015 mg/kg and 0.370 mg/kg, respectively. Initial solvent extractabilities were 47.9% (0.068 mg/kg), 66.3% (1.335 mg/kg) and 47.3% (0.175 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to a PES of 52.1% (0.074 mg/kg), 33.7% (0.680 mg/kg) and 52.7% (0.195 mg/kg), respectively. The extracted residues where characterised by chromatography (Table CA 6.2.1/06-9). The PES were digested in sodium acetate buffer using Viscozyme and Driselase enzymes followed by 2x extraction with 1N HCl and lignin digestion. This released a total of 0.022 mg/kg (15.5% TRR) in the pre-emergence plants and 0.049 mg/kg (13.2% TRR) in the post emergence plants. No further characterisation was performed on the PES samples for single pre-emergence or post-emergence rate plants.

Further analysis was performed on the PES samples for the combined pre-/post emergence application rate. Enzymes and extraction with 1N HCl solubilised 0.232 mg/kg (11.5% of TRR) of the PES residue. Ethyl acetate fractions following partition of enzyme solubilised radioactivity contained an unknown polar component, AMBA, 4/5-hydroxy mesotrione and parent mesotrione. Lignin extraction released 0.312 mg/kg (15.5% TRR). Analysis of the aqueous and tetrahydrofuran (THF) lignin extracts indicated that 14C was incorporated into natural plant products. These processes released an overall total TRR of 27.0% (0.544 mg/kg). Extraction with 0.1M KOH followed by hemicellulose extraction with a 24% KOH solution released an additional 0.046 mg/kg (2.2% of TRR) in total from the PES. A final cellulose digestion with 72% H2SO4 released 0.028 mg/kg (1.4% of TRR) of residue. The remaining PES accounted for 3.1% TRR (0.146 mg/kg).

The residues determined in soybean hay are summarised in Table 6.2.1-19. A summary of the characterisation and identification of residues present in soybean hay PES from [phenyl-U-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-20.

Residues of 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in hay samples treated at all application rates, with higher quantities being detected in the combined pre-/post emergence samples. 4/5-Hydroxy mesotrione residues of 0.013 (9.2%), 0.331 (16.4%) and 0.054 mg/kg (14.6%) were detected in the pre-emergence, combined and post-emergence treatments, respectively. Parent mesotrione residues were detected in each sample at 0.009 mg/kg (6.3%), 0.178 mg/kg (8.8%) and 0.023 mg/kg (6.2%), respectively. The polar residues were detected in pre-emergence, combined and post-emergence samples at 0.006 mg/kg (4.2%), 0.026 mg/kg (1.3%) and 0.006 (1.6%) mg/kg, respectively.

Table 6.2.1-19: Summary of radioactive residues in soybean hay samples following treatment with [phenyl-U-^{14}C]-mesotrione

Crop and Commodity:		**Soybean hay**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		217.7 g a.s./ha		345.5 g a.s./ha*		224.2 g a.s./ha	
Total Radioactive Residue (mg/kg):		0.142		2.015		0.370	
Initial extraction applied to chromatography (mg/kg):		0.068		1.335		0.175	
%TRR:		47.9		66.3		47.3	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction	MNBA	0.015	10.6	0.410a	20.3	0.042	11.4
	AMBA	ND	ND	0.055a	2.7	ND	ND

Crop and Commodity:		Soybean hay					
(acetonitrile:water combined supernatants)	4/5-Hydroxy mesotrione	0.013	9.2	0.331a	16.4	0.054	14.6
	Mesotrione	0.009	6.3	0.178a	8.8	0.023	6.2
	Polar unknowns	0.006	4.2	0.026	1.3	0.006	1.6
	Unassigned peaks (each ≥0.01 mg/kg but <6% TRR)	0.012	8.5	0.335	16.6b	-	-
	Non-defined (each <0.01 mg/kg)	0.013	9.2	0.000	0.0	0.05	13.5
	Total characterised	0.068	47.9	1.335	66.3	0.175	47.3
	PES	0.074	52.1	0.680	33.7	0.195	52.7
Total		**0.142**	**100**	**2.015**	**100**	**0.370**	**100**

- = Not applicable a = TLC confirmed b = <2.6% TRR for [phenyl-U-^{14}C]-mesotrione
ND = Not detected

Table 6.2.1-20: Summary of characterisation and identification of radioactive residues in soybean hay PES samples following treatment with [phenyl-U-^{14}C]-mesotrione

Application Stage		Pre-Emergence		Pre/Post-Emergence		Post-Emergence	
TRR, mg/kg		0.142		2.015		0.370	
Origin of component		**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps		0.074	52.1	0.680	33.7	0.195	52.7
Combined Viscozyme/Driselase, 1N HCl extraction, hydrolysis, and lignin digestion		0.022	15.5	0.544	27.0	0.049	13.2
Organic Fraction		NA	NA	0.337[B]	16.7	0.014	3.8
Chromatography of organic fraction components	Mesotrione	-	-	0.033	1.6	-	-
	AMBA	-	-	0.019	0.9	-	-
	4/5-Hydroxy mesotrione	-	-	0.014	0.7	-	-
	Polar Peak	-	-	0.003	0.1	-	-
	Non-defined (each >0.01mg/kg)	-	-	0.233[C]	11.6	-	-
	Non-defined (each <0.01mg/kg)	-	-	0.034	1.7	-	-
Aqueous Fraction		NA	NA	0.207	10.3	0.035	9.5
Combined 0.1M and 24% KOH		NA	NA	0.046	2.2	NA	NA
72% H_2SO_4 Extraction		NA	NA	0.028	1.4	NA	NA
Total PES Characterization		0.022	15.5	0.618	30.7	0.049	13.2
Final PES (combustion)		0.052[D]	36.6	0.063	3.1	0.146[D]	39.5
Total PES		**0.074**	**52.1**	**0.680**	**33.7**	**0.195**	**52.7**

***** = Residues could not be resolved by HPLC due to high salt content in matrix. Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]. A = Sum of fractions , B = Sum of fractions, C = each <0.082 mg/kg (4.1% of TRR), D = Calculated by subtraction, NA = Not applicable

Cyclohexane label plants

The TRRs in soybean hay treated with [cyclohexane-2-^{14}C] mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.076 mg/kg, 1.632 mg/kg and 0.082 mg/kg, respectively.

Initial solvent extractabilities of the soybean hay were 51.3% (0.039 mg/kg), 78.1% (1.275 mg/kg) and 59.8% (0.049 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to PES of 48.7% (0.037 mg/kg), 21.9% (0.357 mg/kg) and 40.2% (0.033 mg/kg), respectively. The extracted residues where characterised by chromatography (Table 6.2.1-21). For all application rates, the PES was digested in sodium acetate buffer using Viscozyme and Driselase enzymes followed by 2x extraction with 1N HCl and where appropriate, lignin digestion. These combined released a total of 0.014 mg/kg (18.4% TRR) in the pre-emergence plants and 0.008 mg/kg (13.2% TRR) in the post emergence plants. No further characterisation was performed on the PES for single pre-emergence or post-emergence rate plants.

Following enzyme treatment which solubilised 0.139 mg/kg (8.5% of TRR), further characterisation was performed on the PES for the combined pre-/post-emergence application rate. Partitioning of the solubilised radioactivity with ethyl acetate only recovered 0.015 mg/kg (0.9%) of residue. HPLC analysis of the ethyl acetate fraction detected low levels of 4/5-hydroxy mesotrione (0.005 mg/kg), parent mesotrione (0.003 mg/kg) and polar component (0.003 mg/kg). Extraction and hydrolysis with 1N HCl released a further 0.051 mg/kg (3.1% of TRR in total) of the PES residue. Lignin extraction released 0.084 mg/kg (5.1%). These processes released an overall total TRR of 0.274 mg/kg (16.8% TRR) in the combined pre-and post emergence plants. Mild base extraction with 0.1M KOH followed by hemicellulose extraction with 24% KOH solution released an additional 0.016 mg/kg (1.0% of TRR) in total. A final cellulose digestion with 72% H2SO4 released 0.023 mg/kg (1.4% of TRR) of residue. The remaining PES accounted for 2.7% TRR (0.044 mg/kg).

Residues of 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in hay samples treated at all application rates, with the highest quantities being detected in the combined pre-/post emergence samples. 4/5-Hydroxy mesotrione residues of 0.012 mg/kg (15.8%), 0.407 mg/kg (24.9%) and 0.016 mg/kg (19.5%) were detected in the pre-emergence, combined and post-emergence treatments, respectively. Parent mesotrione residues were detected in each sample at 0.005 mg/kg (6.6%), 0.134 mg/kg (8.2%) and 0.006 mg/kg (7.3%), from the pre-emergence, combined and post-emergence treatments, respectively. The polar residues were detected in pre-emergence, combined and post-emergence samples at 0.012 mg/kg (15.8%), 0.243 mg/kg (14.9%) and 0.012 mg/kg (14.6%), respectively.

Further analysis and characterisation was performed on the polar residues peak obtained following initial analysis of the pre-/post emergence hay samples. The peak was isolated using a combination of HPLC and solid phase extraction techniques.

Molecular weight determination suggested that the peak was made up of multiple small molecular weight components (≤0.087 mg/kg, ≤5.3% TRR). Further characterisation indicated that the polar peak did not contain reducing sugars, free hydroxyl groups, accessible carboxylic acid functional groups or malonic acid and/or its derivatives

The residues detected in soybean hay are summarised in Table 6.2.1-21. A summary of the characterisation and identification of residues present in soybean hay PES from [cyclohexane-2-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-22.

Table 6.2.1-21: Summary of radioactive residues in soybean hay samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Crop and Commodity:		**Soybean hay**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		225.8 g a.s./ha		356 g a.s./ha		229.6 g a.s./ha	
Total Radioactive Residue (mg/kg):		0.076		1.632		0.082	
Initial extraction applied to chromatography (mg/kg):		0.039		1.275		0.049	
%TRR:		51.3		78.1		59.8	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction (acetonitrile:water combined supernatants)	4/5-Hydroxy mesotrione	0.012	15.8	0.407a	24.9	0.016	19.5
	Mesotrione	0.005	6.6	0.134a	8.2	0.006	7.3
	Polar unknowns	0.012	15.8	0.243b	14.9	0.012	14.6
	Unassigned peaks (each ≥0.01 mg/kg but <6% TRR)	-	-	0.491	30.1	-	-
	Non-defined (each <0.01 mg/kg)	0.010	13.2	0.000	0.0	0.015	18.3
	Total characterised	0.039	51.3	1.275	78.1	0.049	59.8
	PES	0.037	48.7	0.357	21.9	0.033	40.2
Total		**0.073**	**100**	**1.632**	**100**	**0.082**	**100**

- = Not applicable a = TLC confirmed b = multi-component upon further characterization, each <0.087 mg/kg (5.3%TRR)

Table 6.2.1-22: Summary of characterisation and identification of radioactive residues in soybean hay PES samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Application Stage		**Pre-Emergence**		**Pre/Post-Emergence**		**Post-Emergence**	
TRR, mg/kg		0.076		1.632		0.082	
Origin of component		**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps		0.037	48.7	0.357	21.9	0.033	40.2
Viscozyme/Driselase, 1N HCl extraction, hydrolysis, and lignin digestion		0.014	18.4	0.274	16.8	0.008	13.2
Organic Fraction		NA	NA	0.026[A]	1.6	NA	NA
Chromatography of organic fraction components	Mesotrione	-	-	0.003	0.2	-	-
	4/5-Hydroxy-mesotrione	-	-	0.005	0.3	-	-
	Polar Peak	-	-	0.003	0.2	-	-
	Non-defined (each < 0.01mg/kg)	-	-	0.004	0.2	-	-
Aqueous Fraction		NA	NA	0.248	15.2	NA	NA
Combined 0.1M and 24% KOH		NA	NA	0.016	1.0	NA	NA
72% H_2SO_4 Extraction		NA	NA	0.023	1.4	NA	NA
Total PES Characterization		0.014	18.4	0.313	19.2	0.008	9.8
Final PES (combustion)		0.023[B]	30.3	0.044[B]	2.7	0.025[B]	30.5
Total PES		**0.037**	**48.7**	**0.357**	**21.9**	**0.033**	**40.2**

* = Residues could not be resolved by HPLC due to high salt content in matrix. Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]. A = Sum of fractions , B = Calculated by subtraction, NA = Not applicable

Residues in Mature Soybean Seeds

Phenyl label plants

The TRRs in soybean seeds treated with [phenyl-U-^{14}C]-mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.063 mg/kg, 0.104 mg/kg and 0.052 mg/kg, respectively.

Initial solvent extractabilities of the soybean seeds were 34.9% (0.022 mg/kg), 42.3% (0.044 mg/kg) and 32.7% (0.017 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to a PES of 55.6% (0.035 mg/kg), 50.0% (0.052 mg/kg) and 57.7% (0.030 mg/kg), respectively. The extracted residues where characterised by chromatography (Table 6.2.1-23).

Due to the presence of oils and lipids in the soybean seed samples, additional extraction/partitioning steps were performed using a mixture of acetone and hexane. This released a further 0.006 mg/kg (9.5% TRR), 0.008 mg/kg (7.7% TRR) and 0.005 mg/kg (9.6% TRR) of residue from the single pre-emergence, combined pre-/post emergence and single post emergence application rates, respectively.

The PES from each application rate was digested in sodium acetate buffer using Viscozyme and Driselase enzymes. This released a further 0.020 mg/kg (31.7%), 0.026 mg/kg (25.0%) and 0.018 mg/kg (34.6%) of residues from the single pre-emergence, combined pre-/post emergence and single post-emergence application rates, respectively. The PES enzyme digest extracts from each treatment application rate were subject to acetone precipitation which recovered a further 0.015 mg/kg (23.8%), 0.012 mg/kg (11.5%) and 0.013 mg/kg (25.0%) of the residues. HPLC analysis revealed that the enzyme extracts contained multiple components ranging from ≤0.006 to ≤0.007 mg/kg.

The residues detected in soybean seeds are summarised in Table 6.2.1-21. A summary of the characterisation and identification of residues present in soybean seed PES from [phenyl-U-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-24.

Residues of 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in soybean seed samples treated at all application rates. 4/5-Hydroxy mesotrione was present at low levels in all samples and accounted for 4.8% (0.003 mg/kg), 6.7% (0.007 mg/kg) and 7.7% (0.004 mg/kg) in the single pre-emergence, combined pre-/post emergence and single post-emergence application rates, respectively. Parent mesotrione was the most abundant residue present in the single pre-emergence seed sample and accounted for 9.5% TRR (0.006 mg/kg). The unknown polar component was the most abundant residue in the combined pre-/post emergence and single post-emergence seed samples at 9.6% TRR (0.010 mg/kg) and 15.4 % (0.008 mg/kg), respectively. Low levels of MNBA were detected in the single pre-emergence and combined pre-/post emergence samples and accounted for 0.001 mg/kg (1.6%) and 0.005 mg/kg (4.8% TRR), respectively. AMBA residue was only found in the combined pre-/post emergence samples at 0.002 mg/kg (1.9%).

Table 6.2.1-23: Summary of radioactive residues in soybean seed samples following treatment with [phenyl-U-14C]-mesotrione

Crop and Commodity:		**Soybean seed**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		217.7 g a.s./ha		345.5 g a.s./ha*		224.2 g a.s./ha	
Total Radioactive Residue (mg/kg):		0.063		0.104		0.052	
Initial extraction applied to chromatography (mg/kg):		0.022		0.044		0.017	
%TRR:		34.9		42.3		32.7	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction (acetonitrile:water combined supernatants)	MNBA	0.001	1.6	0.005a	4.8	ND	ND
	AMBA	ND	ND	0.002	1.9	ND	ND
	4/5-Hydroxy mesotrione	0.003	4.8	0.007a	6.7	0.004	7.7
	Mesotrione	0.006	9.5	0.003a	2.9	0.002	3.8
	Polar unknowns	0.004	6.3	0.010b	9.6	0.008	15.4
	Unassigned peaks	-	-	0.010	9.6	-	-
	Non-defined (each <0.01 mg/kg)	0.008	12.7	0.007	6.7	0.003	5.8
	Total characterised	0.022	34.9	0.044	42.3	0.017	32.7
	PES	0.035	55.6	0.052	50.0	0.030	57.7
Acetone/Hexane extractions		0.006	9.5	0.008	7.7	0.005	9.6
Totals		**0.063**	**100**	**0.104**	**100**	**0.052**	**100**

- = Not applicable, ND = not detected, a = TLC confirmed b = Initial characterisation value of 0.01 mg/kg, but two additional extractions and characterisation demonstrated the value to be actually lower, 0.006-0.007 mg/kg

Table 6.2.1-24: Summary of characterisation and identification of radioactive residues in soybean seed PES samples following treatment with [phenyl-U-^{14}C]-mesotrione

Application Stage		**Pre-Emergence**		**Pre/Post-Emergence**		**Post-Emergence**	
TRR, mg/kg		0.063		0.104		0.052	
Origin of component		**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps		0.035	55.6	0.052	50.0	0.030	57.7
Viscozyme and Driselase extracts		0.020	31.7	0.026	25.0	0.018	34.6
Post-acetone precipitation		0.015	23.8	0.012[A]	11.5	0.013	25.0
Chromatography of extract after acetone precipitation	Polar Peak	-	-	0.010[C]	9.6	-	-
	Non-defined (each <0.01mg/kg)	0.015	23.8	0.002	1.9	0.013	25.0
Precipitate (by subtraction		0.005	7.9	0.007	6.7	0.005	9.6
Total PES Characterization		0.020	31.7	0.026	25.0	0.018	34.6
Final PES (combustion)		0.015	23.8	0.026	25.0	0.013	25.0
Total PES		**0.035**	**55.5**	**0.052**	**50.0**	**0.031**	**57.7**

Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]; A = Acetone precipitation on Viscozyme extract only, C = multi-components based on acetonitrile:water extractable polar peak results

Cyclohexane label plants

The TRRs in soybean seeds treated with [cyclohexane-2-^{14}C] mesotrione at a single pre-emergence, combined and a single post-emergence application rates were 0.039 mg/kg, 0.093 mg/kg and

0.015 mg/kg, respectively. Initial solvent extractabilities of the soybean seeds were 30.8% (0.012 mg/kg), 45.2% (0.042 mg/kg) and 33.3% (0.005 mg/kg) from the pre-emergence, combined and post-emergence treatments, respectively. This corresponded to PES of 51.3% (0.020 mg/kg), 41.9% (0.039 mg/kg) and 53.3% (0.008 mg/kg), respectively. The extracted residues where characterised by chromatography (Table 6.2.1-25).

Due to the presence of oils and lipids in the soybean seed samples, additional extraction/partitioning steps were performed using either hexane/acetone (1:1 v/v) and/or 100% hexane. The acetone/hexane extract for the combined pre-/post emergence application contained 0.012 mg/kg and was subjected to saponification, isolation of the fatty acids by selective extraction and TLC analysis. The results from the TLC analysis showed that ^{14}C was associated with fatty acids, indicating incorporation of the radiolabel into natural products.

For the pre-emergence and combined pre-/post emergence application rates, the PES was treated with Viscozyme and Driselase enzymes. This released a further 0.017 mg/kg (43.6% TRR) and 0.033 mg/kg (35.5% TRR) of residues, respectively. The PES Viscozyme extracts were also subjected acetone precipitation which recovered a further 0.013 mg/kg (33.3% TRR) and 0.014 mg/kg (15.1% TRR) of the residue, respectively. HPLC analysis revealed that the extract from the combined pre-/post emergence sample mainly contained the unknown polar peak components (0.011 mg/kg, 11.8% TRR).

The extract from the soybean seed samples treated with the single post-emergence application rate contained <0.010 mg/kg of residue in the acetonitrile:water fraction. Therefore, no HPLC analysis was conducted. The PES contained 0.008 mg/kg of residue, and was not characterized further.

Residues of 4/5-hydroxy mesotrione, parent mesotrione and a polar component were detected in soybean seed samples treated at the single pre-emergence and the combined pre-/post emergence samples. 4/5-Hydroxy mesotrione residues of 0.001 mg/kg (2.6% TRR) and 0.003 mg/kg (3.2% TRR) were detected in each sample respectively. Parent mesotrione residues were detected at 0.002 mg/kg (5.1% TRR) and 0.003 mg/kg (3.2% TRR), respectively. The polar residues detected in pre-emergence and combined pre/-post emergence samples were 0.007 mg/kg (17.9% TRR) and 0.029 mg/kg (31.2% TRR).

Further characterisation was performed on the polar residues peak obtained following initial extraction of the combined pre-/post emergence seed samples. A range of techniques were used including partitioning with organic solvents, acid hydrolysis, HPLC analysis and solid phase extractions. The results demonstrated that the polar peak contained multiple components (each ≤0.007 mg/kg) and the carbon-14 was likely to be incorporated into natural products.

The residues detected in soybean seeds are summarised in Table 6.2.1-25. A summary of the characterisation and identification of residues present in soybean seed PES from [cyclohexane-2-^{14}C]-mesotrione treated plants is detailed in Table 6.2.1-26.

Table 6.2.1-25: Summary of radioactive residues in soybean seed samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Crop and Commodity:		**Soybean seed**					
Treatment regime:		**Pre-emergence**		**Pre-/Post emergence**		**Post-emergence**	
Application Rate:		225.8 g a.s./ha		356 g a.s./ha		229.6 g a.s./ha	
Total Radioactive Residue (mg/kg):		0.039		0.093		0.015	
Initial extraction applied to chromatography (mg/kg):		0.012		0.042		0.005	
%TRR:		30.8		45.2		33.3	
Origin of component	**Component (code)**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
Chromatography of initial extraction (acetonitrile:water combined supernatants)	4/5-Hydroxy mesotrione	0.01	2.6	0.003	3.2	-	-
	Mesotrione	0.02	5.1	0.003	3.2	-	-
	Polar unknowns	0.07	17.9	0.029a	31.2	-	-
	Non-defined (each <0.01 mg/kg)	0.02	5.1	0.007	7.5	-	-
	Total characterised	0.012	30.8	0.042	45.2	-	-
	PES	0.020	51.3	0.039	41.9	0.008	53.3
Acetone/Hexane extractions		0.007	17.9	0.012	12.9	0.002	13.3
Totals		**0.039**	**100**	**0.093**	**100**	**0.015**	**33.3**

a = Multi-component upon further characterization, each <0.007 mg/kg (<6.5% TRR)
- = Not applicable

Table 6.2.1-26: Summary of characterisation and identification of radioactive residues in soybean seed PES samples following treatment with [cyclohexane-2-^{14}C]-mesotrione

Application Stage		**Pre-Emergence**		**Pre/Post-Emergence**		**Post-Emergence**	
TRR, mg/kg		0.039		0.093		0.015	
Origin of component		**mg/kg**	**%TRR**	**mg/kg**	**%TRR**	**mg/kg**	**%TRR**
TRR Not Extracted by Initial Acetonitrile/Water Steps		0.020	51.3	0.039	41.9	0.008	53.3
Viscozyme and Driselase extracts		0.017	43.6	0.033	35.5	-	-
Post-acetone precipitation		0.013	33.3	0.014[A]	15.1	-	-
Chromatography of extract after acetone precipitation	Polar Peak	-	-	0.011[D]	11.8	-	-
	Non-defined (each <0.01mg/kg)	0.013	33.3	0.003	3.2	-	-
Precipitate (by subtraction)		0.004	10.3	0.011	11.8	NA	NA
Total PES Characterization		0.017	43.6	0.033	35.5	NA	NA
Final PES (combustion)		0.003[C]	7.7	0.006[C]	6.5	NA	NA
Total PES		**0.020**	**51.4**	**0.039**	**42.0**	**NA**	**NA**

Total PES Characterization = sum of extracts. Total PES = Total PES Characterization + Final PES [Combustion]; A = Acetone precipitation on Viscozyme extract only, C = Calculated by subtraction. D = multi-components based on acetonitrile:water extractable polar peak results

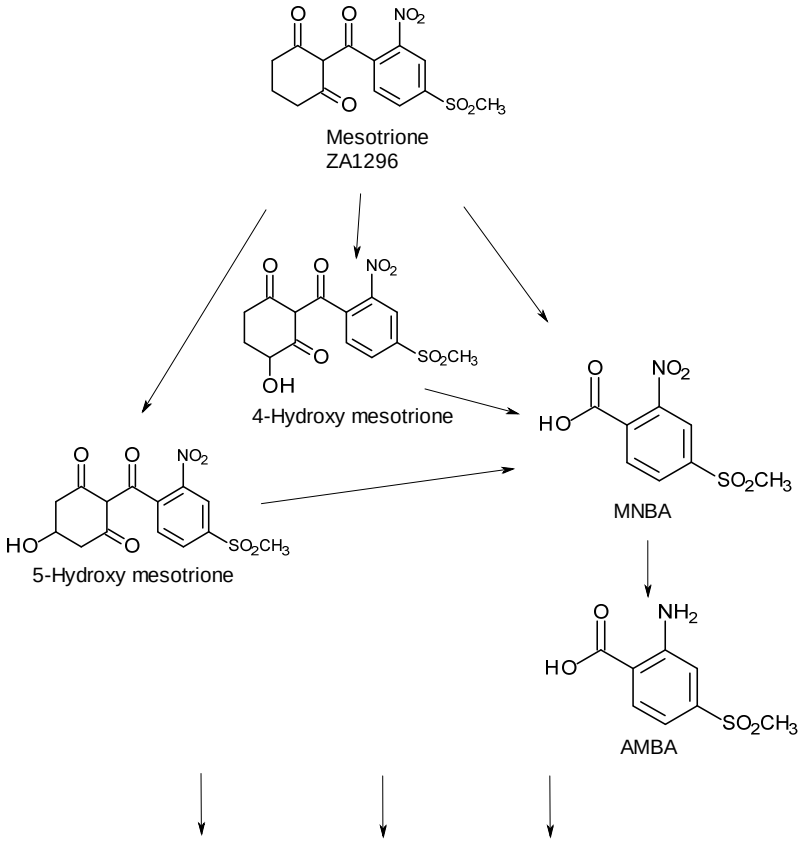
Storage Stability

The initial radiocomponent profiles used to characterise extractable residues in forage, hay and seed samples were obtained within 33 days (approx 1 month) of harvest. Extraction and analysis after 159, 294 and 374 days storage of selected hay and seed samples from cyclohexane and phenyl label treatments indicated that mesotrione and mesotrione metabolites, including 5-hydroxy mesotrione, were stable

during freezer storage of the samples. However there was evidence following extraction, long-term storage and thawing of the extracts that 5-hydroxy mesotrione was susceptible to degradation.

The proposed metabolic of mesotrione in soybeans pathway is presented in Figure 6.2.1-3.

Figure 6.2.1-3: Proposed metabolic pathway for mesotrione in soybean



Conclusions:

Following separate applications of either [phenyl-U-^{14}C]-mesotrione or [cyclohexane-2-^{14}C]-mesotrione to soybeans with three different treatment regimes (a single pre-emergence, a combined pre-/post emergence and a single post-emergence application) samples of forage, hay and mature seeds were harvested.

Total radioactive residues in the edible seeds were 0.052 – 0.104 mg/kg for phenyl label treated plants and 0.015 mg/kg – 0.093 mg/kg for cyclohexane label treated plants, with highest residues (0.104 and 0.093 mg/kg; phenyl and cyclohexane plants respectively) observed in plants receiving the combined pre-/post emergence application. In seeds from all three use patterns, identifiable extractable residues were parent mesotrione, up to 0.006 mg/kg (9.5% TRR), MNBA, up to 0.005 mg/kg (4.8% TRR), AMBA, up to 0.002 mg/kg (1.9% TRR) and 4/5 hydroxy mesotrione, up to 0.007 mg/kg (6.7% TRR). Saponification of a hexane/acetone extract demonstrated carbon-14 incorporation into plant fatty acids and individual components were shown to each account for ≤0.01 mg/kg. The remaining extractable residues in seeds were shown to be comprised of multiple small components all ≤0.01 mg/kg (and/or ≤10% TRR).

Initial PES in seeds were 42-58% TRR reflecting extensive metabolism and carbon-14 incorporation into natural products. Enzyme hydrolyses of these solid residues was particularly effective, releasing 25-44%

TRR as multiple polar components with only extremely small amounts (<0.003 mg/kg) of identifiable metabolites. Final unextractable residues in seeds were <10% TRR and/or <0.05 mg/kg.

In soybean forage, the single post-emergence treatment with the shortest PHI demonstrated the highest residue levels (0.499 and 0.260 mg/kg; phenyl and cyclohexane respectively). Forage was harvested before the second treatment in the combined application regime and residues from this treatment and that of the pre-emergence treatment were 0.162 and 0.212 mg/kg for phenyl labelled plants. Corresponding levels for cyclohexane treated plants were 0.055 mg/kg and 0.077 mg/kg.

In soybean hay, the highest TRR was observed in hay receiving the combined pre-/post emergence application rate (2.015 and 1.632 mg/kg; phenyl and cyclohexane labels respectively) which is likely due to the very short PHI (9 days). Residues in hay from each of the single pre- and post-emergence treatments comprised 0.142 mg/kg and 0.370 mg/kg, respectively for phenyl labelled plants and 0.08 mg/kg for both treatments in cyclohexane labelled plants.

Qualitatively, the metabolic profile was similar in seeds, forage and hay samples, but quantitatively, more radioactivity was readily extractable in forage and hay, particularly in hay with a very short PHI (9 days after the 2nd application).

As in seeds, a similar pattern of identifiable components was observed with parent mesotrione accounting for a maximum of 0.03 mg/kg (14.2% TRR) in forage and 0.178 mg/kg (8.8% TRR) in hay. MNBA was the highest identifiable component, accounting for a maximum of 0.065 mg/kg (13.0% TRR) in forage and 0.410 mg/kg (20.3% TRR) in hay. The 4/5-hydroxy mesotrione moiety accounted for a further 0.073 mg/kg (14.6% TRR) in forage and 0.407 mg/kg (24.9% TRR) in hay, whilst AMBA, the reduced form of MNBA accounted for a maximum of 0.004 mg/kg (0.8% TRR) in forage and 0.055 mg/kg (2.7% TRR) in hay.

It was also demonstrated that a number of small molecular weight components, likely carbon-14 incorporated into natural products were present in both forage and hay samples from all treatment regimes. Hydrolysis of PES samples (using acid and enzymes) released approximately 12-17% TRR in forage and 10-19% TRR in hay in the samples with the highest PES levels. These hydrolysates were shown to be predominantly polar and could not be identified or characterised further. Harsher acid and base extraction of selected forage and hay samples indicated multiple small molecular weight components.

In conclusion, mesotrione in soybeans was metabolised to 4/5-hydroxy mesotrione and two discrete organic acid metabolites lacking the cyclohexanedione ring, MNBA and AMBA. Mesotrione and its metabolites undergo further metabolism to small molecular fragments which are incorporated into natural products and to very polar components.

Summary of metabolism, distribution and expression of residues in crops

Metabolism studies conducted with crops representative of two different crop groups (cereal/grass: maize and oilseed: peanut and mesotrione herbicide tolerant (HT) soybean) and based on the commercially recommended use pattern, i.e. pre- or post- and pre- and post-emergence foliar applications have been submitted. These have provided a detailed understanding of the metabolism of mesotrione (ZA1296) in food and feed commodities showing that the metabolic pathways are similar and support the proposed uses of mesotrione on these crop groups. Furthermore, the metabolism pathways operating in genetically modified HT soybeans are qualitatively similar to those operating in unmodified crops.

Total residues were very low (0.001 to 0.037 mg/kg) in food commodities (maize grain and peanut meat) from the unmodified crops and higher in HT soya seed at 0.015 to 0.104 mg/kg dependent on the use pattern. Total residues in feed items were 0.015-1.066 mg/kg for maize forage and fodder, 0.011 -

0.064 mg/kg for peanut foliage and hay and 0.076 to 2.015 mg/kg for HT soya forage and hay dependent on the use pattern.

Little or no mesotrione was detected in maize grain, peanut meat or HT soya seed (0.001-0.006 mg/kg) or feed items from the unmodified crops (<0.0005-0.008 mg/kg). Higher amounts of mesotrione were measured in the feed items from HT soybean at 0.005-0.178 mg/kg dependent on the use pattern.

The metabolism of mesotrione was extensive in all crops and proceeded via the same routes, primarily through either hydroxylation of the cyclohexanedione ring or by cleavage to form the metabolite MNBA (4-methylsulfonyl-2-nitro benzoic acid), which was further reduced to AMBA (2-amino-4-methylsulfonyl benzoic acid). These metabolites were also present as conjugates. Evidence of incorporation of radioactive residues from further breakdown of the metabolites into natural products (lignin, cellulose, sugars etc.) was seen in all crops.

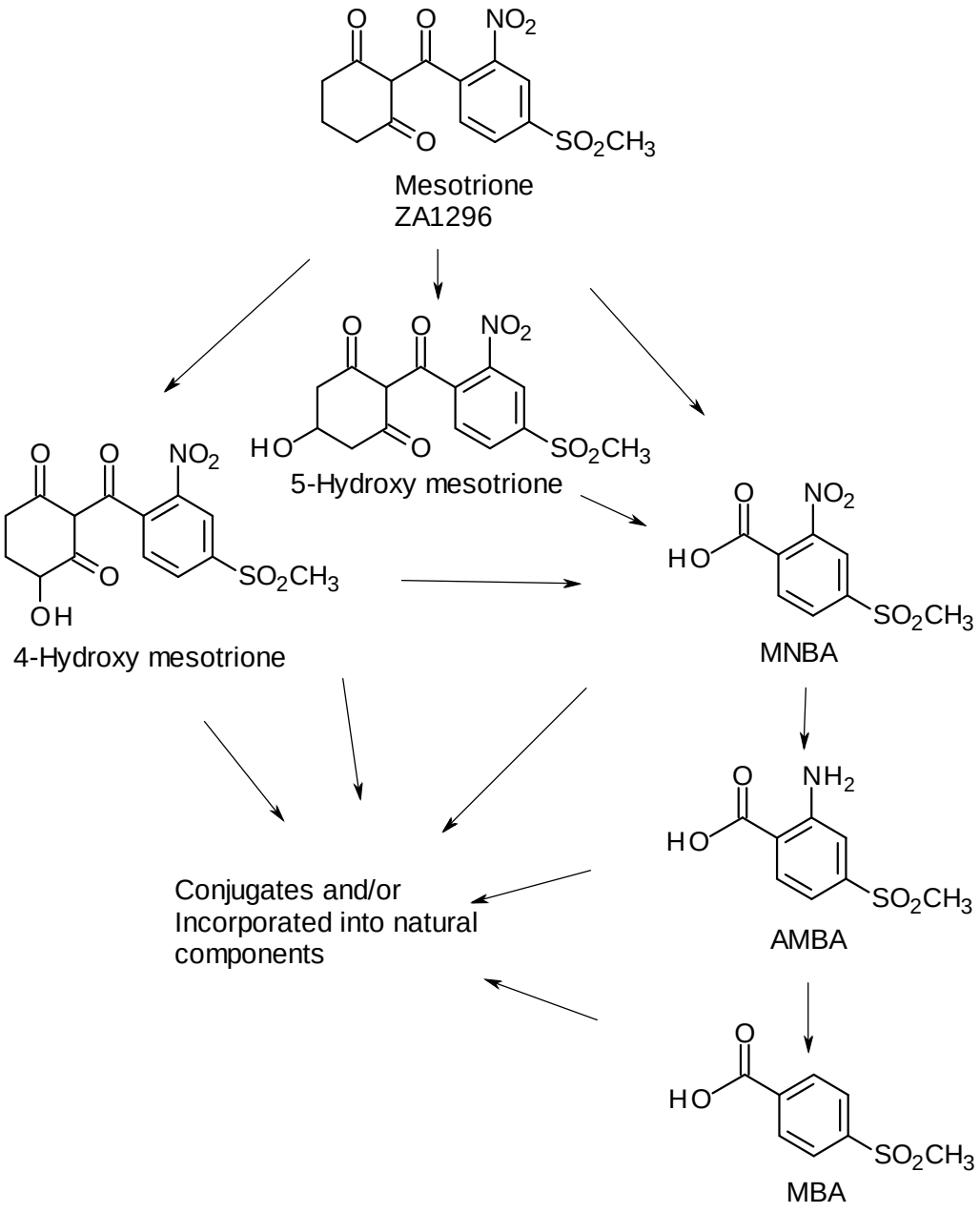
In maize, the pathway was defined in foliage and comprised (i) the cleavage of mesotrione to give MNBA (0.008-0.070 mg/kg) and its subsequent reduction to AMBA (0.02-0.301 mg/kg, free and conjugated) (ii) hydroxylation of the parent compound to give 4-hydroxy-mesotrione (0.006-0.027 mg/kg) (iii) incorporation of mesotrione degradates into natural plant constituents in particular glucose, lignin and cellulose and (iv) conjugation of metabolites.

In peanuts, the metabolic pathway following a pre-emergence application proceeded via cleavage of mesotrione to yield MNBA (<0.001 mg/kg in nutmeat and 0.001-0.007 mg/kg in feed items). MNBA was reduced to its amino analogue, AMBA that was converted to numerous conjugates (<0.001-0.002 mg/kg in nutmeat and <0.001-0.005 mg/kg in feed items). Exceedingly small amounts (<0.001-0.001 mg/kg) of MBA (4-methylsulfonyl benzoic acid) resulting from further degradation of AMBA were also found in nutmeat and feed items. Mesotrione was hydroxylated in the cyclohexanedione ring to give 4-hydroxy mesotrione and found (0.001 mg/kg) in the nutmeat after further extraction of the post-extracted solids.

In HT soybeans, the pathway comprised (i) the cleavage of mesotrione into MNBA (0.001-0.005 mg/kg in soya seed and 0.015-0.410 mg/kg in feed items) and its subsequent reduction to AMBA (0.002 mg/kg in soya seed and 0.001-0.055 mg/kg in feed items), (ii) hydroxylation of the parent compound to give 4-hydroxy-mesotrione and 5-hydroxy-mesotrione (0.001-0.007 mg/kg in soya seed and 0.007-0.407 mg/kg in feed items) and (iii) incorporation of mesotrione degradates into natural plant constituents in particular fatty acids, sugars and amino acids.

The proposed pathways of metabolism are shown in Figure 6.2.1-4.

Figure 6.2.1-4 Metabolism of mesotrione (ZA1296) in plants



CA 6.2.2 Poultry

As shown by dietary burden calculations under Section CA 6.4 the use of mesotrione does not lead to significant residues in livestock feed (<0.1 mg/kg DM total diet and <0.004 mg/kg bw/day) with respect to poultry. Thus, metabolism and distribution studies in poultry are not required according to EU data requirements (**Commission Regulation (EU) No 283/2013, 1 March 2013**).

CA 6.2.3 Lactating ruminants

As shown by dietary burden calculations under Section CA 6.4, the use of mesotrione does not lead to significant residues in livestock feed (<0.1 mg/kg DM total diet and <0.004 mg/kg bw/day) with respect

to dairy or beef cattle. Thus, metabolism and distribution studies in ruminants are not required according to EU data requirements (**Commission Regulation (EU) No 283/2013, 1 March 2013**).

Although not considered to be a metabolite important in the residue definition of mesotrione, AMBA and its conjugates were present in the forage and fodder samples from the maize metabolism study and residues in the diet may exceed 0.1 mg/kg. The significance of AMBA to ruminants is considered rather than establishing the AMBA residue levels under field conditions. This strategy was agreed with selected authority experts since a method could not be developed to analyse AMBA in field samples where non-radiolabelled mesotrione had been applied (see Point CA 6.2.1, Metabolism, distribution and expression of residues in maize).

However, the following data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.2.1, December 1999**).

Species	Author/s	Issue Year	Report Number
Cow	Hand L	1997	R44276/0008

A summary of the study is given below.

Guidelines

Compliant with the recommendations for conducting animal metabolism studies within the framework of EU Directive 91/414/EEC

GLP

The study was carried out according to the principles of good laboratory practice.

Executive Summary

A lactating cow was orally administered AMBA at a dose level of approximately 200 mg/day (equivalent to more than 60 times the maximum calculated daily intake for dairy cows). Results of the study demonstrated that residues of AMBA in tissues was low, typically <0.01 mg/kg, although kidney and perirenal fat samples contained residues of 0.053 mg/kg and 0.018 mg/kg AMBA equivalents respectively (suspected to be due to residual urine in the samples). Mean daily residues levels in milk were found to be between 0.005 mg/L and 0.009 mg/L – accounting for 0.06% of the administered dose. With no or very low residues of AMBA detected at a high dosage rate, no detectable residues are expected after normal field use of mesotrione.

Materials and methods:

A single lactating cow was dosed with ^{14}C-labelled AMBA (radiochemical purity >98.2%) at an exaggerated nominal rate of 10 mg ai/kg in the total diet (equivalent to a total of 200 mg ai/day). This dose is greater than 60 times the likely maximum residue in animal feed, based on a maximum intake of 3.2 mg ai/day in fodder. The cow was dosed once a day (at morning milking) for 7 consecutive days.

Findings:

A total of 88.7% of the dose was recovered in the urine and faeces. The TRR in the milk remained at <0.01 mg/kg throughout the 8 day study period (see Table 6.2.3-1 to Table 6.2.3-3).

At termination, radioactive residues were <0.01 mg/kg AMBA equivalents in the forequarter and hindquarter meat, subcutaneous and omental fat and in the liver. Total radioactive residues of 0.018 and 0.053 mg/kg were found in the perirenal fat and kidney respectively. In these tissues, unmetabolised AMBA was the major identified product, with low levels (<0.01 mg/kg) of other unknown components. The unmetabolised AMBA represented 61.6 and 79.0% of the TRR, equivalent to 0.013 and 0.038 mg/kg. By extrapolation, at likely maximum residue levels of AMBA in animal feed, AMBA residues would be <0.0006 mg/kg and consequently of no concern.

Table 6.2.3-1: Radioactive residues in lactating cow tissues, milk and excreta after oral administration of ^{14}C-AMBA

Tissues	Radioactive residue ^{14}C-AMBA (mg/kg)
Liver	0.005
Kidney	0.053
Muscle (fore)	0.000
Muscle (hind)	0.000
Fat (perirenal)	0.018
Fat (omental)	0.000
Fat (subcutaneous)	0.003
Milk (peak concentration)	0.0090
Urine (% of dose)	32.0%
Faeces (% of dose)	56.7%
Total in excreta (% of dose)	88.7%

Table 6.2.3-2: Mean Daily Radioactive Residues in Milk (mg/kg AMBA equivalents)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8[a]
Mean Daily Radioactive Residues (mg/kg AMBA equivalents))	0.0050	0.0065	0.0070	0.0065	0.0085	0.0090	0.0075	0.0030

a am collection only

Table 6.2.3-3: Nature of the residues of AMBA in perirenal fat and kidney

Tissue	Perirenal fat		Kidney	
Component/Fraction	%TRR[1]	mg/kg	%TRR[1]	mg/kg
AMBA	61.6	0.013	79.0[2]	0.038
Unknown	3.2	0.001	0.5	0.000
Unidentified	16.9	0.004	8.4	0.004
Aqueous fractions[3]	21.3	0.004	5.9	0.003
Organic fractions	-	-	2.5	0.001
Unextracted	9.7	0.002	3.1	0.001
Gains	12.7	0.003	0.6	0.000
Total	100.0	0.021	100.0	0.047[4]

1 Total Radioactive Residue (mg/kg AMBA equivalents).
2 Summation of the % AMBA in 2 major fractions
3 This consists of 2 fractions, the largest of which represents 12.6% (0.003 mg/kg) of the TRR in the perirenal fat and 3.0% (0.001 mg/kg) of the TRR in the kidney
4 Slight discrepancy due to rounding errors.

Conclusion:

This study was conducted using AMBA at a dose rate approximately 60 times greater than the maximum possible intake of a dairy cow following consumption of maize grain, fodder and forage after treatment with mesotrione at 150 g a.s./ha. Consequently, no residues (<0.01 mg/kg) of AMBA products from dairy cattle would result from normal application of mesotrione. In addition, AMBA is not considered to be of toxicological concern (see Bartley G (1998), *AMBA: a Metabolite of ZA1296 Overview of Toxicology and Environmental Fate*).

CA 6.2.4 Pigs

As shown by dietary burden calculations under Point CA 6.4, the use of mesotrione does not lead to significant residues in livestock feed (<0.1 mg/kg DM total diet and <0.004 mg/kg bw/day) with respect to pigs. Thus, metabolism and distribution studies in pigs are not required according to EU data requirements (**Commission Regulation (EU) No 283/2013, 1 March 2013**). Furthermore, based on the expected similarity of metabolic pattern in ruminants and rat, no additional metabolism study in pig is necessary.

CA 6.2.5 Fish

No guideline is available for possible design of fish metabolism studies or for estimation of dietary burden for farmed fish diet. However, from the uses of mesotrione and the magnitude of residues (all <0.01 mg/kg) it can be expected that there is no potential for residues in commercial fish diet.

CA 6.3 Magnitude of Residues Trials in Plants

The use pattern for evaluation for renewal of approval of mesotrione is provided in **Document D1** and summarised below (Table 6.3-1).

Table 6.3-1: Mesotrione - representative use patterns

Crop	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Max. Application		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Maize	Outdoor (NEU)	2-8 leaves BBCH 12-18	1	NA	0.150	100 - 400	NR
Maize	Outdoor (SEU)	2-8 leaves BBCH 12-18	1	NA	0.150	100 - 400	NR

NA- not applicable

NR – not relevant. Application is growth stage dependent and is made before the consumable part of the crop has formed

The representative crop included in the original EU review of mesotrione was also maize and new trials are available for this crop to complement the data originally evaluated.

Residue trials data for the use of mesotrione on sweet corn, oilseeds and soya bean are also presented in this dossier, not evaluated previously. For these crops, supervised residue trials data have been generated and are presented to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). These data are summarised in the following sections and the GAPs considered are shown in Table 6.3-2.

Table 6.3-2: Mesotrione – additional crop use patterns

Crop	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Max. Application		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Sweet corn	Outdoor	BBCH 00-19	1	NA	0.075	300	42
Poppy	Outdoor	BBCH 16-20	1	NA	0.100	500	80
Linseed	Outdoor	BBCH 16-19	1	NA	0.150	300	NR
Oilseed rape	Outdoor	BBCH 16-19	2	21	0.015	500	NR
HT soya bean	Outdoor	BBCH 00-60	2	Defined by growth stage	0.225 0.125	100-200	NR
HT soya bean	Outdoor	BBCH 12	1	NA	0.225	100-200	NR

NA- not applicable
NR – not relevant. Application is growth stage dependent and is made before the consumable part of the crop has formed

CA 6.3.1 Maize

Mesotrione is approved for use on maize according to the following EU critical GAP, detailed in Table 6.3.1-1.

Table 6.3.1–1: Approved EU critical GAPs for mesotrione on maize

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	2-8 leaves BBCH 12-18	1	NA	0.150	100-400	NR
Southern EU	Outdoor	2-8 leaves BBCH 12-18	1	NA	0.150	100-400	NR

NA- not applicable
NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

The residue reports supporting the EU critical GAP for mesotrione on maize are referenced in Table 6.3.1-2 and the data are presented in Table 6.3.1-5.

Table 6.3.1-2: Report references for trials supporting EU critical GAPs for mesotrione on maize

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.1/01*	(1 of 25)	J P Barnes	1997	ZA1296: Residue Levels in Maize from Trials Carried out in France During 1995 (WRC-96-099) Syngenta File No. ZA1296/0412, Syngenta Report No. RR 96-071B
KCA 6.3.1/02*	(2 of 25)	J P Barnes	1997	ZA1296: Residue Levels in Maize from Trials Carried out in Germany During 1995 (WRC-96-114) Syngenta File No. ZA1296/0409, Syngenta Report No. RR 96-078B
KCA 6.3.1/03*	(3 of 25)	J P Barnes	1997	ZA1296: Residue Levels in Maize from Trials Carried out in France During 1996 (Postemergence) Syngenta File No. ZA1296/0421, Syngenta Report No. RR 97-045B
KCA 6.3.1/04	(4 of 25)	M M Miller	1998	ZA1296: Residue Levels in Maize from Trials Carried out in France During 1996 (Preemergence) (WRC-97-138) Syngenta File No. ZA1296/0417, Syngenta Report No. RR 97-062B

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.1/05	(5 of 25)	M.M. Miller	1998	ZA1296: Residue Levels in Maize from Trials Carried out in Germany During 1996 (Pre-emergence) Syngenta File No. ZA1296/0418, Syngenta Report No. RR 97-063B
KCA 6.3.1/06*	(6 of 25)	J P Barnes	1997	ZA1296: Residue Levels in Maize from Trials Carried out in Germany During 1996 (Postemergence) Syngenta File No. ZA1296/0414, Syngenta Report No. RR 97-048B
KCA 6.3.1/07	(7 of 25)	S Klimmek	2008	Mesotrione and Nicosulfuron - Residue study on maize in northern France in 2007 Syngenta File No. A14351BX_10205, Syngenta Report No. T011368-06-REG
KCA 6.3.1/08	(8 of 25)	C Heillaut	2009	Glyphosate (ASF71), Mesotrione (ZA1296) and S-Metolachlor (CGA77102) - Residue study on GA21 (MON-ØØØ21-9) Corn in France (north) and Czech Republic in 2007 Syngenta File No. A15189G_10009, Syngenta Report No. T011085-06-REG
KCA 6.3.1/09	(9 of 25)	H Schulz	2010	Mesotrione and Nicosulfuron - Residue study on maize in France (north) in 2008 Syngenta File No. ZA1296_10049, Syngenta Report No. T009530-07-REG
KCA 6.3.1/10	(10 of 25)	C Heillaut	2009	Glyphosate, Mesotrione and S-Metolachlor - Residue study on GA21 (MON-00021-9) corn in Denmark and Sweden in 2008 Syngenta File No. A15189G_10014, Syngenta Report No. T009533-07-REG
KCA 6.3.1/11	(11 of 25)	M Meyer	2011	Mesotrione - Residue study on Field Corn in Germany and the United Kingdom in 2009 Syngenta File No. A14203B_10105, Syngenta Report No. T000920-09-REG
KCA 6.3.1/12*	(12 of 25)	J P Barnes	1997	Residue Levels in Maize from Trials Carried out in Italy During 1995 Syngenta File No. ZA1296/0411, Syngenta Report No. RR 96-077B
KCA 6.3.1/13*	(13 of 25)	J P Barnes	1997	ZA1296 - Residue levels in Maize from trials carried out in Italy during 1996 (Postemergence) Syngenta File No. ZA1296/0415, Syngenta Report No. RR 97-049B
KCA 6.3.1/14	(14 of 25)	M.M. Miller	1998	ZA1296 - Residue levels in Maize from trials carried out in Italy During 1996 Syngenta File No. ZA1296/0419, Syngenta Report No. RR 97-064B
KCA 6.3.1/15	(15 of 25)	S Richards	2003	Residue Study with A-12812 A (Mesotrione [ZA1296], S-Metolachlor and Terbuthylazine) in or on Maize in Italy Syngenta File No. ZA1296/1112, Syngenta Report No. 02-7036
KCA 6.3.1/16	(16 of 25)	S Richards	2003	Residue Study with A-12812A (Mesotrione (ZA 1296) S-Metolachlor and Terbuthylazine) in or on Maize in Italy Syngenta File No. ZA1296/1122, Syngenta Report No. 02-7037
KCA 6.3.1/17	(17 of 25)	S Richards	2003	Residue Study with A-12812A (Mesotrione (ZA1296), S-Metolachlor and Terbuthylazine) in or on Maize in Italy Syngenta File No. ZA1296/1151, Syngenta Report No. 02-7038
KCA 6.3.1/18	(18 of 25)	S Richards	2003	Residue Study with A-12812A (Mesotrione (ZA 1296), S-Metolachlor and Terbuthylazine) in or on Maize in Italy Syngenta File No. ZA1296/1152, Syngenta Report No. 02-7039
KCA 6.3.1/19	(19 of 25)	C Sole	2004	Residue Study with Mesotrione (ZA1296) and S-Metolachlor (CGA77102) in or on Maize in Italy Syngenta File No. ZA1296/1536, Syngenta Report No. 03-7019
KCA 6.3.1/20	(20 of 25)	S Richards	2004	Residue Study with Mesotrione (ZA1296) and S-Metolachlor (CGA77102) in or on Maize in Italy Syngenta File No. ZA1296/1520, Syngenta Report No. 03-7020
KCA 6.3.1/21	(21 of 25)	C Sole	2004	Residue Study with Mesotrione (ZA1296) and S-Metolachlor (CGA77102) in or on Maize in Italy Syngenta File No. ZA1296/1538, Syngenta Report No. 03-7021

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.1/22	(22 of 25)	C Sole	2004	Residue Study with Mesotrione (ZA1296) and S-Metolachlor (CGA77102) in or on Maize in Italy Syngenta File No. ZA1296/1539, Syngenta Report No. 03-7022
KCA 6.3.1/23	(23 of 25)	S Klimmek	2012	Mesotrione and Nicosulfuron - Residue study on Maize in Italy and Spain in 2007 Syngenta File No. A14351BX_10612, Syngenta Report No. T011369-06
KCA 6.3.1/24	(24 of 25)	H Schulz	2010	Mesotrione and Nicosulfuron - Residue study on Maize in France (south) in 2008 Syngenta File No. ZA1296_10048, Syngenta Report No. T009531-07-REG
KCA 6.3.1/25	(25 of 25)	F Gemrot	2009	Glyphosate, Mesotrione and S-Metolachlor - Residue study on GA21 (MON-00021-9) Corn in Spain in 2008 Syngenta File No. A15189G_10015, Syngenta Report No. T009534-07-REG

***** The residue data from these reports were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (Vol.3, Annex B, Section B.7.6.1, December 1999). They are included in this submission to provide a complete overview of available data

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Fifty supervised residue trials were conducted on maize between 1995 and 2009, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.1-3.

Table 6.3.1-3: Summary of mesotrione residue trials on maize

Northern Europe							
Country	**1995***	**1996***	**2002**	**2003**	**2007**	**2008**	**2009**
France (north)	1 Decline	1 Decline 1 Harvest	-	-	2 Decline 3 Harvest	2 Decline	-
Germany	4 Decline	3 Decline 3 Harvest	-	-	-	-	1 Harvest
United Kingdom	-	-	-	-	-	-	1 Harvest
Czech Republic	-	-	-	-	1 Harvest	-	-
Denmark	-	-	-	-	1 Harvest	-	-
Sweden	-	-	-	-	1 Harvest	-	-
Southern Europe							
Country	**1995***	**1996***	**2002**	**2003**	**2007**	**2008**	**2009**
France (south)	2 Decline	2 Decline 2 Harvest	-	-	-	2 Decline	-
Italy	2 Harvest	2 Harvest 2 Harvest	4 Harvest	4 Harvest	1 Decline	-	-
Spain	-	-	-	-	1 Decline	3 Harvest	-

* The residue data from these years were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (Vol.3, Annex B, Section B.7.6.1, December 1999). They are included in this submission to provide a complete overview of available data

Maize is a major crop in northern and southern Europe and therefore generally requires eight trials in each residue region. According to EU guidance (**Document 7525/VI/95 – rev.9, March 2011**), trials on maize involving application before the consumable part of the crop has formed are sufficient to support registration on millet and sorghum.

Treatments with mesotrione were conducted as pre- or early post emergence (BBCH 00-18) spray applications utilising a number of formulation as detailed in Table 6.3.1-4 at application rates between 0.147 and 0.200 kg a.s./ha. The water volumes during application ranged from 200 to 408 L/ha.

Table 6.3.1-4: Summary of mesotrione Formulations used in the Presented Trials

Product code	Formulation type	Composition
A12738B	SC	480 g/L mesotrione
A12739A	SC	100 g/L mesotrione
A12807H	SC	60 g/L mesotrione + 500 g/L S-metolachlor
A12812A	SE	37.5 g/L mesotrione + 187.5 g/L terbuthylazine + 312.5 g/L S-metolachlor
A13385B	SC	100 g/L mesotrione
A14351BX	OD	75 g/L mesotrione + 30 g/L nicosulfuron
A15189G	ZC	25 g/L mesotrione, 250 g/L glyphosate, 250 g/L S-metolachlor
A14203B	WG	500 g/kg mesotrione
WF2411	SC	100 g/L mesotrione
WF2515	SC	100 g/L mesotrione

Samples of various parts of mature and immature maize plants were taken and analysed for residues of mesotrione and MNBA. Therefore, the available trials are sufficient to support the EU critical GAP for maize.

Allowing for a 25% deviation from the proposed maximum application rate, rates in all trials cover the critical EU GAP.

In twenty nine trials, suspension concentrate (SC) formulation types were used, which when applied more than seven days prior to harvest, are expected to produce comparable residues to a water dispersible granule (WG) formulation type according to EU Guidelines (**EU guideline Document 7525/VI/95 rev. 9, March 2011**). A further four trials were conducted using a suspo-emulsion (SE) formulation, eight trials were conducted using an oil dispersion (OD) formulation, seven trials were conducted using a mixed formulation of CS and SC (ZC) formulation and two trials were conducted using a water dispersible granule (WG) formulation. The range of formulations used enables an assessment on the affect formulation type has on residue.

No PHI is proposed in the critical EU GAP since the application is made pre- or early post-emergence and the maize grain is harvested at maturity.

Table 6.3.1-5: Summary of Residue Data Supporting the EU Critical GAP for mesotrione on Maize

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Northern Europe									
Report: RR 96-071B Study: 1296-95-MR-02 Trial: 94-FR-95-851 - Study to GLP - Study carried out in 1995**	Maize (Banguy)	FRANCE (Europe North)	150 g a.s./ha WF2411	6-8 leaves	0	Whole plant	4.58	0.15	MNBA Forage Mean = 108% RSD = N/A (n = 2 in 0.01 - 0.20 mg/kg spiking range) MNBA Grain Mean = 88% RSD = 7% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 90% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 75% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Forage Mean = 89% RSD = 17% (n = 3 in 0.01 - 1.00 mg/kg spiking range) Mesotrione Grain Mean = 91% RSD = 11% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 99% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 91% RSD = 32% (n = 3 in 0.01 - 10.00 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					63	Forage	≤ 0.01	< 0.01	
					80	Silage	< 0.01	< 0.01	
					120	Cob + Grain	< 0.01	< 0.01	
					120	Cob + Grain + Husk	< 0.01	< 0.01	
					120	Grain	≤ 0.01	< 0.01	
Report: RR 97-045B Study: 1296-96-MR-02 Trial: 94-FR-96-263 - Study to GLP - Study carried out in 1996**	Maize (LG 2243)	FRANCE (Europe North)	200 g a.s./ha WF2515	BBCH 16 - 18	0	Whole plant	21.60, 18.30 (Mean=20.0)	0.10, 0.10 (Mean=0.10)	MNBA Forage Mean = 82% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 75% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 108% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 86% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					56	Forage	≤ 0.01†	-	
					90	Silage	< 0.01†	-	
					119	Cob + Grain	< 0.01†	-	
					119	Cob + Grain + Husk	< 0.01†	-	
					119	Grain	≤ 0.01†	-	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate / Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: RR 96-078B Study: 1296-95-MR-03 Trial: RS-9512-B1 (94-GR-95-854) - Study to GLP - Study carried out in 1995**	Maize (Diamant)	GERMANY (Europe North)	150 g a.s./ha WF2411	BBCH 17	0	Whole plant	9.23	0.08	MNBA Grain Mean = 96% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 95% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 83% RSD = 0% (n = 1 in 0.50 - 0.50 mg/kg spiking range) Mesotrione Grain Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 88% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 77% RSD = 0% (n = 1 in 15.00 - 15.00 mg/kg spiking range)
					13	Whole plant	< 0.01	< 0.01	
					32	Forage	≤ 0.01	< 0.01	
					68	Silage	< 0.01	< 0.01	
					78	Cob + Grain	< 0.01	< 0.01	
					78	Cob + Grain + Husk	< 0.01	< 0.01	
					78	Grain	≤ 0.01	< 0.01	
Report: RR 96-078B Study: 1296-95-MR-03 Trial: RS-9512-G1 (94-GR-95-855) - Study to GLP - Study carried out in 1995**	Maize (General)	GERMANY (Europe North)	150 g a.s./ha WF2411	BBCH 17	0	Whole plant	10.31	0.08	MNBA Forage Mean = 112% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 99% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 91% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Forage Mean = 103% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 107% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 84% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					32	Forage	≤ 0.01	< 0.01	
					73	Silage	< 0.01	< 0.01	
					114	Cob + Grain	< 0.01	< 0.01	
					114	Cob + Grain + Husk	< 0.01	< 0.01	
					114	Grain	≤ 0.01	< 0.01	
Report: RR 96-078B Study: 1296-95-MR-03 Trial: RS-9512-G2 (94-GR-95-856) - Study to GLP - Study carried out in 1995**	Maize (Graf)	GERMANY (Europe North)	150 g a.s./ha WF2411	BBCH 16 - 17	0	Whole plant	11.57, 11.54, (Mean=11.6)	0.09, 0.07, 0.09 (Mean=0.08)	MNBA Whole plant Mean = 104% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 102% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					32	Forage	≤ 0.01	< 0.01	
					73	Silage	< 0.01	< 0.01	
					114	Cob + Grain	< 0.01	< 0.01	
					114	Cob + Grain + Husk	< 0.01	< 0.01	
					114	Grain	≤ 0.01	< 0.01	
Report: RR 96-078B Study: 1296-95-MR-03 Trial: RS-9512-K1 (94-GR-95-857) - Study to GLP - Study carried out in	Maize (Anjou 207)	GERMANY (Europe North)	150 g a.s./ha WF2411	BBCH 16 - 17	0	Whole plant	5.81, 6.14, (Mean=6.0)	0.19, 0.21, 0.20 (Mean=0.20)	MNBA Whole plant Mean = 127% RSD = 0% (n = 1 in 0.20 - 0.20 mg/kg spiking range) Mesotrione Whole plant Mean = 78% RSD = 0% (n = 1 in 15.00 - 15.00 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					32	Forage	≤ 0.01	< 0.01	
					73	Silage	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
1995**					114	Cob + Grain	< 0.01	< 0.01	
					114	Cob + Grain + Husk	< 0.01	< 0.01	
					114	Grain	< 0.01	< 0.01	
Report: RR 97-048B Study: ZA1296-96-MR-03 Trial: RS-9604-B1 (94-GR-96-271) - Study to GLP - Study carried out in 1996**	Maize (Janna)	GERMANY (Europe North)	200 g a.s./ha WF2515	BBCH 16	0	Whole plant	24.30, 22.00 (Mean=11.62)	0.10, 0.09, (Mean=0.10)	MNBA Forage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 86% RSD = 18% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 84% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 24% (n = 4 in 0.01 - 0.30 mg/kg spiking range) Mesotrione Forage Mean = 72% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 89% RSD = 24% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 94% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 79% RSD = 3% (n = 4 in 0.01 - 25.00 mg/kg spiking range)
					14	Whole plant	0.05	0.06	
					44	Forage	< 0.01†	-	
					86	Silage	< 0.01†	-	
					109	Cob + Grain	< 0.01†	-	
					109	Cob + Grain + Husk	< 0.01†	-	
					109	Grain	< 0.01†	-	
Report: RR 97-048B Study: ZA1296-96-MR-03 Trial: RS-9604-G1 (94-GR-96-272) - Study to GLP - Study carried out in 1996**	Maize (Ilias)	GERMANY (Europe North)	200 g a.s./ha WF2515	BBCH 17	0	Whole plant	10.90	0.10	MNBA Forage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 86% RSD = 18% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 84% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 24% (n = 4 in 0.01 - 0.30 mg/kg spiking range) Mesotrione Forage Mean = 72% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 89% RSD = 24% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 94% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 79% RSD = 3% (n = 4 in 0.01 - 25.00 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					36	Forage	< 0.01†	-	
					88	Silage	< 0.01†	-	
					126	Cob + Grain	< 0.01†	-	
					126	Cob + Grain + Husk	< 0.01†	-	
					126	Grain	< 0.01†	-	
Report: RR 97-048B Study: ZA1296-96-MR-03 Trial: RS-9604-K1 (94-	Maize (Helix)	GERMANY (Europe North)	200 g a.s./ha WF2515	BBCH 18	0	Whole plant	9.23, 9.18 (Mean=9.2)	0.08, 0.08 (Mean=0.08)	MNBA Forage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 86% RSD = 18% (n =
					14	Whole plant	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
GR-96-273) - Study to GLP - Study carried out in 1996**					36	Forage	≤ 0.01†	-	3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 84% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 24% (n = 4 in 0.01 - 0.30 mg/kg spiking range) Mesotrione Forage Mean = 72% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 89% RSD = 24% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 94% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 79% RSD = 3% (n = 4 in 0.01 - 25.00 mg/kg spiking range)
					88	Silage	< 0.01†	-	
					126	Cob + Grain	< 0.01†	-	
					126	Cob + Grain + Husk	< 0.01†	-	
					126	Grain	≤ 0.01†	-	
Report: RR 97-062B Study: 1296-96-MR-05 Trial: 94-FR-96-289 - Study to GLP - Study carried out in 1996**	Maize (LG 2243)	FRANCE (Europe North)	200 g a.s./ha A12738B	Pre-emergence	28	Whole plant	< 0.01	< 0.01	MNBA Forage Mean = 90% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 92% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 83% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 84% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Forage Mean = 96% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 100% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 95% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 94% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range)
					42	Whole plant	< 0.01	< 0.01	
					60	Forage	< 0.01†	-	
					90	Silage	< 0.01†	-	
					168	Cob + Grain	< 0.01†	-	
					168	Cob + Grain + Husk	< 0.01†	-	
					168	Grain	< 0.01†	-	
Report: RR 97-063B Study: 1296-96-MR-06 Trial: RS-9608-B1 (94-GR-96-292) - Study to GLP - Study carried out in 1996**	Maize (Janna)	GERMANY (Europe North)	200 g a.s./ha A12738B	BBCH 05	40	Whole plant	< 0.01	< 0.01	MNBA Forage Mean = 86% RSD = N/A (n = 2 in 0.03 - 0.03 mg/kg spiking range) MNBA Grain Mean = 80% RSD = 1% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 77% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 12% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 90% RSD = N/A (n = 2 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Grain Mean = 95% RSD = 5% (n
					65	Whole plant	< 0.01	< 0.01	
					84	Forage	≤ 0.01	< 0.01	
					126	Silage	< 0.01	< 0.01	
					149	Cob + Grain + Husk	< 0.01	< 0.01	
					149	Cob + Grain	< 0.01	< 0.01	
					149	Grain	≤ 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
									= 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 71% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = 15% (n = 3 in 0.01 - 0.03 mg/kg spiking range)
Report: RR 97-063B Study: 1296-96-MR-06 Trial: RS-9608-G1(94-GR-96-293) - Study to GLP - Study carried out in 1996**	Maize (Ilias)	GERMANY (Europe North)	200 g a.s./ha A12738B	BBCH 07	33	Whole plant	< 0.01	< 0.01	MNBA Forage Mean = 86% RSD = N/A (n = 2 in 0.03 - 0.03 mg/kg spiking range) MNBA Grain Mean = 80% RSD = 1% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 77% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 12% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 90% RSD = N/A (n = 2 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Grain Mean = 95% RSD = 5% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 71% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = 15% (n = 3 in 0.01 - 0.03 mg/kg spiking range)
					47	Whole plant	< 0.01	< 0.01	
					68	Forage	≤ 0.01	< 0.01	
					143	Silage	< 0.01	< 0.01	
					168	Cob + Grain	< 0.01	< 0.01	
					168	Cob + Grain + Husk	< 0.01	< 0.01	
					168	Grain	≤ 0.01	< 0.01	
Report: RR 97-063B Study: 1296-96-MR-06 Trial: RS-9608-K1(94-GR-96-294) - Study to GLP - Study carried out in 1996**	Maize (Helix)	GERMANY (Europe North)	200 g a.s./ha A12738B	BBCH 05	40	Whole plant	< 0.01	< 0.01	MNBA Forage Mean = 86% RSD = N/A (n = 2 in 0.03 - 0.03 mg/kg spiking range) MNBA Grain Mean = 80% RSD = 1% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 77% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 12% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 90% RSD = N/A (n = 2 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Grain Mean = 95% RSD = 5% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 71% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = 15% (n = 3 in 0.01 - 0.03 mg/kg spiking range)
					62	Whole plant	< 0.01	< 0.01	
					81	Forage	≤ 0.01	< 0.01	
					133	Silage	< 0.01	< 0.01	
					171	Cob + Grain	< 0.01	< 0.01	
					171	Cob + Grain + Husk	< 0.01	< 0.01	
					171	Grain	≤ 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: T011368-06-REG Study: SYN-0731 Trial: FR-HR-07-0121 - Study to GLP - Study carried out in 2007	Maize (Anjou 248)	FRANCE (Europe North)	149.1 g a.s./ha A14351BX	BBCH 18	24	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 87% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 89% RSD = 12% (n = 4 in 0.01 - 0.10 mg/kg spiking range); MNBA Cobs without kernels Mean = 95% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 82% RSD = 19% (n = 3 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 90% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); Mesotrione Cobs without kernels Mean = 88% RSD = 14% (n = 3 in 0.01 - 0.10 mg/kg spiking range).
					38	Whole Plant	< 0.01	< 0.01	
					44	Whole Plant	< 0.01	< 0.01	
					60	Whole Plant	< 0.01	< 0.01	
					75	Kernel	< 0.01	< 0.01	
					75	Cob without kernels	< 0.01	< 0.01	
					75	Remaining plant(1)	< 0.01	< 0.01	
					94	Kernel	< 0.01	< 0.01	
					94	Cob without kernels	< 0.01	< 0.01	
					94	Remaining plant(1)	< 0.01	< 0.01	
					99	Whole Plant	< 0.01	< 0.01	
					120	Kernel	< 0.01	< 0.01	
					120	Cob without kernels	< 0.01	< 0.01	
					120	Remaining plant(1)	< 0.01	< 0.01	
Report: T011368-06-REG Study: SYN-0731 Trial: FR-HR-07-0122 - Study to GLP - Study carried out in 2007	Maize (Marcello)	FRANCE (Europe North)	148.0 g a.s./ha A14351BX	BBCH 18	34	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 87% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 89% RSD = 12% (n = 4 in 0.01 - 0.10 mg/kg spiking range); MNBA Cobs without kernels Mean = 95% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 82% RSD = 19% (n = 3 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 90% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); Mesotrione Cobs without kernels Mean = 88% RSD = 14% (n = 3 in 0.01 - 0.10 mg/kg spiking range).
					40	Whole Plant	< 0.01	< 0.01	
					43	Whole Plant	< 0.01	< 0.01	
					60	Whole Plant	< 0.01	< 0.01	
					70	Kernel	< 0.01	< 0.01	
					70	Cob without kernels	< 0.01	< 0.01	
					70	Remaining plant(1)	< 0.01	< 0.01	
					90	Kernel	< 0.01	< 0.01	
					90	Cob without kernels	< 0.01	< 0.01	
					90	Remaining plant(1)	< 0.01	< 0.01	
					106	Whole Plant	< 0.01	< 0.01	
					130	Kernel	< 0.01	< 0.01	
					130	Cob without kernels	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
					130	Remaining plant(1)	< 0.01	< 0.01	
Report: T009530-07-REG Study: IF-08/01104631 Trial: PDA-08-4166-FR01 - Study to GLP - Study carried out in 2008	Maize (PR37F73)	FRANCE (Europe North)	150.4 g a.s./ha A14351BX	BBCH 18	30	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 92% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 83% RSD = 9% (n = 4 in 0.01 – 0.10 mg/kg spiking range); MNBA Cobs Mean = 97% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). MNBA Leaf sheaths Mean = 88% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 107% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 87% RSD = 9% (n = 4 in 0.01 – 0.10 mg/kg spiking range); Mesotrione Cobs Mean = 93% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range).
					33	Whole Plant	≤ 0.01	< 0.01	
					42	Cobs	< 0.01	< 0.01	
					42	Remaining plant(1)	< 0.01	< 0.01	
					63	Kernel	≤ 0.01	< 0.01	
					63	Cob without kernels	< 0.01	< 0.01	
					63	Leaf sheaths	< 0.01	< 0.01	
					63	Remaining plant(1) (BBCH 78)	< 0.01	< 0.01	
					63	Whole Plant	< 0.01	< 0.01	
					76	Whole Plant	< 0.01	< 0.01	
					92	Kernel	< 0.01	< 0.01	
					92	Cob without kernels	< 0.01	< 0.01	
					92	Remaining plant(1)	< 0.01	< 0.01	
					124	Kernel	≤ 0.01	< 0.01	
					124	Cob without kernels	< 0.01	< 0.01	
					124	Remaining plant(1)	< 0.01	< 0.01	
Report: T009530-07-REG Study: IF-08/01104631 Trial: PDA-08-4166-FR02 - Study to GLP - Study carried out in 2008	Maize (Kornadi)	FRANCE (Europe North)	156.1 g a.s./ha A14351BX	BBCH 18	25	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 92% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 83% RSD = 9% (n = 4 in 0.01 – 0.10 mg/kg spiking range); MNBA Cobs Mean = 97% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). MNBA Leaf sheaths Mean = 88% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 107% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 87% RSD = 9% (n = 4 in 0.01 – 0.10 mg/kg spiking range); Mesotrione Cobs Mean = 93% RSD = NA (n
					36	Whole Plant	≤ 0.01	< 0.01	
					42	Cobs	< 0.01	< 0.01	
					42	Remaining plant(1)	< 0.01	< 0.01	
					58	Kernel	≤ 0.01	< 0.01	
					58	Cob without kernels	< 0.01	< 0.01	
					58	Leaf sheaths	< 0.01	< 0.01	
					58	Remaining plant(1)	< 0.01	< 0.01	
					64	Whole Plant	< 0.01	< 0.01	
					77	Whole Plant	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
					91	Kernel	< 0.01	< 0.01	= 2 in 0.01 - 0.10 mg/kg spiking range).
					91	Cob without kernels	< 0.01	< 0.01	
					91	Remaining plant(1)	< 0.01	< 0.01	
					130	Grain	< 0.01	< 0.01	
					130	Cob without kernels (BBCH 89)	< 0.01	< 0.01	
					130	Remaining plant(1)	< 0.01	< 0.01	
Report: T011085-06-REG Study: T011085-06 Trial: CZ-HR-07-0064 - Study to GLP unchecked - Study carried out in 2007 (F)	Corn (GA21 (MON-00021-9))	CZECH REPUBLIC (Europe North)	156.00 g a.s./ha A15189G	BBCH 15 - 16	65	Whole plant	≤ 0.01	< 0.01	MNBA Cob Mean = 90% RSD = 5% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 89% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 85% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 92% RSD = 3% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 89% RSD = 4% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 88% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 98% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					98	Cob	< 0.01	< 0.01	
					98	Cob + Kernel	< 0.01 +	< 0.01 +	
					98	Kernel	≤ 0.01	< 0.01	
					98	Remaining Plant	< 0.01	< 0.01	
					104	Whole plant	< 0.01	< 0.01	
					134	Cob	< 0.01	< 0.01	
					134	Cob + Kernel	< 0.01 +	< 0.01 +	
					134	Kernel	≤ 0.01	< 0.01	
					134	Remaining Plant	< 0.01	< 0.01	
Report: T011085-06-REG	Corn (GA21	FRANCE	158.00 g	BBCH 15	61	Whole plant	≤ 0.01	< 0.01	MNBA Cob Mean = 90% RSD = 5% (n = 4

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Study: T011085-06 Trial: FR-HR-07-0063 - Study to GLP unchecked - Study carried out in 2007 (F)	(MON-00021-9))	(Europe North)	a.s./ha A15189G		92	Cob	< 0.01	< 0.01	in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 89% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 85% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 87% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 92% RSD = 3% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 89% RSD = 4% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 88% RSD = 7% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 98% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					92	Cob + Kernel	< 0.01 +	< 0.01 +	
					92	Kernel	< 0.01	< 0.01	
					92	Remaining Plant	< 0.01	< 0.01	
					109	Whole plant	< 0.01	< 0.01	
					137	Cob	< 0.01	< 0.01	
					137	Cob + Kernel	< 0.01 +	< 0.01 +	
					137	Kernel	< 0.01	< 0.01	
					137	Remaining Plant	< 0.01	< 0.01	
Report: T009533-07-REG Study: T009533-07 Trial: SE-HR-08-0003 - Study to GLP unchecked - Study carried out in 2008 (F)	Corn (GA21 (MON-00021-9))	SWEDEN (Europe North)	155.30 g a.s./ha A15189G	BBCH 16 - 17	65	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 100% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 84% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 100% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 91% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range)
					94	Cob	< 0.01	< 0.01	
					94	Cob + Kernel	< 0.01 +	< 0.01 +	
					94	Kernel	< 0.01	< 0.01	
					94	Remaining Plant	< 0.01	< 0.01	
					120	Cob + Kernel	< 0.01 +	< 0.01 +	
					120	Cob	< 0.01	< 0.01	
					120	Kernel	< 0.01	< 0.01	
					120	Remaining Plant	< 0.01	< 0.01	
	Corn (GA21		148.50 g	BBCH 16 - 17	65	Whole plant	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
	(MON-00021-9))		a.s./ha A15189G		94	Cob	< 0.01	< 0.01	Mesotrione Remaining Plant Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					94	Cob + Kernel	< 0.01 +	< 0.01 +	
					94	Kernel	< 0.01	< 0.01	
					94	Remaining Plant	< 0.01	< 0.01	
					120	Cob	< 0.01	< 0.01	
					120	Cob + Kernel	< 0.01 +	< 0.01 +	
					120	Kernel	< 0.01	< 0.01	
					120	Remaining Plant	< 0.01	< 0.01	
Report: T009533-07-REG Study: T009533-07 Trial: SE-HR-08-0007 - Study to GLP unchecked - Study carried out in 2008 (F)	Corn (GA21 (MON-00021-9))	DENMARK (Europe North)	147.00 g a.s./ha A15189G	BBCH 15	63	Whole plant	< 0.01	-	MNBA Cob Mean = 100% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 84% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 100% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 91% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01
					92	Cob	< 0.01	< 0.01	
					92	Cob + Kernel	< 0.01 +	< 0.01 +	
					92	Kernel	< 0.01	< 0.01	
					92	Remaining Plant	< 0.01	< 0.01	
					128	Cob	< 0.01	< 0.01	
					128	Cob + Kernel	< 0.01 +	< 0.01 +	
					128	Kernel	< 0.01	< 0.01	
					128	Remaining Plant	< 0.01	< 0.01	
	Corn (GA21 (MON-00021-9))		167.70 g a.s./ha A15189G	BBCH 15	63	Whole plant	< 0.01	-	
					92	Cob	< 0.01	< 0.01	
					92	Cob + Kernel	< 0.01 +	< 0.01 +	
					92	Kernel	< 0.01	< 0.01	
					92	Remaining Plant	< 0.01	< 0.01	
					128	Cob	< 0.01	< 0.01	
					128	Cob + Kernel	< 0.01 +	< 0.01 +	
					128	Kernel	< 0.01	< 0.01	
					128	Remaining Plant	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
									MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01
Report: T000920-09-REG Study: IF-09/01385983 Trial: 09-DE-059 - Study to GLP unchecked - Study carried out in 2009 (F)	Field Corn (Nescio)	GERMANY (Europe North)	143.00 g a.s./ha A14203B	BBCH 16 - 18	34	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 84% RSD = 2% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 81% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 90% RSD = 12% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 92% RSD = 17% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 98% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 96% RSD = 10% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01, modified Mesotrione (Cob + Kernel) RAM 366/01, modified Mesotrione (Kernel) RAM 366/01, modified Mesotrione (Remaining Plant) RAM 366/01, modified Mesotrione (Whole plant) RAM 366/01, modified MNBA (Cob) RAM 366/01, modified MNBA (Cob + Kernel) RAM 366/01, modified MNBA (Kernel) RAM 366/01, modified MNBA (Remaining Plant) RAM 366/01, modified MNBA (Whole plant) RAM 366/01, modified
					47	Cob + Kernel	< 0.01	< 0.01	
					47	Remaining Plant	< 0.01	< 0.01	
					47	Whole plant	< 0.01	< 0.01	
					66	Whole plant	< 0.01	< 0.01	
					82	Cob	< 0.01	< 0.01	
					82	Kernel	< 0.01	< 0.01	
					82	Remaining Plant	< 0.01	< 0.01	
					91	Cob	< 0.01	< 0.01	
					91	Kernel	< 0.01	< 0.01	
					91	Remaining Plant	< 0.01	< 0.01	
					110	Whole plant	< 0.01	< 0.01	
					143	Cob	< 0.01	< 0.01	
					143	Kernel	< 0.01	< 0.01	
					143	Remaining Plant	< 0.01	< 0.01	
Report: T000920-09-REG Study: IF-09/01385983 Trial: 09-UK-060 - Study to GLP unchecked - Study carried out in 2009 (F)	Field Corn (Ohio)	UNITED KINGDOM (Europe North)	147.00 g a.s./ha A14203B	BBCH 16 - 17	20	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 84% RSD = 2% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 81% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 90% RSD = 12% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 92% RSD = 17% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 98% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range)
					35	Whole plant	< 0.01	< 0.01	
					41	Cob + Kernel	< 0.01	< 0.01	
					41	Remaining Plant	< 0.01	< 0.01	
					53	Cob + Kernel	< 0.01	< 0.01	
					53	Remaining Plant	< 0.01	< 0.01	
					60	Whole plant	< 0.01	< 0.01	
					87	Whole plant	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
					98	Cob	< 0.01	< 0.01	Mesotrione Remaining Plant Mean = 96% RSD = 10% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01, modified Mesotrione (Cob + Kernel) RAM 366/01, modified Mesotrione (Kernel) RAM 366/01, modified Mesotrione (Remaining Plant) RAM 366/01, modified Mesotrione (Whole plant) RAM 366/01, modified MNBA (Cob) RAM 366/01, modified MNBA (Cob + Kernel) RAM 366/01, modified MNBA (Kernel) RAM 366/01, modified MNBA (Remaining Plant) RAM 366/01, modified MNBA (Whole plant) RAM 366/01, modified
					98	Kernel	< 0.01	< 0.01	
					98	Remaining Plant	< 0.01	< 0.01	
					112	Cob	< 0.01	< 0.01	
					112	Kernel	< 0.01	< 0.01	
					112	Remaining Plant	< 0.01	< 0.01	
Southern Europe									
Report: RR 96-071B Study: 1296-95-MR-02 Trial: 94-FR-95-852 - Study to GLP - Study carried out in 1995**	Maize (Cecilia)	FRANCE (Europe South)	150 g a.s./ha WF2411	6-8 leaves	0	Whole plant	2.57	0.03	MNBA Silage Mean = 89% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 93% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 97% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 93% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range)
					15	Whole plant	< 0.01	< 0.01	
					60	Forage	< 0.01	< 0.01	
					91	Silage	< 0.01	< 0.01	
					109	Cob+ Grain+ Husk	< 0.01	< 0.01	
					109	Cob + Grain	< 0.01	< 0.01	
					109	Grain	< 0.01	< 0.01	
Report: RR 96-071B Study: 1296-95-MR-02 Trial: 94-FR-95-853 - Study to GLP - Study carried out in 1995*	Maize (Cecilia)	FRANCE (Europe South)	150 g a.s./ha WF2411	6-8 leaves	0	Whole plant	7.57	0.06,	MNBA Whole plant Mean = 93% RSD = N/A (n = 2 in 0.01 - 0.20 mg/kg spiking range) Mesotrione Whole plant Mean = 115% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					60	Forage	< 0.01	< 0.01	
					77	Silage	< 0.01	< 0.01	
					128	Cob + Grain	< 0.01	< 0.01	
					128	Cob+ Grain+ Husk	< 0.01	< 0.01	
					128	Grain	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: RR 97-045B Study: 1296-96-MR-02 Trial: 94-FR-96-261 - Study to GLP - Study carried out in 1996**	Maize (Volga)	FRANCE (Europe South)	200 g a.s./ha WF2515	BBCH 17	0	Whole plant	19.20, 18.70 (Mean=19.0)	0.18, 0.23 (Mean=0.21),	AMBA Whole plant Mean = 97% RSD = 7% (n = 9 in 0.01 - 25.00 mg/kg spiking range) MNBA Forage Mean = 82% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 75% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 108% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 86% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					12	Whole plant	< 0.01	< 0.01	
					61	Forage	≤ 0.01†	-	
					91	Silage	< 0.01†	-	
					126	Cob + Grain	< 0.01†	-	
					126	Cob+ Grain+ Husk	< 0.01†	-	
					126	Grain	≤ 0.01†	-	
Report: RR 97-045B Study: 1296-96-MR-02 Trial: 94-FR-96-262 - Study to GLP - Study carried out in 1996**	Maize (Cecilia)	FRANCE (Europe South)	200 g a.s./ha WF2515	BBCH 16	0	Whole plant	14.40	0.12	AMBA Whole plant Mean = 97% RSD = 7% (n = 9 in 0.01 - 25.00 mg/kg spiking range) MNBA Forage Mean = 82% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 75% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 108% RSD = 0% (n = 1 in 0.03 - 0.03 mg/kg spiking range) Mesotrione Forage Mean = 86% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 82% RSD = 5% (n = 3 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 85% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					14	Whole plant	< 0.01	< 0.01	
					61	Forage	≤ 0.01†		
					92	Silage	< 0.01†		
					146	Cob + Grain	< 0.01†	-	
					146	Cob+ Grain+ Husk	< 0.01†	-	
					146	Grain	≤ 0.01†	-	
Report: RR 96-077B Study: 1296-95-MR-04 Trial: 94-IT-95-858 - Study to GLP - Study carried out in 1995**	Maize (Samantha)	ITALY (Europe South)	150 g a.s./ha A12739A	7 leaves - 8 leaves	76	Silage	≤ 0.01	< 0.01	MNBA Grain Mean = 90% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 92% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 92% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 91% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					98	Cob+ Grain+ Husk	< 0.01	< 0.01	
					121	Cob + Grain	< 0.01	< 0.01	
					121	Cob+ Grain+ Husk	< 0.01	< 0.01	
					121	Grain	≤ 0.01	< 0.01	
Report: RR 96-077B	Maize	ITALY	150 g a.s./ha	7 leaves - 8	65	Silage	≤ 0.01	< 0.01	MNBA Grain Mean = 79% RSD = 0% (n = 1

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Study: 1296-95-MR-04 Trial: 94-IT-95-859 - Study to GLP - Study carried out in 1995**	(Summer 2)	(Europe South)	A12739A	leaves	98	Cob+ Grain+ Husk	< 0.01	< 0.01	in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 99% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
Report: RR 97-049B Study: 1296-96-MR-04 Trial: 94-IT-96-281 - Study to GLP - Study carried out in 1996**	Maize (Cecilia)	ITALY (Europe South)	200 g a.s./ha A13385B	BBCH 17 - 18	84	Silage	≤ 0.01†	-	MNBA Grain Mean = 96% RSD = 10% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 79% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 103% RSD = 8% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 80% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					121	Cob + Grain	< 0.01†	-	
					121	Cob+ Grain+ Husk	< 0.01†	-	
					121	Grain	≤ 0.01†	-	
Report: RR 97-049B Study: 1296-96-MR-04 Trial: 94-IT-96-282 - Study to GLP - Study carried out in 1996**	Maize (Caterina)	ITALY (Europe South)	200 g a.s./ha A13385B	6 leaves - 8 leaves	91	Silage	≤ 0.01†	-	MNBA Grain Mean = 96% RSD = 10% (n = 3 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 79% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 103% RSD = 8% (n = 3 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 80% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					129	Cob + Grain	< 0.01†	-	
					129	Cob + Grain + Husk	< 0.01†	-	
					129	Grain	≤ 0.01†	-	
Report: RR 97-062B Study: 1296-96-MR-05 Trial: 94-FR-96-287 - Study to GLP - Study carried out in 1996**	Maize (Volga)	FRANCE (Europe South)	200 g a.s./ha A12738B	Pre-emergence	29	Whole plant	< 0.01†	-	MNBA Forage Mean = 90% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 92% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 83% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 84% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Forage Mean = 96% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 100% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 95% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 94% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range)
					42	Whole plant	< 0.01†	-	
					63	Forage	< 0.01†	-	
					91	Silage	< 0.01†	-	
					156	Cob + Grain	< 0.01†	-	
					156	Cob + Grain + Husk	< 0.01†	-	
					156	Grain	< 0.01†	-	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: RR 97-062B Study: 1296-96-MR-05 Trial: 94-FR-96-288 - Study to GLP - Study carried out in 1996*	Maize (Cecilia)	FRANCE (Europe South)	200 g a.s./ha A12738B	Pre-emergence	29	Whole plant	< 0.01	< 0.01	MNBA Forage Mean = 90% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 92% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) MNBA Silage Mean = 83% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) MNBA Whole plant Mean = 84% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Forage Mean = 96% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 100% RSD = 18% (n = 4 in 0.01 - 0.03 mg/kg spiking range) Mesotrione Silage Mean = 95% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Whole plant Mean = 94% RSD = 12% (n = 5 in 0.01 - 0.10 mg/kg spiking range)
					42	Whole plant	< 0.01	< 0.01	
					63	Forage	< 0.01†	-	
					88	Silage	< 0.01†	-	
					130	Silage	< 0.01†	-	
					184	Cob + Grain	< 0.01†	-	
					184	Cob + Grain + Husk	< 0.01†	-	
					184	Grain	< 0.01†	-	
Report: RR 97-064B Study: 1296-96-MR-07 Trial: 94-IT-96-297 - Study to GLP - Study carried out in 1996**	Maize (Cecilia)	ITALY (Europe South)	200 g a.s./ha A12738B	1 day after planting	125	Silage	< 0.01†	-	MNBA Grain Mean = 89% RSD = 13% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 82% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 93% RSD = 13% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 99% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					162	Cob + Grain	< 0.01†	-	
					162	Cob + Grain + Husk	< 0.01†	-	
					162	Grain	< 0.01†	-	
Report: RR 97-064B Study: 1296-96-MR-07 Trial: 94-IT-96-298 - Study to GLP - Study carried out in 1996**	Maize (Caterina)	ITALY (Europe South)	200 g a.s./ha A12738B	2 days after planting	132	Silage	< 0.01†	-	MNBA Grain Mean = 89% RSD = 13% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Silage Mean = 82% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 93% RSD = 13% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Silage Mean = 99% RSD = 0% (n = 1 in 0.01 - 0.01 mg/kg spiking range)
					171	Cob + Grain	< 0.01†	-	
					171	Cob + Grain + Husk	< 0.01†	-	
					171	Grain	< 0.01†	-	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 02-7036 Study: 02-7036 Trial: 02-7036 - Study to GLP - Study carried out in 2002	Maize (Helder 550)	ITALY (Europe South)	168.75 g a.s./ha A12812A	BBCH 01	101	Cob + Grain	< 0.01	< 0.01	MNBA Grain Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Stover (fodder) Mean = 95% RSD = 11% (n = 6 in 0.01 - 0.01 mg/kg spiking range) MNBA Cob Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 110% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 94% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 103% RSD = 6% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 101% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range)
					101	Cob + Grain	< 0.01	< 0.01	
					101	Stover (fodder)	< 0.01	< 0.01	
					101	Stover (fodder)	< 0.01	< 0.01	
					150	Grain	< 0.01	< 0.01	
					150	Grain	< 0.01	< 0.01	
					150	Cob	< 0.01	< 0.01	
					150	Cob	< 0.01	< 0.01	
					150	Stover (fodder)	< 0.01	< 0.01	
					150	Stover (fodder)	< 0.01	< 0.01	
	Maize (Helder 550)		150 g a.s./ha A12812A	BBCH 13	74	Cob + Grain	< 0.01	< 0.01	
					74	Cob + Grain	< 0.01	< 0.01	
					74	Stover (fodder)	< 0.01	< 0.01	
					74	Stover (fodder)	< 0.01	< 0.01	
					123	Grain	< 0.01	< 0.01	
					123	Grain	< 0.01	< 0.01	
					123	Cob	< 0.01	< 0.01	
					123	Cob	< 0.01	< 0.01	
					123	Stover (fodder)	< 0.01	< 0.01	
					123	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 02-7037 Study: 02-7037 Trial: 02-7037 - Study to GLP - Study carried out in 2002	Maize (Leonardo)	ITALY (Europe South)	168.75 g a.s./ha A12812A	BBCH 07	91	Cob + Grain	< 0.01	< 0.01	MNBA Grain Mean = 98% RSD = 3% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Stover (fodder) Mean = 93% RSD = 7% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Cob Mean = 96% RSD = 7% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 104% RSD = 3% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 102% RSD = 2% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 102% RSD = 13% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Cob Mean = 103% RSD = 5% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 102% RSD = 4% (n = 4 in 0.01 - 0.01 mg/kg spiking range)
					91	Cob + Grain	< 0.01	< 0.01	
					91	Stover (fodder)	< 0.01	< 0.01	
					91	Stover (fodder)	< 0.01	< 0.01	
					147	Grain	< 0.01	< 0.01	
					147	Grain	< 0.01	< 0.01	
					147	Cob	< 0.01	< 0.01	
					147	Cob	< 0.01	< 0.01	
					147	Stover (fodder)	< 0.01	< 0.01	
					147	Stover (fodder)	< 0.01	< 0.01	
	Maize (Leonardo)		150 g a.s./ha A12812A	BBCH 14	77	Cob + Grain	≤ 0.01	< 0.01	
					77	Cob + Grain	< 0.01	< 0.01	
					77	Stover (fodder)	≤ 0.01	< 0.01	
					77	Stover (fodder)	< 0.01	< 0.01	
					133	Grain	≤ 0.01	< 0.01	
					133	Grain	< 0.01	< 0.01	
					133	Cob	< 0.01	< 0.01	
					133	Cob	< 0.01	< 0.01	
					133	Stover (fodder)	< 0.01	< 0.01	
					133	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 02-7038 Study: 02-7038 Trial: 02-7038 - Study to GLP - Study carried out in 2002	Maize (LG 2306)	ITALY (Europe South)	167.6 g a.s./ha A12812A	Pre-emergence	87	Cob + Grain	< 0.01	< 0.01	MNBA Grain Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Stover (fodder) Mean = 103% RSD = 1% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Cob Mean = 74% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 103% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 109% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 99% RSD = 2% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Cob Mean = 114% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 96% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range)
					87	Cob + Grain	< 0.01	< 0.01	
					87	Stover (fodder)	< 0.01	< 0.01	
					87	Stover (fodder)	< 0.01	< 0.01	
					132	Grain	< 0.01	< 0.01	
					132	Grain	< 0.01	< 0.01	
					132	Cob	< 0.01	< 0.01	
					132	Cob	< 0.01	< 0.01	
					132	Stover (fodder)	< 0.01	< 0.01	
					132	Stover (fodder)	< 0.01	< 0.01	
	Maize (LG 2306)		152 g a.s./ha A12812A	BBCH 13 - 14	59	Cob + Grain	< 0.01	< 0.01	
					59	Cob + Grain	< 0.01	< 0.01	
					59	Stover (fodder)	< 0.01	< 0.01	
					59	Stover (fodder)	< 0.01	< 0.01	
					104	Grain	< 0.01	< 0.01	
					104	Grain	< 0.01	< 0.01	
					104	Cob	< 0.01	< 0.01	
					104	Cob	< 0.01	< 0.01	
					104	Stover (fodder)	< 0.01	< 0.01	
					104	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 02-7039 Study: 02-7039 Trial: Az. Recchiuti Casimiro - Study to GLP - Study carried out in 2002	Maize (Panama)	ITALY (Europe South)	175.5 g a.s./ha A12812A	BBCH 00	88	Cob + Grain	< 0.01	< 0.01	MNBA Grain Mean = 98% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Stover (fodder) Mean = 104% RSD = 6% (n = 4 in 0.01 - 0.01 mg/kg spiking range) MNBA Cob Mean = 104% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Grain Mean = 100% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 110% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 96% RSD = 6% (n = 4 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Cob Mean = 110% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) Mesotrione Grain Mean = 112% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range)
					88	Cob + Grain	< 0.01	< 0.01	
					88	Stover (fodder)	< 0.01	< 0.01	
					88	Stover (fodder)	< 0.01	< 0.01	
					130	Grain	< 0.01	< 0.01	
					130	Grain	< 0.01	< 0.01	
					130	Cob	< 0.01	< 0.01	
					130	Cob	< 0.01	< 0.01	
					130	Stover (fodder)	< 0.01	< 0.01	
					130	Stover (fodder)	< 0.01	< 0.01	
	Maize (Panama)		157.3 g a.s./ha A12812A	BBCH 14	73	Cob + Grain	≤ 0.01	< 0.01	
					73	Cob + Grain	< 0.01	< 0.01	
					73	Stover (fodder)	≤ 0.01	< 0.01	
					73	Stover (fodder)	< 0.01	< 0.01	
					115	Grain	≤ 0.01	< 0.01	
					115	Grain	< 0.01	< 0.01	
					115	Cob	< 0.01	< 0.01	
					115	Cob	< 0.01	< 0.01	
					115	Stover (fodder)	< 0.01	< 0.01	
					115	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 03-7019 Study: 03-7019 Trial: 03-7019 - Study to GLP - Study carried out in 2003	Maize (Proxima)	ITALY (Europe South)	157.7 g a.s./ha A12807H	BBCH 13	77	Forage	< 0.01	< 0.01	MNBA Cob Mean = 82% RSD = 15% (n = 7 in 0.01 - 0.10 mg/kg spiking range) MNBA Grain Mean = 103% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Stover (fodder) Mean = 95% RSD = 14% (n = 7 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 84% RSD = 13% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Grain Mean = 98% RSD = 17% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 91% RSD = 17% (n = 8 in 0.01 - 0.10 mg/kg spiking range) S-Metolachlor Cob Mean = 89% RSD = 12% (n = 8 in 0.02 - 0.20 mg/kg spiking range) S-Metolachlor Grain Mean = 91% RSD = 15% (n = 4 in 0.02 - 0.20 mg/kg spiking range) S-Metolachlor Stover (fodder) Mean = 98% RSD = 13% (n = 8 in 0.02 - 0.20 mg/kg spiking range)
					77	Forage	< 0.01	< 0.01	
					77	K+cwhr	< 0.01	< 0.01	
					77	K+cwhr	< 0.01	< 0.01	
					121	Cob	< 0.01	< 0.01	
					121	Cob	< 0.01	< 0.01	
					121	Grain	< 0.01	< 0.01	
					121	Grain	< 0.01	< 0.01	
					121	Stover (fodder)	< 0.01	< 0.01	
					121	Stover (fodder)	< 0.01	< 0.01	
	Maize (Proxima)		166.2 g a.s./ha A12807H	BBCH 00	91	Forage	< 0.01	< 0.01	
					91	Forage	< 0.01	< 0.01	
					91	K+cwhr	< 0.01	< 0.01	
					91	K+cwhr	< 0.01	< 0.01	
					135	Cob	< 0.01	< 0.01	
					135	Cob	< 0.01	< 0.01	
					135	Grain	< 0.01	< 0.01	
					135	Grain	< 0.01	< 0.01	
					135	Stover (fodder)	< 0.01	< 0.01	
					135	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate / Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 03-7020 Study: 03-7020 Trial: 03-7020 - Study to GLP - Study carried out in 2003	Maize (Pioneer PR32D12)	ITALY (Europe South)	171.15 g a.s./ha A12807H	BBCH 00	104	Forage	< 0.01	< 0.01	MNBA Cob Mean = 72% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range) MNBA Forage Mean = 81% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA Grain Mean = 72% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA K+cwhr Mean = 68% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Cob Mean = 103% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Forage Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Grain Mean = 85% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione K+cwhr Mean = 84% RSD = N/A (n = 2 in 0.01 - 0.01 mg/kg spiking range)
					104	Forage	< 0.01	< 0.01	
					104	K+cwhr	< 0.01	< 0.01	
					104	K+cwhr	< 0.01	< 0.01	
					133	Cob	< 0.01	< 0.01	
					133	Cob	< 0.01	< 0.01	
					133	Grain	< 0.01	< 0.01	
					133	Grain	< 0.01	< 0.01	
					133	Stover (fodder)	< 0.01	< 0.01	
					133	Stover (fodder)	< 0.01	< 0.01	
	Maize (Pioneer PR32D12)		148.5 g a.s./ha A12807H	BBCH 13 - 14	88	Forage	≤ 0.01	< 0.01	
					88	Forage	< 0.01	< 0.01	
					88	K+cwhr	≤ 0.01	< 0.01	
					88	K+cwhr	< 0.01	< 0.01	
					117	Cob	< 0.01	< 0.01	
					117	Cob	< 0.01	< 0.01	
					117	Grain	≤ 0.01	< 0.01	
					117	Grain	< 0.01	< 0.01	
					117	Stover (fodder)	< 0.01	< 0.01	
					117	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 03-7021 Study: 03-7021 Trial: 03-7021 - Study to GLP - Study carried out in 2003	Maize (Furio)	ITALY (Europe South)	171.4 g a.s./ha A12807H	pre-emergence	86	Forage	< 0.01	< 0.01	MNBA Cob Mean = 82% RSD = 15% (n = 7 in 0.01 - 0.10 mg/kg spiking range) MNBA Grain Mean = 103% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Stover (fodder) Mean = 95% RSD = 14% (n = 7 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 84% RSD = 13% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Grain Mean = 98% RSD = 17% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 91% RSD = 17% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
					86	Forage	< 0.01	< 0.01	
					86	K+cwhr	0.02(2)	< 0.01	
					86	K+cwhr	< 0.01	< 0.01	
					136	Cob	< 0.01	< 0.01	
					136	Cob	< 0.01	< 0.01	
					136	Grain	< 0.01	< 0.01	
					136	Grain	< 0.01	< 0.01	
					136	Stover (fodder)	< 0.01	< 0.01	
					136	Stover (fodder)	< 0.01	< 0.01	
	Maize (Furio)		151.5 g a.s./ha A12807H	BBCH 13 - 14	65	Forage	< 0.01	< 0.01	
					65	Forage	< 0.01	< 0.01	
					65	K+cwhr	< 0.01	< 0.01	
					65	K+cwhr	< 0.01	< 0.01	
					115	Cob	< 0.01	< 0.01	
					115	Cob	< 0.01	< 0.01	
					115	Grain	< 0.01	< 0.01	
					115	Grain	< 0.01	< 0.01	
					115	Stover (fodder)	< 0.01	< 0.01	
					115	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: 03-7022 Study: 03-7022 Trial: 03-7022 - Study to GLP - Study carried out in 2003	Maize (PR32W92)	ITALY (Europe South)	171.8 g a.s./ha A12807H	BBCH 05	105	Forage	< 0.01	< 0.01	MNBA Cob Mean = 82% RSD = 15% (n = 7 in 0.01 - 0.10 mg/kg spiking range) MNBA Grain Mean = 103% RSD = 8% (n = 4 in 0.01 - 0.10 mg/kg spiking range) MNBA Stover (fodder) Mean = 95% RSD = 14% (n = 7 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 84% RSD = 13% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Grain Mean = 98% RSD = 17% (n = 4 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Stover (fodder) Mean = 91% RSD = 17% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
					105	Forage	< 0.01	< 0.01	
					105	K+cwhr	< 0.01	< 0.01	
					105	K+cwhr	< 0.01	< 0.01	
					144	Cob	< 0.01	< 0.01	
					144	Cob	< 0.01	< 0.01	
					144	Grain	< 0.01	< 0.01	
					144	Grain	< 0.01	< 0.01	
					144	Stover (fodder)	< 0.01	< 0.01	
					144	Stover (fodder)	< 0.01	< 0.01	
	Maize (PR32W92)		156.9 g a.s./ha A12807H	BBCH 13 - 14	81	Forage	≤ 0.01	< 0.01	
					81	Forage	< 0.01	< 0.01	
					81	K+cwhr	≤ 0.01	< 0.01	
					81	K+cwhr	< 0.01	< 0.01	
					144	Cob	< 0.01	< 0.01	
					144	Cob	< 0.01	< 0.01	
					144	Grain	≤ 0.01	< 0.01	
					144	Grain	< 0.01	< 0.01	
					144	Stover (fodder)	< 0.01	< 0.01	
					144	Stover (fodder)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: T011369-06-REG Study: SYN-0732 Trial: AF/11508/SY/1 - Study to GLP - Study carried out in 2007	Maize (PRA-68)	SPAIN (Europe South)	152.0 g a.s./ha A14351BX	BBCH 18	8	Whole Plant	0.02	< 0.01	MNBA Grain Mean = 95% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 104% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); MNBA Cobs without kernels Mean = 97% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Grain Mean = 93% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 90% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); Mesotrione Cobs without kernels Mean = 69% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range).
					27	Whole Plant	≤ 0.01	< 0.01	
					41	Kernel	≤ 0.01	< 0.01	
					41	Cob without kernels	< 0.01	< 0.01	
					41	Remaining plant(1)	< 0.01	< 0.01	
					62	Whole Plant	< 0.01	< 0.01	
					91	Kernel	< 0.01	< 0.01	
					91	Cob without kernels	< 0.01	< 0.01	
					91	Remaining plant(1)	< 0.01	< 0.01	
					103	Kernel	≤ 0.01	< 0.01	
					103	Cob without kernels	< 0.01	< 0.01	
					103	Remaining plant(1)	< 0.01	< 0.01	
Report: T011369-06-REG Study: SYN-0732 Trial: IT-HR-07-0120 - Study to GLP - Study carried out in 2007	Maize (PRA 36 B08)	ITALY (Europe South)	163.3 g a.s./ha A14351BX	BBCH 18	27	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 95% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 104% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); MNBA Cobs without kernels Mean = 97% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 93% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 90% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range); Mesotrione Cobs without kernels Mean = 69% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range).
					35	Whole Plant	< 0.01	< 0.01	
					42	Whole Plant	< 0.01	< 0.01	
					60	Whole Plant	≤ 0.01	< 0.01	
					68	Kernel	≤ 0.01	< 0.01	
					68	Cob without kernels	< 0.01	< 0.01	
					68	Remaining plant(1)	< 0.01	< 0.01	
					75	Whole Plant	< 0.01	< 0.01	
					96	Kernel	≤ 0.01	< 0.01	
					96	Cob without kernels	< 0.01	< 0.01	
					96	Remaining plant(1)	< 0.01	< 0.01	
Report: T009531-07-REG Study: IF-08/01136896 Trial: PDA-08-4166-FR03 - Study to GLP - Study carried out in 2008	Maize (FAM050)	FRANCE (Europe South)	154.2 g a.s./ha A14351BX	BBCH 18	22	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 76% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 81% RSD = NA (n = 2 in 0.01 mg/kg spiking range); MNBA Cobs Mean = 77% RSD = NA (n = 2
					41	Whole Plant	≤ 0.01	< 0.01	
					41	Cobs	< 0.01	< 0.01	
					41	Remaining plant(1)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
					53	Kernel	< 0.01	< 0.01	in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 81% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 87% RSD = NA (n = 2 in 0.01 mg/kg spiking range); Mesotrione Cobs Mean = 87% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range).
					53	Cob without kernels	< 0.01	< 0.01	
					53	Remaining plant(1))	< 0.01	< 0.01	
					60	Whole Plant	< 0.01	< 0.01	
					77	Whole Plant	< 0.01	< 0.01	
					91	Kernel	< 0.01	< 0.01	
					91	Cob without kernels	< 0.01	< 0.01	
					91	Remaining plant(1)	< 0.01	< 0.01	
					124	Kernel	< 0.01	< 0.01	
					124	Cob without kernels	< 0.01	< 0.01	
					124	Remaining plant(1)	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: T009531-07-REG Study: IF-08/01136896 Trial: PDA-08-4166-FR04 - Study to GLP - Study carried out in 2008	Maize (PR35T06)	FRANCE (Europe South)	146.8 g a.s./ha A14351BX	BBCH 18	20	Whole Plant	< 0.01	< 0.01	MNBA Kernel Mean = 76% RSD = N/A (n = 2 at 0.01 mg/kg spiking); MNBA Plant Mean = 81% RSD = NA (n = 2 in 0.01 mg/kg spiking range); MNBA Cobs Mean = 77% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range). Mesotrione Kernel Mean = 81% RSD = N/A (n = 2 at 0.01 mg/kg spiking); Mesotrione Plant Mean = 87% RSD = NA (n = 2 in 0.01 mg/kg spiking range); Mesotrione Cobs Mean = 87% RSD = NA (n = 2 in 0.01 - 0.10 mg/kg spiking range).
					34	Whole Plant	< 0.01	< 0.01	
					41	Cobs)	< 0.01	< 0.01	
					41	Remaining plant(2	< 0.01	< 0.01	
					54	Kernel	< 0.01	< 0.01	
					54	Cob without kernels	< 0.01	< 0.01	
					54	Remaining plant(1)	< 0.01	< 0.01	
					62	Whole Plant	< 0.01	< 0.01	
					92	Kernel	< 0.01	< 0.01	
					92	Cob without kernels	< 0.01	< 0.01	
					92	Remaining plant(1)	< 0.01	< 0.01	
Report: T009534-07-REG Study: T009534-07 Trial: S08-02210-01 - Study to GLP - Study carried out in 2008 (F)	Corn (GA21 (MON-00021-9))	SPAIN (Europe South)	155.00 g a.s./ha (A15189G)	BBCH 15	58	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 79% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 88% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 91% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 96% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01
					86	Cob	< 0.01	< 0.01	
					86	Cob + Kernel	< 0.01 +	< 0.01 +	
					86	Kernel	< 0.01	< 0.01	
					86	Remaining Plant	< 0.01	< 0.01	
					86	Whole plant	< 0.01	< 0.01	
					147	Cob	< 0.01	< 0.01	
					147	Cob + Kernel	< 0.01 +	< 0.01 +	
					147	Kernel	< 0.01	< 0.01	
					147	Remaining Plant	< 0.01	< 0.01	
	Corn (GA21 (MON-00021-9))		152.00 g a.s./ha (A15189G)	BBCH 15	58	Whole plant	< 0.01	< 0.01	
					86	Cob	< 0.01	< 0.01	
					86	Cob + Kernel	< 0.01 +	< 0.01 +	
					86	Kernel	< 0.01	< 0.01	
					86	Remaining Plant	< 0.01	< 0.01	
					86	Whole plant	< 0.01	< 0.01	
					147	Cob	< 0.01	< 0.01	
					147	Cob + Kernel	< 0.01 +	< 0.01 +	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
					147	Kernel	< 0.01	< 0.01	Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					147	Remaining Plant	< 0.01	< 0.01	
Report: T009534-07-REG Study: T009534-07 Trial: S08-02210-02 - Study to GLP - Study carried out in 2008 (F)	Corn (GA21 (MON-00021-9))	SPAIN (Europe South)	150.00 g a.s./ha (A15189G)	BBCH 15	56	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 79% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Remaining Plant Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 88% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 91% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 96% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range)
					72	Whole plant	< 0.01	< 0.01	
					97	Cob	< 0.01	< 0.01	
					97	Cob + Kernel	< 0.01 +	< 0.01 +	
					97	Kernel	< 0.01	< 0.01	
					97	Remaining Plant	< 0.01	< 0.01	
					128	Cob	< 0.01	< 0.01	
					128	Cob + Kernel	< 0.01 +	< 0.01 +	
					128	Kernel	< 0.01	< 0.01	
					128	Remaining Plant	< 0.01	< 0.01	
	Corn (GA21 (MON-00021-9))		151.00 g a.s./ha (A15189G)	BBCH 15	56	Whole plant	< 0.01	< 0.01	Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					72	Whole plant	< 0.01	< 0.01	
					97	Cob	< 0.01	< 0.01	
					97	Cob + Kernel	< 0.01 +	< 0.01 +	
					97	Kernel	< 0.01	< 0.01	
					97	Remaining Plant	< 0.01	< 0.01	
					128	Cob	< 0.01	< 0.01	
					128	Cob + Kernel	< 0.01 +	< 0.01 +	
					128	Kernel	< 0.01	< 0.01	
					128	Remaining Plant	< 0.01	< 0.01	
Report: T009534-07-REG Study: T009534-07 Trial: S08-02210-03 - Study to GLP	Corn (GA21 (MON-00021-9))	SPAIN (Europe South)	153.00 g a.s./ha (A15189G)	BBCH 15	57	Whole plant	< 0.01	< 0.01	MNBA Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Kernel Mean = 79% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range)
					78	Whole plant	< 0.01	< 0.01	
					97	Cob	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate / Product Code	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
- Study carried out in 2008 (F)					97	Cob + Kernel	< 0.01 +	< 0.01 +	MNBA Remaining Plant Mean = 102% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) MNBA Whole plant Mean = 88% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Cob Mean = 91% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Kernel Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Remaining Plant Mean = 96% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Whole plant Mean = 86% RSD = N/A (n = 2 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Cob) RAM 366/01 Mesotrione (Cob + Kernel) RAM 366/01 Mesotrione (Kernel) RAM 366/01 Mesotrione (Remaining Plant) RAM 366/01 Mesotrione (Whole plant) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Cob + Kernel) RAM 366/01 MNBA (Kernel) RAM 366/01 MNBA (Remaining Plant) RAM 366/01 MNBA (Whole plant) RAM 366/01
					97	Kernel	< 0.01	< 0.01	
					97	Remaining Plant	< 0.01	< 0.01	
					130	Cob	< 0.01	< 0.01	
					130	Cob + Kernel	< 0.01 +	< 0.01 +	
					130	Kernel	< 0.01	< 0.01	
					130	Remaining Plant	< 0.01	< 0.01	
	Corn (GA21 (MON-00021-9))		152.00 g a.s./ha (A15189G)	BBCH 15	57	Whole plant	< 0.01	< 0.01	
					78	Whole plant	< 0.01	< 0.01	
					97	Cob	< 0.01	< 0.01	
					97	Cob + Kernel	< 0.01 +	< 0.01 +	
					97	Kernel	< 0.01	< 0.01	
					97	Remaining Plant	< 0.01	< 0.01	
					130	Cob	< 0.01	< 0.01	
					130	Cob + Kernel	< 0.01 +	< 0.01 +	
					130	Kernel	< 0.01	< 0.01	
					130	Remaining Plant	< 0.01	< 0.01	

(DBA) Days Before Application
(†) Analysis of combined mesotrione plus MNBA residue expressed as mesotrione equivalents
(1) Remaining plant after cobs removed
(2) This data point has been demonstrated to be an outlier using Dixon's Q test and was not considered suitable for inclusion in MRL calculations
(*) Indicates sample taken prior to last application
(#) Indicates corrected Residue values
(+) Indicates calculated Residue value
(N/A) Not applicable
K+cwhr = kernel + cob with husk removed

Results dotted underlined are those considered suitable for extrapolation to sweet corn. See point CA 6.3.2

(**) The residue data from these trials were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (Vol.3, Annex B, Section B.7.6.1, December 1999). They are included in this submission to provide a complete overview of available data

Findings

MRLs for maize grain have been calculated for northern and southern Europe according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The mesotrione residue values used in the MRL and STMR calculations are underlined in Table 6.3.1-5. Only trials treated post emergence have been considered as a worst case. The calculated outputs are presented in Table 6.3.1-6.

Table 6.3.1-6: MRL and STMR calculations for mesotrione on maize (grain) – approved EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	22 x <0.01	0.010	0.01	0.01	0.01
Southern EU	Outdoor	22 x <0.01	0.010	0.01	0.01	0.01
Combined EU	Outdoor	44 x <0.01	0.010	0.01	0.01	0.01

The available data clearly show all mesotrione data from the critical GAP are below the analytical LOQ of 0.01 mg/kg. MNBA residue concentrations are also insignificant. There is an existing EU MRL of <0.05* mg/kg for mesotrione on maize grain (as the sum of mesotrione and MNBA (4-methylsulfonyl-2-nitro benzoic acid), expressed as mesotrione. To support the proposed new definition of residue of mesotrione only (no MNBA metabolite) a new MRL is proposed. The EU MRL is presented in Table CA 6.3.1-8, with the corresponding STMR and HR.

MRLs for maize forage as a potential livestock feed item have been calculated for northern and southern Europe according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The residue values for forage or silage used in the MRL and STMR calculations are double underlined in Table 6.3.1-5. Only trials treated post emergence have been considered as a worst case. The calculated outputs are presented in Table 6.3.1-7.

Table 6.3.1-7: MRL and STMR calculations for mesotrione on maize (forage) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	22 x <0.01	0.010	0.01	0.01	0.01
Southern EU	Outdoor	23 x <0.01	0.010	0.01	0.01	0.01
Combined EU	Outdoor	45 x <0.01	0.010	0.01	0.01	0.01

The available data clearly show all mesotrione data from the critical GAP for are below the analytical LOQ of 0.01 mg/kg. Currently there are no EU MRLs set for forage or for any livestock feed items. For use in dietary burden estimations, a new pseudo MRL for mesotrione only is presented. These data are presented in Table 6.3.1-8, with the corresponding STMR and HR.

Table 6.3.1-8: EU MRL, STMR and HR for mesotrione on maize

Commodity (code)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Maize grain (500030)	0.01	0.01	0.01
Maize forage (not applicable)	0.01	0.01	0.01

CA 6.3.2 Sweet corn

This crop is included to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). Mesotrione is used on sweet corn according to the following EU critical GAP, detailed in Table 6.3.2-1.

Table 6.3.2–1: Approved EU critical GAPs for mesotrione on sweet corn (extrapolation from maize)

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	2-8 leaves BBCH 12-18	1	NA	0.150	100-400	NR
Southern EU	Outdoor	2-8 leaves BBCH 12-18	1	NA	0.150	100-400	NR

NA- not applicable

NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

Residue data from immature maize grain can be used to represent sweet corn according to EU guidelines (**EU guideline Document 7525/VI/95 rev. 9**). Immature maize grain samples, taken at BBCH 75-79, presented in Section CA 6.3.1 above are considered appropriate to extrapolate to sweet corn.

Sweet corn is considered to be a minor crop in both Southern and Northern Europe and therefore generally requires a minimum of four trials in both regions (**Commission Regulation (EU) No 284/2013, 1 March 2013**). However, as an early application herbicide, residues are foreseen to be under the limit of quantification and hence a minimum of three residue trials are sufficient (**EU guideline Document 7525/VI/95 rev. 9 and Commission Regulation (EU) No 284/2013, 1 March 2013**).

A sufficient number of trials are available in which mesotrione was applied as an SC, SE, OD, WG or ZC formulation and grain samples at BBCH 75-79 were taken. A summary of the data is presented in Table 6.3.2-2 below. The full results of the trials are presented in Table 6.3.1-5 above in which the residue values considered are dotted underlined.

Table 6.3.2–2: Summary of residues of mesotrione and MNBA in immature maize grain commodities (sweet corn)

Region	Formulation type (number of trials)	Maize commodity	PHI (days)	Residues (mg/kg)	
				mesotrione	MNBA
North EU	OD (4 trials)	Immature grain	58 - 90	4 x <0.01	4 x <0.01
	ZC (4 trials)	Immature grain	92 - 98	4 x <0.01	4 x <0.01
	WG (2 trials)	Kernels + cobs (with husk removed)	47 - 53	2 x <0.01	2 x <0.01
South EU	SC (4 trials)	Kernels + cobs (with husk removed)	65 - 88	4 x <0.01	4 x <0.01
	SE (4 trials)	Kernels + cobs (with husk removed)	59 - 77	4 x <0.01	4 x <0.01
	OD (4 trials)	Immature grain	41 - 68	4 x <0.01	4 x <0.01
	ZC (3 trials)	Immature grain	86 - 97	3 x <0.01	3 x <0.01

Good Agricultural Practice (GAP) - Sweet corn

An additional national GAP is available in the EU in which mesotrione can be applied to sweet corn and harvested with a short pre harvest interval. This application is not proposed for maize and hence extrapolation is not considered appropriate. These data were not previously submitted in Europe however have been included here to provide a complete data package.

Mesotrione is used on sweet corn according to the following EU National GAP, detailed in Table 6.3.2-3.

Table 6.3.2–3: EU National GAP for mesotrione on sweet corn

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Southern EU	Outdoor	0-9 leaves BBCH 00-19	1	NA	0.075	300	42

NA- not applicable

NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

The residue reports supporting the EU National GAP for mesotrione on sweet corn are referenced in Table 6.3.2-4 and the data are presented in Table 6.3.2-6.

Table 6.3.2-4: Report references for trials supporting EU National GAPs for mesotrione on sweet corn

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.2/01	(1 of 5)	J P Gill	2002	Mesotrione: Residue Levels in Sweet Maize from Trials conducted in Northern France during 2001 Syngenta File No. ZA1296/0824, Syngenta Report No. RJ3298B
KCA 6.3.2/02	(2 of 5)	J Gill	2002	Mesotrione: Residue Levels in Sweet Maize from Trials conducted in Southern France during 2001 Syngenta File No. ZA1296/0823, Syngenta Report No. RJ3297B
KCA 6.3.2/03	(3 of 5)	S Richards	2004	Residue Study with Mesotrione (ZA 1296) in or on Sweet Corn in France (South) Syngenta File No. ZA1296/1358, Syngenta Report No. 03-7049
KCA 6.3.2/04	(4 of 5)	S Richards	2004	Residue Study with Mesotrione (ZA 1296) in or on Sweet Corn in France (South) Syngenta File No. ZA1296/1359, Syngenta Report No. 03-7050
KCA 6.3.2/05	(5 of 5)	S Richards	2005	Residue study with Mesotrione (ZA1296) in or on Sweet Corn in France (South) Syngenta File No. ZA1296/1798, Syngenta Report No. 04-7012

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Eight supervised residue trials were conducted on sweet corn between 2001 and 2003, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.2-5.

Table 6.3.2-5: Summary of mesotrione residue trials on sweet corn

Northern Europe			
Country	**2001**	**2003**	**2004**
France (north)	1 Harvest	-	-
Southern Europe			
Country	**2001**	**2003**	**2004**
France (south)	3 Harvest	2 Harvest	2 Harvest

Sweet corn is a minor crop in northern and southern Europe and therefore generally requires four trials in each residue region (**Document 7525/VI/95 – rev.9, March 2011**).

In four trials, treatments with mesotrione as single spray applications were conducted at a late growth stage (BBCH 19-59) as an SC 100 formulation at application rates between 0.098 and 0.104 kg a.s./ha. The water volumes during application ranged from 288 to 295 L/ha. Samples of sweet corn kernel or cob (with husk removed) were taken 38 to 39 days after application. Additionally in all trials, an application of mesotrione was made according to the GAP extrapolated from maize; a single early post-emergence (BBCH 12 to 15) spray application as an SC 100 formulation at application rates between 0.143 to 0.154 kg a.s./ha. Samples of sweet corn kernel and cobs were taken 38 to 83 days after application.

All samples were analysed for residues of mesotrione and MNBA. . The four trials conducted at BBCH 19 – 59 are sufficient to satisfy the requirements for a minor crop in one region (**EU guideline Document 7525/VI/95 rev. 9**). The additional early post-emergence applications made in the trials (at the GAP extrapolated from maize) conducted in Southern Europe are also sufficient to satisfy EU Guideline requirements for a minor crop in one region. From the two application regimes, there is sufficient data to make a comparison between the GAP proposed for sweet corn and the GAP extrapolated from maize.

Allowing for a 25% deviation from the proposed maximum application rate, rates in all trials cover or exceed the National EU GAP. However as all samples gave residues below the analytical LOQ the GAP is supported.

A minimum PHI of 42 days is proposed for the critical EU GAP for sweet corn.

Table 6.3.2-6: Summary of Residue Data Supporting the EU National GAP for mesotrione on Sweet corn

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Northern Europe									
Report: RJ3298B Study: 01JH065 Trial: AF/5941/SY/1 - Study to GLP - Study carried out in 2001 (F)	Sweet maize (El Toro)	FRANCE (Europe North)	100.0 g a.s./ha (YF11645)	BBCH 15	83	*Kernel*	< 0.01	< 0.01	MNBA Cob K+cwhr Mean = 105% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) MNBA Kernel K+cwhr Mean = 101% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Cob K+cwhr Mean = 100% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Kernel K+cwhr Mean = 98% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione (Cob) SOP RAM 366/01 Mesotrione (Kernel) SOP RAM 366/01 MNBA (Cob) SOP RAM 366/01 MNBA (Kernel) SOP RAM 366/01
					83	*Cob*	< 0.01	< 0.01	
Southern Europe									
Report: RJ3297B Study: 01JH064 Trial: AF/5940/SY/1 - Study to GLP - Study carried out in 2001 (F)	Sweet maize (Royalty)	FRANCE (Europe South)	100.0 g a.s./ha (YF11645)	BBCH 14	72	*Kernel*	< 0.01	< 0.01	MNBA Cob K+cwhr Mean = 105% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) MNBA Kernel K+cwhr Mean = 101% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Cob K+cwhr Mean = 100% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Kernel K+cwhr Mean = 98% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione (Cob) SOP RAM 366/01 Mesotrione (Kernel) SOP RAM 366/01 MNBA (Cob) SOP RAM 366/01 MNBA (Kernel) SOP RAM 366/01
					72	*Cob*	< 0.01	< 0.01	
Report: RJ3297B Study: 01JH064 Trial: AF/5940/SY/2 - Study to GLP - Study carried out in 2001 (F)	Sweet maize (Bomus)	FRANCE (Europe South)	100.0 g a.s./ha (YF11645)	BBCH 14	72	*Kernel*	< 0.01	< 0.01	MNBA Cob K+cwhr Mean = 105% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) MNBA Kernel K+cwhr Mean = 101% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Cob K+cwhr Mean = 100% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking
					72	*Cob*	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
									range) Mesotrione Kernel K+cwhr Mean = 98% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione (Cob) SOP RAM 366/01 Mesotrione (Kernel) SOP RAM 366/01 MNBA (Cob) SOP RAM 366/01 MNBA (Kernel) SOP RAM 366/01
Report: RJ3297B Study: 01JH064 Trial: AF/5940/SY/3 - Study to GLP - Study carried out in 2001 (F)	Sweet maize (Royalty)	FRANCE (Europe South)	100.0 g a.s./ha (YF11645)	BBCH 14	72	*Kernel*	< 0.01	< 0.01	MNBA Cob K+cwhr Mean = 105% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) MNBA Kernel K+cwhr Mean = 101% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Cob K+cwhr Mean = 100% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione Kernel K+cwhr Mean = 98% RSD = N/A (n = 2 in 0.02 - 0.02 mg/kg spiking range) Mesotrione (Cob) SOP RAM 360/01 Mesotrione (Kernel) SOP RAM 366/01 MNBA (Cob) SOP RAM 360/01 MNBA (Kernel) SOP RAM 366/01
					72	*Cob*	< 0.01	< 0.01	
Report: 03-7049 Study: 03-7049 Trial: Loustalet - Study to GLP - Study carried out in 2003 (F)	Sweet maize (620 Spirit)	FRANCE (Europe South)	102.2 g a.s./ha (A12739A)	BBCH 19	38	Cob	< 0.01	< 0.01	MNBA Cob Mean = 76% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA Kernel Mean = 76% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Cob Mean = 77% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Kernel Mean = 94% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione (Cob) RAM 366/01, modified Mesotrione (Kernel) RAM 366/01, modified MNBA (Cob) RAM 366/01, modified MNBA (Kernel) RAM 366/01, modified
					38	Kernel	< 0.01	< 0.01	
	Sweet maize (620 Spirit)		153.3 g a.s./ha (A12739A)	BBCH 12	61	Cob	< 0.01	< 0.01	
					61	Kernel	< 0.01	< 0.01	
Report: 03-7050 Study: 03-7050 Trial: Souprosse - Study to GLP unchecked - Study carried out in 2003 (F)	Sweet maize (620 Spirit)	FRANCE (Europe South)	97.9 g a.s./ha (A12739A)	BBCH 19	38	Kernel	< 0.01	< 0.01	MNBA Cob Mean = 71% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA Kernel Cob Mean = 89% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Cob Mean = 76% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Kernel Cob Mean = 94% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking
					38	Cob	< 0.01	< 0.01	
	Sweet maize (620 Spirit)		143.4 g a.s./ha (A12739A)	BBCH 12	62	Kernel	< 0.01	< 0.01	
					62	Cob	< 0.01	< 0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
									range) Mesotrione (Cob) RAM 366/01 Mesotrione (Kernel) RAM 366/01 MNBA (Cob) RAM 366/01 MNBA (Kernel) RAM 366/01
Report: 04-7012 Study: 04-7012 Trial: FR-HR-04-0106 - Study to GLP - Study carried out in 2004 (F)	Sweet maize (620 Spirit)	FRANCE (Europe South)	104.4 g a.s./ha (A12739A)	BBCH 59	39	Cob	< 0.01	< 0.01	MNBA Cob Mean = 103% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA Kernel Mean = 87% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Kernel Mean = 81% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione (Cob) RAM 366/01, modified Mesotrione (Kernel) RAM 366/01, modified MNBA (Cob) RAM 366/01, modified MNBA (Kernel) RAM 366/01, modified
					39	Kernel	< 0.01	< 0.01	
	Sweet maize (620 Spirit)		152.7 g a.s./ha (A12739A)	BBCH 12	61	Cob	< 0.01	< 0.01	
					61	Kernel	< 0.01	< 0.01	
					74	Cob	< 0.01	< 0.01	
					74	K+cwhr			
					74	Kernel	< 0.01	< 0.01	
Report: 04-7012 Study: 04-7012 Trial: FR-HR-04-0107 - Study to GLP - Study carried out in 2004 (F)	Sweet maize (620 Spirit)	FRANCE (Europe South)	102.9 g a.s./ha (A12739A)	BBCH 59	39	Cob	< 0.01	< 0.01	MNBA Cob Mean = 103% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) MNBA Kernel Mean = 87% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Cob Mean = 97% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione Kernel Mean = 81% RSD = N/A (n = 2 in 0.01 - 0.02 mg/kg spiking range) Mesotrione (Cob) RAM 366/01, modified Mesotrione (Kernel) RAM 366/01, modified MNBA (Cob) RAM 366/01, modified MNBA (Kernel) RAM 366/01, modified
					39	Kernel	< 0.01	< 0.01	
	Sweet maize (620 Spirit)		153.75 g a.s./ha (A12739A)	BBCH 12	61	Cob	< 0.01	< 0.01	
					61	Kernel	< 0.01	< 0.01	
					74	Cob	< 0.01	< 0.01	
					74	Kernel	< 0.01	< 0.01	

(DBA) Days Before Application
(*) Indicates sample taken prior to last application
(#) Indicates corrected Residue values
(+) Indicates calculated Residue value
(N/A) Not applicable
(^) PHI calculated using cut date

Findings

MRLs for sweet corn have been calculated for northern and southern Europe according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The mesotrione residue values used in the MRL and STMR calculations are dotted underlined in Table 6.3.1-5 and underlined in Table 6.3.2-6. The calculated outputs are presented in Table 6.3.2-7.

Table 6.3.2-7: MRL and STMR calculations for mesotrione on sweet corn – EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	13 x <0.01	0.010	0.01	0.01	0.01
Southern EU	Outdoor	22 x <0.01	0.010	0.01	0.01	0.01

The available data clearly show all mesotrione data from the critical GAP are below the analytical LOQ of 0.01 mg/kg. MNBA residue concentrations are also insignificant. These data support the proposed new definition of residue of mesotrione only (no MNBA metabolite).

CA 6.3.3 Poppy seed

This crop is included to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). Mesotrione is approved for use on poppy seed crops according to the following EU critical GAP, detailed in Table 6.3.3-1.

Table 6.3.3–1: Approved EU critical GAPs for mesotrione on poppy seed

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 16-20	1	NA	0.100	500	80
Southern EU	Outdoor	BBCH 16-20	1	NA	0.100	500	80

NA- not applicable

The residue reports supporting the EU critical GAP for mesotrione on poppy are referenced in Table 6.3.3-2 and the data are presented in Table 6.3.3-4.

Table 6.3.3-2: Report references for trials supporting EU critical GAPs for mesotrione on poppy

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.3/01	(1 of 1)	P Simon	2004	Residues of Mesotrione after Application of A12739A in Poppy Seed, Austria 2003. Syngenta File No. ZA1296/1361, Syngenta Report No. gpp067003

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Four supervised residue trials were conducted on poppy in 2003, in northern Europe. A summary of the trials conducted is presented in Table 6.3.3-3.

Table 6.3.3-3: Summary of mesotrione residue trials on poppy

Northern Europe	
Country	**2003**
Austria	4 Harvest

Poppy seed is a minor crop in northern and southern Europe and therefore generally requires four trials in each residue region (**Document 7525/VI/95 – rev.9, March 2011**).

Treatments with mesotrione were conducted as single spray applications at a late growth stage (BBCH 16-20) as an SC 100 formulation at application rates of 0.100 kg a.s./ha. The water volume used during application was 300 L/ha. Samples of poppy seeds were taken 79 to 90 days after application.

All samples of poppy seeds were analysed for residues of mesotrione and MNBA. The four trials conducted at BBCH 16- 20 in Austria in a single year are sufficient to satisfy the requirements for a minor crop in one region (**Document 7525/VI/95 – rev.9, March 2011 and Commission Regulation (EU) No 283/2013, 1 March 2013**) where non-relevant residues are expected with a high degree of probability.

A minimum PHI of 80 days is proposed for the critical EU GAP for poppy seed crops.

Table 6.3.3-4: Summary of Residue Data Supporting the EU critical GAP for mesotrione on poppy seed

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Northern Europe									
Report: gpp067003 Study: gpp067003 Trial: H-03-A-037-02 - Study to GLP - Study carried out in 2003	Opium poppy (Zeno)	AUSTRIA (Europe North)	100 g a.s./ha (A12739A)	BBCH 16 - 18	89	Seed	<u>< 0.003</u>	< 0.006	MNBA Seed Mean = 100% RSD = 12% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 93% RSD = 5% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
			75 g a.s./ha		89	Seed	< 0.003	< 0.003	
Report: gpp067003 Study: gpp067003 Trial: H-03-A-037-03 - Study to GLP - Study carried out in 2003	Opium poppy (Zeno) A12739A	AUSTRIA (Europe North)	100 g a.s./ha (A12739A)	BBCH 16	79	Seed	<u>< 0.003</u>	< 0.003	MNBA Seed Mean = 100% RSD = 12% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 93% RSD = 5% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
			75 g a.s./ha		79	Seed	< 0.003	< 0.003	
Report: gpp067003 Study: gpp067003 Trial: H-03-A-037-04 - Study to GLP - Study carried out in 2003	Opium poppy (Zeno) A12739A	AUSTRIA (Europe North)	100 g a.s./ha (A12739A)	BBCH 16 - 18	84	Seed	<u>< 0.003</u>	< 0.008	MNBA Seed Mean = 100% RSD = 12% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 93% RSD = 5% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
			75 g a.s./ha		84	Seed	< 0.003	< 0.008	
Report: gpp067003 Study: gpp067003 Trial: H-03-A-037-06 - Study to GLP - Study carried out in 2003	Opium poppy (Zeno) A12739A	AUSTRIA (Europe North)	100 g a.s./ha (A12739A)	BBCH 18 - 20	90	Seed	<u>< 0.003</u>	< 0.003	MNBA Seed Mean = 100% RSD = 12% (n = 8 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 93% RSD = 5% (n = 8 in 0.01 - 0.10 mg/kg spiking range)
			75 g a.s./ha		90	Seed	< 0.003	< 0.003	

DBA) Days Before Application
(*) Indicates sample taken prior to last application
(#) Indicates corrected Residue values
(+) Indicates calculated Residue value
(N/A) Not applicable
Underlined values represent those values considered appropriate to support the cGAP for Poppy Seeds

Findings

MRLs for poppy seed have been calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The mesotrione residue values used in the MRL and STMR calculations are underlined in Table 6.3.3-4. The calculated outputs are presented in Table 6.3.3-5.

Table 6.3.3-5: MRL and STMR calculations for mesotrione on poppy seed – EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	4 x <0.003	0.010	0.01	0.003	0.003

The available data clearly show all mesotrione data from the critical GAP are below the analytical LOQ of 0.003 mg/kg and therefore below the default MRL level of 0.01 mg/kg. MNBA residue concentrations are also insignificant, being below the analytical LOQs employed of 0.003, 0.006 or 0.008 mg/kg. These data support the proposed new definition of residue of mesotrione only (no MNBA metabolite).

CA 6.3.4 Linseed

This crop is included to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). Mesotrione is approved for use on linseed crops according to the following EU critical GAP, detailed in Table 6.3.4-1.

Table 6.3.4–1: Approved EU critical GAPs for mesotrione on linseed

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 16-19	1	NA	0.150	300	NR

NA - Not applicable
NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

The residue reports supporting the EU critical GAP for mesotrione on linseed are referenced in Table 6.3.4-2 and the data are presented in Table 6.3.4-4.

Table 6.3.4-2: Report references for trials supporting EU critical GAPs for mesotrione on linseed

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.4/01	(1 of 1)	P Simon	2004	Residues of Mesotrione after application of A12739A in Linseed, Germany 2003 Syngenta File No. ZA1296/1360, Syngenta Report No. gli058003

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Four supervised residue trials were conducted on linseed rape in 2003, in northern Europe. A summary of the trials conducted is presented in Table 6.3.4-3.

Table 6.3.4-3: Summary of mesotrione residue trials on linseed

Northern Europe	
Country	**2003**
Germany	4 Harvest

Linseed is a very minor crop in northern Europe and therefore generally requires four trials in each residue zone region (**Document 7525/VI/95 – rev.9, March 2011**).

Treatments with mesotrione were conducted as single applications at early post emergence growth stage (BBCH 03-05) as an SC 100 formulation at application rates of 0.150 kg a.s./ha. The water volume used during application ranged from 282 to 294 L/ha. Samples of seed were taken 128 to 144 days after application. The application timings in these trials are earlier than the approved GAP, however the data are appropriate for the purpose of supporting the proposed new definition of residue, mesotrione only.

All samples were analysed for residues of mesotrione and MNBA. The four trials conducted in northern Europe over a single season are sufficient to satisfy the requirements for a very minor crop where non-relevant residues are expected with a high degree of probability (**Document 7525/VI/95 – rev.9, March 2011 and Commission Regulation (EU) No 283/2013, 1 March 2013**). Application rates in all trials cover the critical EU GAP.

No PHI is proposed in the critical EU GAP since the application is made pre- or early post-emergence and linseed is harvested at maturity.

Table 6.3.4-4 Summary of Residue Data Supporting the EU critical GAP for mesotrione on linseed

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Northern Europe									
Report: gli058003 Study: gli058003 Trial: FR02/03/60 - Study conducted to GLP - Study carried out in 2003 (F)	Linseed (Lirina)	GERMANY (Europe North)	150 g a.s./ha (A12739A)	BBCH 05	131	Seed	< 0.003	< 0.003	MNBA Seed Mean = 103% RSD = 12% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 94% RSD = 11% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Seed) RAM 366/01, modified MNBA (Seed) RAM 366/01, modified
Report: gli058003 Study: gli058003 Trial: FR02/03/40 - Study conducted to GLP - Study carried out in 2003 (F)	Linseed (Flanders)	GERMANY (Europe North)	150 g a.s./ha (A12739A)	BBCH 03	133	Seed	< 0.003	< 0.003	MNBA Seed Mean = 103% RSD = 12% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 94% RSD = 11% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Seed) RAM 366/01, modified MNBA (Seed) RAM 366/01, modified
Report: gli058003 Study: gli058003 Trial: FR02/03/41 - Study conducted to GLP - Study carried out in 2003 (F)	Linseed (Lirina)	GERMANY (Europe North)	150 g a.s./ha (A12739A)	BBCH 05	128	Seed	< 0.003	< 0.003	MNBA Seed Mean = 103% RSD = 12% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 94% RSD = 11% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Seed) RAM 366/01, modified MNBA (Seed) RAM 366/01, modified
Report: gli058003 Study: gli058003 Trial: FR02/03/50 - Study conducted to GLP - Study carried out in 2003 (F)	Linseed (Lirina)	GERMANY (Europe North)	150 g a.s./ha (A12739A)	BBCH 03 BBCH 05	144	Seed	< 0.003	< 0.003	MNBA Seed Mean = 103% RSD = 12% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 94% RSD = 11% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Mesotrione (Seed) RAM 366/01, modified MNBA (Seed) RAM 366/01, modified

(DBA) Days Before Application
(*) Indicates sample taken prior to last application
(#) Indicates corrected Residue values
(+) Indicates calculated Residue value
(N/A) Not applicable
(^) PHI calculated using cut date

Findings

MRLs for linseed have been calculated for northern Europe according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The mesotrione residue values used in the MRL and STMR calculations are underlined in Table 6.3.4-4. The calculated outputs are presented in Table 6.3.4-5.

Table 6.3.4-5: MRL and STMR calculations for mesotrione on linseed – EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	4 x <0.003	0.010	0.01	0.003	0.003

The available data clearly show all mesotrione data from the critical GAP are below the analytical LOQ of 0.003 mg/kg and therefore below the default MRL level of 0.01 mg/kg. MNBA residue concentrations are also insignificant, being below the analytical LOQ of 0.003 mg/kg. These data support the proposed new definition of residue of mesotrione only (no MNBA metabolite).

CA 6.3.5 Oilseed rape

This crop is included to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). Mesotrione is proposed for use on oilseed rape crops according to the following EU critical GAP, detailed in Table 6.3.5-1.

Table 6.3.5–1: Proposed EU critical GAPs for mesotrione on oilseed rape

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 16-19	2	21	0.015	500	NR
Southern EU	Outdoor	BBCH 16-19	2	21	0.015	500	NR

NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

The residue reports supporting the EU critical GAP for mesotrione on oilseed rape are referenced in Table 6.3.5-2 and the data are presented in Table 6.3.5-4.

Table 6.3.5-2: Report references for trials supporting EU critical GAPs for mesotrione on oilseed rape

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.5/01	(1 of 2)	Malet J-C, Allard L	2010	Residues of mesotrione, after 2 applications of CALLISTO in fodder colza in support of the registration for minor crops. Syngenta Report No. RXCO00307, Syngenta File No. ZA1296_10054
KCA 6.3.5/02	(2 of 2)	Malet J-C, Allard L	2010	Residues of mesotrione, after 2 applications of CALLISTO in fodder colza in support of the registration for minor crops. Syngenta Report No. RXCO00608, Syngenta File No. ZA1296_10053

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Eight supervised residue trials were conducted on oilseed rape in 2006 or 2007, in northern and southern Europe. A summary of the trials conducted is presented in Table 6.3.5-3.

Table 6.3.5-3: Summary of mesotrione residue trials on oilseed rape

Northern Europe		
Country	**2006**	**2007**
France (North)	1 Harvest	3 Harvest
Southern Europe		
Country	**2006**	**2007**
France (South)	2 Harvest	2 Harvest

Oilseed rape is a major crop in northern and southern Europe and therefore generally requires eight trials in each residue zone region (**Document 7525/VI/95 – rev.9, March 2011**).

Treatments with mesotrione were conducted as two spray applications at early post emergence growth stage (BBCH 16-19) as an SC 100 formulation at application rates of 0.014 or 0.015 kg a.s./ha. The water volume used during application ranged from 230 to 510 L/ha. Samples of oilseed rape seeds and remaining plant were taken 197 to 231 days after application.

All samples were analysed for residues of mesotrione and MNBA. The eight trials conducted in northern and southern Europe (four per region) over two years are sufficient to satisfy the requirements for a major crop where non-relevant residues are expected with a high degree of probability (**Document 7525/VI/95 – rev.9, March 2011 and Commission Regulation (EU) No 283/2013, 1 March 2013**). Allowing for a 25% deviation from the proposed maximum application rate, rates in all trials cover the critical EU GAP.

No PHI is proposed in the critical EU GAP since the application is made early post-emergence and oil seed rape is harvested at maturity.

Table 6.3.5-4 Summary of Residue Data Supporting the EU critical GAP for mesotrione on oilseed rape

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Northern Europe									
Report: RXCO00307 Study: RXCO00307 Trial: RE07003 - Study to GLP - Study carried out in 2006	Rape (Astrid)	FRANCE (Europe North)	15 g a.s./ha 14 g a.s./ha (A12739A)	BBCH 16 BBCH 17 - 18	231	Seed	< 0.01	< 0.01	Mesotrione Plant Mean = 73% RSD = 4% (n = 10 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 77% RSD = 6% (n = 10 in 0.01 - 0.10 mg/kg spiking range) MNBA Seed Mean = 68% RSD = 9% (n = 10 in 0.01 - 0.10 mg/kg spiking range)
					231	Plant	< 0.01	< 0.01	
Report: RXCO00608 Study: RXCO00608 Trial: RE08013 - Study to GLP - Study carried out in 2007	Rape (Catalina)	FRANCE (Europe North)	15 g a.s./ha 14 g a.s./ha (A12739A)	BBCH 16 BBCH 16	210	Seed	< 0.01	< 0.01	Mesotrione Seed Mean = 81% RSD = N?A (n = 1 at 0.01 mg/kg spiking) MNBA Seed Mean = 62% RSD = N/A% (n = 1 at 0.01 mg/kg spiking)
Report: RXCO00608 Study: RXCO00608 Trial: RE08014 - Study to GLP - Study carried out in 2007	Rape (Catalina)	FRANCE (Europe North)	15 g a.s./ha 15 g a.s./ha (A12739A)	BBCH 17 BBCH 17	216	Seed	< 0.01	< 0.01	Mesotrione Seed Mean = 81% RSD = N?A (n = 1 at 0.01 mg/kg spiking) MNBA Seed Mean = 62% RSD = N/A% (n = 1 at 0.01 mg/kg spiking)
Report: RXCO00608 Study: RXCO00608 Trial: RE08015 - Study to GLP - Study carried out in 2007	Rape (Mendel)	FRANCE (Europe North)	15 g a.s./ha 14 g a.s./ha (A12739A)	BBCH 16 BBCH 17	210	Seed	< 0.01	< 0.01	Mesotrione Seed Mean = 81% RSD = N?A (n = 1 at 0.01 mg/kg spiking) MNBA Seed Mean = 62% RSD = N/A% (n = 1 at 0.01 mg/kg spiking)
Southern Europe									
Report: RXCO00307 Study: RXCO00307 Trial: RE07002 - Study to GLP - Study carried out in 2006	Rape (Corail) A12739A	FRANCE (Europe South)	15 g a.s./ha 14 g a.s./ha (A12739A)	BBCH 16 BBCH 18 - 19	226	Seed	< 0.01	< 0.01	Mesotrione Plant Mean = 73% RSD = 4% (n = 10 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 77% RSD = 6% (n = 10 in 0.01 - 0.10 mg/kg spiking range) MNBA Seed Mean = 68% RSD = 9% (n = 10 in 0.01 - 0.10 mg/kg spiking range)
Report: RXCO00307 Study: RXCO00307 Trial: RE07001 - Study to GLP - Study carried out in 2006	Rape (-)	FRANCE (Europe South)	15 g a.s./ha 15 g a.s./ha (A12739A)	BBCH 16 BBCH 16 - 19	216	Seed	< 0.01	< 0.01	Mesotrione Plant Mean = 73% RSD = 4% (n = 10 in 0.01 - 0.10 mg/kg spiking range) Mesotrione Seed Mean = 77% RSD = 6% (n = 10 in 0.01 - 0.10 mg/kg spiking range) MNBA Seed Mean = 68% RSD = 9% (n = 10 in 0.01 - 0.10 mg/kg spiking range)
Report: RXCO00608 Study: RXCO00608 Trial: RE08016 - Study to GLP - Study carried out in 2007	Rape (Vectra)	FRANCE (Europe South)	15 g a.s./ha 15 g a.s./ha (A12739A)	BBCH 18 BBCH 19	218	Seed	< 0.01	< 0.01	Mesotrione Seed Mean = 81% RSD = N?A (n = 1 at 0.01 mg/kg spiking) MNBA Seed Mean = 62% RSD = N/A% (n = 1 at 0.01 mg/kg spiking)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: RXCO00608 Study: RXCO00608 Trial: RE08015 - Study to GLP - Study carried out in 2007	Rape (Hibridstar)	FRANCE (Europe South)	15 g a.s./ha 15 g a.s./ha (A12739A)	BBCH 16 BBCH 19	197	Seed	<u>< 0.01</u>	< 0.01	Mesotrione Seed Mean = 81% RSD = N?A (n = 1 at 0.01 mg/kg spiking) MNBA Seed Mean = 62% RSD = N/A% (n = 1 at 0.01 mg/kg spiking)

(DBA) Days Before Application
(*) Indicates sample taken prior to last application
(#) Indicates corrected Residue values
(+) Indicates calculated Residue value
(N/A) Not applicable
Underlined values represent those values considered appropriate to support the cGAP for Oil Seed Rape

Findings

MRLs for oilseed rape have been calculated for northern Europe according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The mesotrione residue values used in the MRL and STMR calculations are underlined in Table 6.3.5-4. The calculated outputs are presented in Table 6.3.5-5.

Table 6.3.5-5: MRL and STMR calculations for mesotrione on oilseed rape – EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	4 x <0.01	0.010	0.01	0.01	0.01
Southern EU	Outdoor	4 x <0.01	0.010	0.01	0.01	0.01
Combined	Outdoor	8 x <0.01	0.010	0.01	0.01	0.01

The available data clearly show all mesotrione data from the critical GAP are below the analytical LOQ of 0.01 mg/kg. MNBA residue concentrations are also insignificant, being below the analytical LOQ of 0.01 mg/kg. These data support the proposed new definition of residue of mesotrione only (no MNBA metabolite).

CA 6.3.6 HT soya bean

This crop is included to demonstrate the residue levels of MNBA in support of the proposed new definition of residue, mesotrione only (see Section CA 6.7). Mesotrione is proposed for use on herbicide tolerant (HT) soya bean crops according to the following global critical GAP, detailed in Table 6.3.6-1.

Table 6.3.6–1: Global critical GAPs for mesotrione on HT soya bean

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
USA	Outdoor	BBCH 00-60	2	Defined by growth stage	0.225 0.125	100-200	NR
USA	Outdoor	BBCH 12	1	NA	0.225	100-200	NR

NA - Not applicable
NR – not relevant. Last application is made before the consumable part of the crop has formed and crops harvested at maturity

The residue reports supporting the global critical GAP for mesotrione on HT soya bean are referenced in Table 6.3.6-2 and the data are presented in Table 6.3.6-4.

Table 6.3.6-2: Report references for trials supporting global critical GAPs for mesotrione on HT soya bean

Annex Pt.	Number.	Author/s	Issue Year	Report Title
KCA 6.3.6/01	(1 of 1)	Oakes, T.	2012	Mesotrione: Mesotrione SC (A12738A) – Magnitude of the Residues in or on Mesotrione Tolerant Soybean, Syngenta File No. A12738A_50039, Syngenta Report No. T000908-07

Guidelines

The listed reports generally meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are also compatible with OECD Guideline for the Testing of Chemicals, Crop Field Trial (**OECD 509, 07/09/2009**).

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of GLP.

Materials and Methods

Twenty supervised residue trials were conducted on HT soya bean in 2009, in the USA. A summary of the trials conducted is presented in Table 6.3.6-3.

Table 6.3.6-3: Summary of mesotrione residue trials on HT soya bean

USA	
Country	**2009**
USA EPA region 2	1 Harvest
USA EPA region 4	3 Harvest
USA EPA region 5	16 Harvest

Soya bean is a major crop in the USA. To provide data to support the proposed new definition of residue, mesotrione only, more than eight trials in the USA region are presented here which is consistent with EU requirements (**Document 7525/VI/95 – rev.9, March 2011**).

Treatments with mesotrione were conducted as either a double pre-emergence and post emergence applications (BBCH 00 and BBCH 16-63) or as a single early post-emergence application (BBCH 12). Treatments were made using an SC 480 formulation at application rates of 0.225 kg a.s./ha for the first or single application and 0.125 kg a.s./ha for plots receiving a second application. The water volume used during applications ranged from 116 to 277 L/ha for pre-emergence and 145 to 223 L/ha for the second post-emergence treatment. Plots receiving a single post-emergence application received water volumes from 54 to 232 L/ha. Samples of soya bean seed were taken 45 to 151 days after single or final application. At two trials additional plots were conducted at exaggerated application rates up to 1.147 kg a.s./ha to produce samples for processing.

All samples were analysed for residues of mesotrione and MNBA. All twenty trials conducted in the USA over a single season are sufficient to support the EU requirements for a major crop where non-relevant residues are usually expected with a high degree of probability (**Document 7525/VI/95 – rev.9, March 2011 and Commission Regulation (EU) No 283/2013, 1 March 2013**). Allowing for a 25% deviation from the proposed maximum application rate, rates in all trials cover the critical global GAP. These data from trials outside of the EU are appropriate to support the proposed new definition of residue, mesotrione only.

No PHI is proposed in the critical global GAP since the application is made pre- or early post-emergence and soya beans are harvested at maturity. PHI is dependent on growth stage and time to reach maturity.

Table 6.3.6-4 Summary of Residue Data Supporting the global critical GAP (USA) for mesotrione on HT soya bean

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
USA									
Report: T000908-07 Study: ML10-1620-SYN Trial: E11-9652 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 2)	226 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 60 (R1)	89	seed (m)	<u><0.01</u>	<0.01	Procedural recoveries: Mesotrione in soya bean seed: Mean = 85%; RSD = 13; n = 42 Spiking range = 0.01 - 0.10 mg/kg Mesotrione RAM 366/01, modified Maximum storage periods: Seed: 13.4 months Fractions: 4.0 months
			225 g a.s./ha (A12738A)	BBCH 14 (V2)	98	seed (m)	<0.01	<0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C24-9653 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 4)	226 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 60	50 76	seed seed (m)	<0.01 <u><0.01</u>	<0.01 <0.01	
			226 g a.s./ha (A12738A)	BBCH 14 (V2)	59 79 85 92 99	seed seed (-7d) seed (m) seed (+7d) seed (+14d)	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: E18-9654 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 4)	234 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 61	45	seed (m)	<u>0.01</u>	<0.01	
			234 g a.s./ha (A12738A)	BBCH 12	66	seed (m)	<0.01	<0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C23-9655 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 4)	225 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 63	49 58	seed seed (m)	0.01 <u>0.02</u>	<0.01 <0.01	
			226 g a.s./ha 124 g a.s./ha (A12738A)	BBCH 00 BBCH 63	49 58	seed seed (m)	0.01 0.02	<0.01 <0.01	
			225 (A12738A g a.s./ha)	BBCH 12	67 76	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C18-9656 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	226 g a.s./ha 126 g a.s./ha (A12738A)	BBCH 00 BBCH 16	48 102	seed seed (m)	<0.01 <u><0.01</u>	<0.01 <0.01	
			222 g a.s./ha (A12738A)	BBCH 12.5	97 151	seed seed (m)	<0.01 <0.01	<0.01 <0.01	Procedural recoveries: Mesotrione in soya bean seed:

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
			1130 g a.s./ha 623 g a.s./ha (A12738A)	BBCH 00 BBCH 16	102	seed (m) meal hulls crude oil refine oil AGF flour milk tofu soy sauce miso	<0.01 <0.01 <0.01 <0.01 0.01 <0.01 0.02 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.001 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	Mean = 85%; RSD = 13; n = 42 Spiking range = 0.01 - 0.10 mg/kg Mesotrione in soya bean meal: Mean = 97%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean hulls: Mean = 86%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean crude oil: Mean = 95%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean refined oil: Mean = 96%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean AGF: Mean = 78%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean flour: Mean = 91%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean milk: Mean = 89%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean Tofu: Mean = 84%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean soy sauce: Mean = 77%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean miso: Mean = 88%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg
Report: T000908-07 Study: ML10-1620-SYN Trial: C18-0657 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	228 g a.s./ha 123 g a.s./ha (A12738A)	BBCH 00 BBCH 18	45 85	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			224 g a.s./ha (A12738A)	BBCH 12	66 106	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C18-0658 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	227 g a.s./ha 122 g a.s./ha (A12738A)	BBCH 00 BBCH 59	47 90	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			223 g a.s./ha (A12738A)	BBCH 12	73 116	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C30-9659 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	226 g a.s./ha 117 g a.s./ha (A12738A)	BBCH 00 BBCH 63	45 76	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			222 g a.s./ha (A12738A)	BBCH 12	77 108	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			1147 g a.s./ha 640 g a.s./ha (A12738A)	BBCH 00 BBCH 63	76	seed (m) meal hulls crude oil refine oil AGF flour milk tofu	0.04 0.01 0.01, 0.02 <0.01 <0.01 0.02 0.07 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.001 <0.01 <0.01 <0.01 <0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
						soy sauce miso	<0.01 <0.01	<0.01 <0.01	Procedural recoveries: Mesotrione in soya bean seed: Mean = 85%; RSD = 13; n = 42 Spiking range = 0.01 - 0.10 mg/kg Mesotrione in soya bean meal: Mean = 97%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean hulls: Mean = 86%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean crude oil: Mean = 95%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean refined oil: Mean = 96%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean AGF: Mean = 78%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean flour: Mean = 91%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean milk: Mean = 89%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean Tofu: Mean = 84%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean soy sauce: Mean = 77%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg Mesotrione in soya bean miso: Mean = 88%; RSD = n/a; n = 2 Spiking range = 0.01 - 1.0 mg/kg
Report: T000908-07 Study: ML10-1620-SYN Trial: C30-9660 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	233 g a.s./ha 118 g a.s./ha (A12738A)	BBCH 00 BBCH 63	43 75	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			224 g a.s./ha (A12738A)	BBCH 12	70 102	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C19-9661 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	226 g a.s./ha 121 g a.s./ha (A12738A)	BBCH 00 R1-R2	47 69	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			225 g a.s./ha (A12738A)	2nd Trifoliate	82 93 104 110 117	seed seed (-7d) seed (m) seed (+7d) seed (+14d)	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C19-9662 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	230 g a.s./ha 121 g a.s./ha (A12738A)	BBCH 00 BBCH 60 (R1-R2)	47 70	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			229 g a.s./ha (A12738A)	Mostly 2nd Trifoliate, Occasional 1st	76 99	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C03-9663 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	224 g a.s./ha 124 g a.s./ha (A12738A)	BBCH 00 BBCH 60 (V8,R1)	45 76	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			225 g a.s./ha (A12738A)	BBCH 14 (V2)	81 112	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C23-9664 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	228 g a.s./ha 128 g a.s./ha (A12738A)	BBCH 00 BBCH 61	47 55	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			223 g a.s./ha (A12738A)	BBCH 12	64 72	seed seed (m)	<0.01 <0.01	<0.01 <0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: T000908-07 Study: ML10-1620-SYN Trial: E13-9665 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	228 g a.s./ha 123 g a.s./ha (A12738A)	BBCH 00 BBCH 61	46 85	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			227 g a.s./ha (A12738A)	BBCH 12	76 115	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: E13-9666 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	225 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 61	48 94	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			231 g a.s./ha (A12738A)	BBCH 12	83 129	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: E13-9667 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	219 g a.s./ha 123 g a.s./ha (A12738A)	BBCH 00[5] BBCH 61	49 86	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			230 g a.s./ha (A12738A)	BBCH 12	76 113	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C01-9668 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	227 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 61	47 87	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			226 g a.s./ha (A12738A)	BBCH 12	66 106	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: C01-9669 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	227 g a.s./ha 124 g a.s./ha (A12738A)	BBCH 00 BBCH 61	47 87	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			230 g a.s./ha (A12738A)	BBCH 12	67 107	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
Report: T000908-07 Study: ML10-1620-SYN Trial: E19-9670 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack/ SYHT04R	USA (EPA region 5)	222 g a.s./ha 126 g a.s./ha (A12738A)	BBCH 00 BBCH 61	46 123	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			231 g a.s./ha (A12738A)	BBCH 12	68 145	seed seed (m)	<0.01 <0.01	<0.01 <0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (Product Code)	Growth Stage at application	PHI (days)	Crop Part	Residue Found (Uncorrected)		Recovery Data
							mesotrione mg/kg	MNBA mg/kg	
Report: T000908-07 Study: ML10-1620-SYN Trial: E10-9671 - Study to GLP - Study carried out in 2009	GM Soya bean/ Jack	USA (EPA region 2)	226 g a.s./ha 125 g a.s./ha (A12738A)	BBCH 00 BBCH 62	50 79	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
			223 g a.s./ha (A12738A)	BBCH 13	67 96	seed seed (m)	<0.01 <0.01	<0.01 <0.01	
(m) denotes mature seed (earliest normal harvest)									

Findings

MRLs for HT soya bean have been calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO(2011)2, 1 March 2011**) using the proposed new definition of residue for mesotrione only. The STMR is the median residue, and the HR is the highest residue value found. In these calculations a single data point from each trial supporting the global critical GAP (USA) has been considered. The mesotrione residue values used in the MRL and STMR calculations are underlined in Table 6.3.6-4. The calculated outputs are presented in Table 6.3.6-5.

Table 6.3.6-5: MRL and STMR calculations for mesotrione on HT soya bean – global GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
USA	Outdoor	18 x <0.01, 0.01, 0.02	0.020	0.02	0.01	0.02

The available data clearly show that the majority of mesotrione data values from the GAP for are below the analytical LOQ of 0.01 mg/kg with just two trials showing mesotrione residues at or just above the LOQ. All samples showed MNBA residues below the analytical LOQ of 0.01 mg/kg. These data support the proposed new definition of residue of mesotrione only (no MNBA metabolite).

CA 6.4 Feeding Studies

Dietary burden calculations

It is an EU data requirement (**Commission Regulation (EU) No 283/2013, 1 March 2013**) and guideline requirement (**OECD 505, Residues in Livestock**) to estimate the dietary intakes for poultry, dairy cattle, beef cattle and pigs if residues are likely in crops or part of crops fed to animals.

The potential dietary exposure to mesotrione residues in the supported representative crop of maize or its processed products has been calculated using the EU methodologies described. According to available guidance, for the crops considered in the current document, only products from maize as grain or forage items (silage) may form a part of livestock diets. As shown in Section CA 6.3.1 of this document, residues in maize silage following treatment at the EU GAP for mesotrione are all below the LOQ (0.01 mg/kg). Therefore it is very unlikely that any significant residues would occur in commercial livestock diet, however to demonstrate this according to the accepted EU procedure the dietary burden has been estimated here.

The dietary inputs into the calculation are summarised in Table CA 6.4-1. The highest residues in supervised trials (HR) are used to calculate the maximum potential dietary intake except for feed commodities that are bulked, where the STMR is used, or processed, where the STMR-P is used, as detailed in Table 6.4-1.

Table 6.4-1: Mesotrione residue values used for calculation of livestock dietary burdens

Commodity	Crop Group[1]	STMR (mg/kg)	Processing factor	STMR-P (mg/kg)	HR (mg/kg)	Origin
Maize forage	I Green forages	0.01	NA	-	0.01	Residue data in CA 6.3.1
Maize grain	II Grains	0.01	NA	-	0.01	Residue data in CA 6.3.1

1 - As defined in EU Doc. 7031/VI/95 rev.4; 22/7/96

Table 6.4-2 to Table 6.4-5 contain details of the exposure calculations for mesotrione in dairy ruminants, meat ruminants, poultry and pigs.

Table 6.4-2: Dietary Burden of Dairy Ruminants

Bodyweight (kg): 550

Daily Maximum Feed (kg dry matter): 20

Maximum dietary burden (mg/kg bw/day):	**0.001818**
Maximum dietary burden (mg/kg feed DM):	0.050000
Highest contributing commodity:	Maize silage
Median dietary burden (mg/kg bw/day):	0.001818
Median dietary burden (mg/kg feed DM):	0.050000
Highest contributing commodity:	Maize silage

DM – dry matter; bw – body weight

Table 6.4-3: Dietary Burden of Meat Ruminants

Bodyweight (kg): 550

Daily Maximum Feed (kg dry matter): 20

Maximum dietary burden (mg/kg bw/day):	**0.002143**
Maximum dietary burden (mg/kg feed DM):	0.050000
Highest contributing commodity:	Maize silage
Median dietary burden (mg/kg bw/day):	0.002143
Median dietary burden (mg/kg feed DM):	0.050000
Highest contributing commodity:	Maize silage

DM – dry matter; bw – body weight

Table 6.4-4: Dietary Burden of Poultry

Bodyweight (kg): 550

Daily Maximum Feed (kg dry matter): 20

Maximum dietary burden (mg/kg bw/day):	**0.000514**
Maximum dietary burden (mg/kg feed DM):	0.008140
Highest contributing commodity:	Maize grain
Median dietary burden (mg/kg bw/day):	0.000514
Median dietary burden (mg/kg feed DM):	0.008140
Highest contributing commodity:	Maize grain

DM – dry matter; bw – body weight

Table 6.4-5: Dietary Burden of Pigs

Bodyweight (kg): 550

Daily Maximum Feed (kg dry matter): 20

Maximum dietary burden (mg/kg bw/day):	**0.000486**
Maximum dietary burden (mg/kg feed DM):	0.012151
Highest contributing commodity:	Maize silage
Median dietary burden (mg/kg bw/day):	0.000486
Median dietary burden (mg/kg feed DM):	0.012151
Highest contributing commodity:	Maize silage

DM – dry matter; bw – body weight

CA 6.4.1 Poultry

Calculated only for the supported crop use in this submission, the maximum dietary burden of mesotrione in poultry is shown to be not relevant (<0.004 mg/kg bw/day). Therefore, a residue transfer study with mesotrione in poultry is not required.

CA 6.4.2 Ruminants

Calculated only for the supported crop use in this submission, the maximum dietary burden of mesotrione in ruminants is shown to be not relevant (<0.004 mg/kg bw/day). Therefore, a residue transfer study with mesotrione in ruminants is not required.

CA 6.4.3 Pigs

Calculated only for the supported crop use in this submission, the maximum dietary burden of mesotrione in pigs is shown to be not relevant (<0.004 mg/kg bw/day). Therefore, a residue transfer study with mesotrione in pigs is not required.

CA 6.4.4 Fish

According to guideline SANCO/11187/2013, 31 January 2013 rev. 3 there is no requirement to consider the possible fish metabolism of mesotrione as its log Pow is <3. In addition, from the uses of mesotrione and the magnitude of residues (all <0.01 mg/kg) it can be expected that there is no potential for significant residues in commercial fish diet.

CA 6.5 Effects of Processing

Processing studies are not necessary as no significant or analytically determinable residues (i.e. greater than 0.1 mg/kg) occur in the crops considered in this submission and the total theoretical maximum daily intake (TMDI) is calculated to be less than <10% of the ADI.

CA 6.5.1 Nature of the residue

Residues in the Raw Agricultural Commodity are <0.01 mg/kg. Therefore, since no significant residues occur in any relevant commodity, no studies are required for the renewal of approval on the nature of residue.

CA 6.5.2 Distribution of the residue in inedible peel and pulp

There are no crops in this submission for which distribution of the residues in peel/pulp is relevant.

CA 6.5.3 Magnitude of residues in processed commodities

The proposed uses of mesotrione in maize will not give rise to residues in the grain above 0.01 mg/kg. Since no significant residues occur in any relevant commodity and the total theoretical maximum daily intake (TMDI) is calculated to be less than <10% of the ADI, no studies are required for the renewal of approval.

CA 6.6 Residues in Rotational Crops

Succeeding crop studies are deemed unnecessary as the rate of degradation in soil is rapid - DT_{90} from field soil dissipation studies is less than 100 days (**DT_{90f}: 36-78 days. SANCO/1416/2001 – Final, 14 April 2003**). Additionally, residue decline trials showed a significant decrease of residues in maize with

time (Section CA 6.3.1); residues of mesotrione were close to or below the limit of quantification within 14 days after application.

However, two separate confined rotational crop studies were conducted using [^{14}C] labelled mesotrione. These studies were in the original approval evaluation for Europe (Monograph) and are summarised below for information.

CA 6.6.1 Metabolism in rotational crops

Two separate confined rotational crop studies were conducted using [^{14}C] labelled mesotrione labelled in either the cyclohexane or phenyl ring to address the potential uptake and metabolism of mesotrione residues into succeeding or rotated crops following an application to the primary crop.

The following data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.1.3, December 1999**).

Confined/Outdoor	Author/s	Issue Year	Report Number
Confined	Spillner C, Bowler D, Diaz D	1997	IIA 6.6.2/01 (ZA1296/0427)
Confined	Gorder G.W, Cheung A.C, Bowler D.T, Schwab G	1997	IIA 6.6.2/02 (ZA1296/0428)

Executive Summary

Two confined accumulation studies on rotational crops were carried out using mesotrione [^{14}C] radiolabelled at both relevant substructures ([cyclohexane-2-^{14}C] mesotrione and [phenyl-U-^{14}C] mesotrione). Wheat (*Triticum aestivum*), endive (*Cichorium endiva*), and radish (*Raphanus sativus*) were used as test commodities. [^{14}C]-mesotrione was applied at a nominal rate of 165 g a.s./ha to bare soil in pots. The studies were carried out under greenhouse conditions. Wheat, endive, and radish were planted at 120 and 300 days after treatment. Harvested crops were separated into raw agricultural commodities (RAC).

RACs were combusted, extracted, and analysed. Residues >0.01 mg/kg were characterised and quantified using HPLC and reference compounds.

The total radioactive residues in relevant commodities of crops planted 120 days after treatment were low (<0.05 mg/kg for the parts used for animal feeds and ≤0.01 mg/kg for those parts used for human food). Thus, samples of crops planted 300 days after treatment were not analysed. In all crops at each interval analysed, the metabolism of mesotrione was similar. The parent compound mesotrione and its metabolites MNBA and AMBA were <0.01 mg/kg with the exception of MNBA in forage (0.011 mg/kg).

The results indicated that mesotrione was metabolised to MNBA and AMBA. This pathway is similar to the pathway in primary crops.

CA 6.6.2 Magnitude of residues in rotational crops

A limited crop rotation study was conducted to address the residue situation of mesotrione in succeeding or rotated crops under field conditions.

The following data were evaluated under Council Directive 91/414/EEC and are presented in the mesotrione monograph (**Vol.3, Annex B, Section B.7.10, December 1999**).

Confined/Outdoor	Author/s	Issue Year	Report Number
Outdoor	Barnes J.P, Wiebe L.A	1997	IIA 6.6.2/01 (ZA1296/0429)

Executive Summary:

A crop rotation study was carried out under field conditions in the USA during 1995/1996 using soya beans, endive, radish, millet, winter wheat, and sorghum as succeeding crops. Mesotrione was applied at rates of 337 g a.s./ha for the 30 day plant back interval and 562 g a.s./ha for the 100 and 300 day plant back intervals. These rates are more than 3x higher than the EU critical GAP for maize.

Samples were taken at normal harvest and analysed for mesotrione and its metabolite, MNBA. Residues of mesotrione and MNBA were found to be below the limit of quantification (<0.01 mg/kg).

Summary of residues in succeeding crops

Metabolism studies in rotational crops showed that the metabolic pathway in primary and succeeding crops is essentially the same: mesotrione was metabolised to MNBA which is further reduced to AMBA.

Under field conditions, no significant residues of mesotrione or MNBA were found in rotated crops even after application at levels at least twice the proposed critical EU GAP.

These results are consistent with the conclusions that additional field studies in succeeding crops are not required due the low soil DT_{90f} value (<100 days) for mesotrione and its rapid decline observed in crop residue field studies.

CA 6.7 Proposed Residue Definitions and Maximum Residue Levels

CA 6.7.1 Proposed residue definitions

Crops

The existing agreed residue definition in plants in the EU is the sum of mesotrione and MNBA (4-methylsulfonyl-2-nitro benzoic acid), expressed as mesotrione, for both risk assessment and monitoring. However, in the United States and Japan the DoR for crops for both risk assessment and monitoring is mesotrione only. To simplify analysis by the use of a new multiresidue method for mesotrione for enforcement purposes, the monitoring DoR position is proposed as mesotrione only. In addition a body of data in many crops, maize, sweetcorn, poppy seed, linseed, oilseed rape and herbicide tolerant soya bean show no residues of MNBA above 0.01 mg/kg thus, the current DoR position for risk assessment of including MNBA for crops in Europe is revisited and a new ‘global’ DoR proposal is made.

The definition of the residue for monitoring and for risk assessment of mesotrione in crops has been evaluated in the light of data generated from primary crop metabolism studies, confined rotational crop studies, field residue trials, field rotational crop studies and toxicological data on selected metabolites.

The metabolism of mesotrione was investigated in maize, Herbicide Tolerant (HT) soybeans, and peanuts at or above the GAP used in the field. Little or no mesotrione was detected in maize grain, peanut meat or HT soya seed (0.001-0-006 mg/kg), nor in feed items from the unmodified crops (<0.0005 - 0.001 mg/kg). Higher amounts of mesotrione were measured in the feed items from HT soya bean, at 0.002-0.178 mg/kg dependent on the use pattern. However, commodities for animal feed are not included on the label for the use of mesotrione on HT soya crops and thus will not be used for animal feed.

The metabolism of mesotrione was extensive in all crops and proceeded via the same routes, primarily through either hydroxylation of the cyclohexanedione ring or by cleavage to form the metabolite MNBA (4-methylsulfonyl-2-nitro benzoic acid), which was further reduced to AMBA (2-amino-4-methylsulfonyl benzoic acid). These metabolites were also present as conjugates. Evidence of incorporation of radioactive residues from further breakdown of the metabolites into natural products (lignin, cellulose, sugars etc.) was seen in all crops.

The TRR and residues of AMBA in animal feed items from maize were both above 10% TRR and 0.01 mg/kg (maize fodder 28.2% TRR (0.301 mg/kg). To assess if AMBA residues in the animal feed would result in residues in edible animal commodities, a cow metabolism study was conducted with AMBA at 60X the anticipated dietary burden (DB) and showed no or very low residues in any edible animal commodities. Thus, at the anticipated dietary burden, AMBA residues in animal commodities would be below LOQ (0.01 mg/kg)

The confined rotational crop studies, conducted at 2-3 times the field GAP, showed low uptake of parent into the rotational crops. No residues were detected in any human food commodities for parent mesotrione or for metabolites MNBA or AMBA. Higher levels of MNBA and AMBA were observed in the animal feed commodities, wheat forage, 30 day plant back interval: MNBA 62% TRR (0.624 mg/kg) and AMBA 13% TRR (0.204 mg/kg). However, as shown above the AMBA cow metabolism study shows that at realistic dietary burdens, residues in feed item do not result in residues in any edible animal food commodity.

Numerous residue trials have been conducted with mesotrione on a number of different crops: maize (50 trials), sweet corn (8 trials), poppy seed (4 trials), linseed (4 trials), oilseed rape (8 trials) and herbicide tolerant soya (20 trials). With the exception of two HT soya trials, all trials showed mesotrione residues of < LOQ of 0.01 mg/kg. In the two HT soya trials where mesotrione residues were detected, with the highest at 0.02 mg/kg. For all these crops and in all the trials presented, MNBA residues were below 0.01 mg/kg. These data demonstrate that in diverse crops and in a large number of trials, MNBA is not found above the LOQ of 0.01 mg/kg. Therefore MNBA should not be included in the DoR for either monitoring or risk assessment purposes, since residues are essentially not detectable and any exposure to MNBA is negligible.

Toxicological information is available on MNBA and AMBA please refer to the Toxicology section in the DAR of the previous EU review for details of studies with the active substance and major metabolites. 28 and 90 day oral studies, genotox and acute toxicological studies all show both MNBA and AMBA to be of low toxicity. Thus, MNBA and AMBA can be considered to be of no toxicological concern. On this basis, from both exposure and toxicological grounds there is no scientific reason to include MNBA or AMBA in the DoR for monitoring and risk assessment for crops.

Supported by the scientific positions given above, the availability of a new multi-residue for mesotrione and because a DoR of mesotrione only will facilitate analysis for enforcement purposes, it is proposed that the definition of the residue for monitoring in crops should be parent mesotrione only.

Similarly, because MNBA and AMBA are of no toxicological concern, and because detectable residues of MNBA or AMBA are almost never found in human food commodities, as well as to facilitate harmonization of the definition of residues across different countries and regions, it is proposed that the definition of the residue for risk assessment purposes in crops should be parent mesotrione only.

Animal products

According to EU guidance, (EU guideline Document 7031/VI/95 rev. 4) and the dietary burden calculations (see Section CA-6.4), the proposed uses of mesotrione will not result in significant residue levels in any animal tissue, milk or eggs. Consequently, the setting of MRLs in animal products is not relevant and no proposal for a residue definition in animal commodities is required; none has been made.

Proposed DoR summary

Endpoint	Proposed EU endpoints
Definition of the residue in crops for enforcement purposes	Parent mesotrione only
Definition of the residue in crops for risk assessment purposes	Parent mesotrione only
Definition of the residue in animal products for enforcement purposes	Not required
Definition of the residue in animal products for risk assessment purposes	Not required

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

EU MRLs for mesotrione are currently detailed in Annexes of Regulation (EC) No 396/2005. EU MRLs for commodities relevant to this submission are detailed in Table 6.7.2–1. The residue values used and the calculations for MRL are presented in Section CA 6.3.

A change to the residue definition for enforcement (see section CA 6.7.1) and the EU MRL for maize grain is proposed as a result of this submission. The EU does not currently set MRLs in livestock feed commodities, but may do so in future. A "pseudo MRL" of 0.01 mg/kg is proposed for mesotrione in maize forage / silage.

Table 6.7.2–1: Established and proposed MRLs for mesotrione for commodities in this submission

Code	Commodity	Current EU MRL[1] (mg/kg)	Proposed EU MRL[2] (mg/kg)
500030	Maize (grain)	<0.05*	<0.01*
-	Maize forage (silage)	Not applicable	<0.01*

1 – Based on the current definition of the residue for monitoring (Sum of mesotrione and MNBA (4-methylsulfonyl-2-nitro benzoic acid), expressed as mesotrione)

2 – Based on the proposed definition of the residue for monitoring (mesotrione alone, no metabolites)

* MRL set or proposed at the LOQ

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

Not applicable.

CA 6.8 Proposed Safety Intervals

Pre-harvest intervals

Proposed pre-harvest intervals for the use of mesotrione on the representative use crop (maize) are detailed in Table 6.8.1-1.

Table 6.8.1-1: Proposed Pre-harvest Intervals

Crop	Application method	Pre-Harvest Interval (days)
Maize (cereal)	Foliar spray (BBCH 12-18)	Not relevant[1]

1 - Application is growth stage dependent and is made before the consumable part of the crop has formed

Re-entry intervals for livestock to areas to be grazed

A re-entry interval for livestock of 14 days is proposed as all residues are below 0.01 mg/kg in the crop at this time.

Re-entry period for man into treated areas

The worker re-entry risk assessments for the representative use were conducted assuming the maximum rate with no allowance for any decline in the default dislodgeable foliar residue and passed. Thus, no re-entry period is required.

Withholding periods for animal feeding stuffs

All residues of mesotrione in maize feed comodities are below 0.01 mg/kg after 14 days. So additional period of withholding is not required if feed commodities taken after this time point.

Waiting period between last application and sowing or planting the crops to be protected

As mesotrione can be applied to post emergence crops no waiting period is required.

Waiting period between last application and handling treated products

The worker re-entry risk assessments for the representative use were conducted assuming the maximum rate with no allowance for any decline in the default dislodgeable foliar residue and passed. Thus, no waiting period is required.

Waiting periods between last application and sowing or planting succeeding crops

The rotational crop studies showed that even at minimum 30 day plant back interval no residues of mesotrione above 0.01 mg/kg were observed. Thus, a waiting period is not required.

CA 6.9 Estimation of the Potential and Actual Exposure through Diet and other Sources

Acceptable Daily Intake (ADI) and Dietary Exposure Calculation

No change from the existing EU end-point value of 0.01 mg/kg body weight/day for mesotrione (see **SANCO/1416/2001 – Final, 14 April 2003** and **Document M-CA, Section 5** of this submission) is proposed.

Long-term consumer exposure to potential residues resulting from the proposed representative use of mesotrione is estimated according to the EFSA PRIMo model[1] for chronic risk assessment.

The TMDI values are calculated based on proposed MRL values as listed in Table 6.7.2-1. The residue as entered into the EFSA model is for maize grain at the MRL.

The TMDI calculations give unrealistic worst-case estimates of intake because they assume that all commodities with established and proposed uses will contain residues at the MRL or MRL-P. No account is taken of the potential reduction in residues during transport and storage or during commercial and domestic processing. In practice, the actual intake is likely to be much lower than the calculated values.

The TMDI calculations for mesotrione using the EFSA PRIMo model are presented in Table 6.9-1. The highest TMDI is for WHO cluster diet B and represents 0.25% of the ADI.

The results indicate that there is no unacceptable chronic risk to human health from the consumption of maize commodities treated with mesotrione according to the use considered.

[1] Revision 2.0 of the EFSA model. Reasoned Opinion on the Potential Chronic and Acute Risk to Consumers' Health Arising from Proposed Temporary EU MRLs According to Regulation (EC) No 396/2005 on Maximum Residue Levels of Pesticides in Food and Feed of Plant and Animal Origin, European Food Safety Authority, 15 March 2007

Table 6.9-1: TMDI for mesotrione using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU MRL values have been used.

Mesotrione

Status of the active substance:	Approved	Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.01	ARfD (mg/kg bw):	0.02
Source of ADI:	COM	Source of ARfD:	COM
Year of evaluation:	2003	Year of evaluation:	2003

Explain choice of toxicological reference values.
The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

TMDI (range) in % of ADI
minimum - maximum
0.25

No of diets exceeding ADI: ---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
0.25	WHO Cluster diet B	0.25	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.23	IE adult	0.23	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.10	UK Infant	0.10	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.06	WHO cluster diet E	0.06	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.05	WHO cluster diet D	0.05	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.05	PT General population	0.05	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.03	ES child	0.03	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.01	DE child	0.01	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.01	WHO regional European diet	0.01	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.01	NL child	0.01	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.01	WHO Cluster diet F	0.01	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.01	ES adult	0.01	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	NL general	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	IT kids/toddler	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	FI adult	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	IT adult	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	UK Toddler	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	UK vegetarian	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	LT adult	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	UK Adult	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
0.00	PL general population	0.00	Maize		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	
	DK adult		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Mesotrione is unlikely to present a public health concern.

Calculation of National Estimated Daily Intake (NEDI)

The TMDI values are significantly less than the ADI for mesotrione so it is not necessary to calculate NEDI values for mesotrione to give more realistic estimates of intake.

Acute Reference Dose (ARfD) and Dietary Exposure Calculation

No change from the existing EU end-point value of 0.02 mg/kg body weight/day (see **SANCO/1416/2001 – Final, 14 April 2003 and Document M-CA, Section 5** of this submission) is proposed.

Acute dietary risk assessments are presented for potential residues arising from the proposed representative use of mesotrione. Short-term consumer exposure to potential mesotrione residues is estimated according to the EFSA PRIMO model[2] for acute risk assessment.

IESTI (International Estimate of Short-Term Intake) values are generally calculated assuming that residues are present at the HR, except for commodities bulked or blended during processing, where the STMR is used. In this case the proposed EU-MRLs for the intended crops are used; this exhibits a worst-case scenario and does not take into account that some commodities can be considered as blended. The IESTI values are calculated based on proposed MRL values as listed in Table 6.7.2-1. The residue as entered into the EFSA model is for maize grain at the MRL.

The IESTI results for mesotrione obtained using the EFSA PRIMo model (Rev. 2.0) are presented in Table 6.9-2. The highest estimated short-term intake is for the consumption of maize by children (based on consumption data from UK Infant) and represents 0.3% of the ARfD.

The results indicate that there is no unacceptable acute risk to human health from the consumption of maize commodities treated with mesotrione according to the uses considered.

[2] Revision 2.0 of the EFSA model. Reasoned Opinion on the Potential Chronic and Acute Risk to Consumers' Health Arising from Proposed Temporary EU MRLs According to Regulation (EC) No 396/2005 on Maximum Residue Levels of Pesticides in Food and Feed of Plant and Animal Origin, European Food Safety Authority, 15 March 2007

Table 6.9-2: IESTI for mesotrione using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU MRL values have been used.

Acute risk assessment /children						Acute risk assessment / adults / general population					
The acute risk assessment is based on the ARfD. For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation. In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3. **Threshold MRL** is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	0.3	Maize	0.01 / -	0.3	Maize	0.01 / -	0.1	Maize	0.01 / -	0.1	Maize	0.01 / -
	No of critical MRLs (IESTI 1)		---				**No of critical MRLs (IESTI 2)**		---			
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**		---				**No of commodities for which ARfD/ADI is exceeded:**		---			
			*****)**						*****)**			
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)				Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)			
	0.2	Maize flour	0.01 / -				0.0	Maize flour	0.01 / -			
*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported. **) pTMRL: provisional temporary MRL ***) pTMRL: provisional temporary MRL for unprocessed commodity												
Conclusion: For Mesotrione IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available. No exceedance of the ARfD/ADI was identified for any unprocessed commodity. For processed commodities, no exceedance of the ARfD/ADI was identified.												

CA 6.10 Other Studies

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

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

Mesotrione is not a systemic herbicide and is not known to have any toxic effects to bees and therefore data from field studies conducted on bees are not available. Furthermore, for the supported representative use of mesotrione on maize, applied at early growth stages (typically BBCH 02 to 18), there is no likelihood of mesotrione exposure to honey bees and residues of mesotrione in pure blossom honey or other bee products will not occur from this use.