FINAL REGISTRATION REPORT
Part B
Section 4: Metabolism and Residues
Detailed summary of the risk assessment

Product code: TOTO 75/ HERKULES 75/TYTAN 75

Active Substance: Thifensulfuron-methyl – 68.2%

Metsulfuron-methyl – 6.8%

Central Zone
Zonal Rapporteur Member State: N/A

CORE ASSESSMENT- renewal of authorisation

Applicant: **Innvigo Sp z o.o.**

Date: **January, 2019**

October, 2020

July 2021

October 2022

Version history

When	What
July 2021	ZRMs evaluated submitted dRR.
October 2022	The Final version

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IIIA 8 METABOLISM AND RESIDUES DATA

New data was highlighted in turquoise.

NOTE: zRMS comments/corrections are market in grey

zRMS summary is on pages 61 and 62 in point *IIIA 8.11 Summary and Evaluation of Residue Behaviour.*

This document reviews the metabolism and residue data relevant for the product TOTO 20 containing metsulfuron-methyl which was included into Annex I of Directive 91/414 by Commission Directive 2000/49/EC of 26 July 2000 and has been renewed by Commission Implementing Regulation (EU) 2016/139 of 2 February 2016.

This document reviews the metabolism and residue data relevant for the product TOTO 20 containing thifensulfuron-methyl which was included into Annex I of Directive 91/414 by Commission Directive 2000/49/EC of 26 July 2000 and has been renewed by Commission Implementing Regulation (EU) 2016/1424 of 25 August 2016.

The SANTE document for metsulfuron methyl (SANTE/10319/2015 Rev ~~3~~ 4) are considered to provide the relevant review information or a reference to where such information can be found. The following table provides the EU endpoints to be used in the evaluation.

The SANTE document for thifensulfuron methyl (SANTE/10150/2016 rev. 2) are considered to provide the relevant review information or a reference to where such information can be found. The following table provides the EU endpoints to be used in the evaluation.

Metsulfuron - methyl

- Reference to Inclusion Directive: Commission Directive 2000/49/EC of 26 July 2000;
- Reference to Review Report/EFSA Scientific Report: SANCO/7593/VI/97-final 14 August 2000 and SCP/METSU/002-Final 5 April 2000;

Thifensulfuron – methyl

- Reference to Inclusion Directive: Commission Directive 2001/99/EC of 20 November 2001;
- Reference to Review Report/EFSA Scientific Report: SANCO/7577/VI/97-final 12 December 2001;

Agreed EU End-points (SANCO/7593/VI/97-final 14 August 2000 [Met] and SANCO/7577/VI/97-final 12 December 2001 [Thifen])

End-Point	Metsulfuron-methyl	Thifensulfuron-methyl
Acceptable Daily Intake (ADI)	0.22 mg/kg bw/d, 2 year rat, safety factor 100	0.01 mg/kg bw/d, 2 year rat, safety factor 100
Acute Reference Dose (ARfD)	Not proposed because toxicological end points are not relevant for acute oral dietary exposure	Not proposed because toxicological end points are not relevant for acute oral dietary exposure

Agreed EU End-points (SANTE/10319/2015 Rev 3 and SANTE/10150/2016 rev. 2)

Metsulfuron methyl	
End-Point	**Active Substance**
Acceptable Daily Intake (ADI)	0.22 mg/kg bw/d, 2 year rat, safety factor 100
Acute Reference Dose (ARfD)	0.25 mg/kg bw*.
Thifensulfuron methyl	
End-Point	**Active Substance**
Acceptable Daily Intake (ADI)	0.01 mg/kg bw per day, 2-yr rat study
Acute Reference Dose (ARfD)	2 mg/kg bw, Rat developmental toxicity study

* The acute reference dose (**ARfD**) is 0.25 mg/kg bw based on the maternal NOAEL of 25 mg/kg bw per day for reduced body weight gain in the first days of dosing from the rabbit developmental toxicity study, 100 UF applied.

The Commission Implementing Regulation for metsulfuron-methyl 2016/139 provides specific provisions under Part B which need to be considered by the applicant in the preparation of their renewal of authorisation and by the MS prior to granting a renewal of authorisation.

For the implementation of the uniform principles of Annex VI, the conclusions of the review report on the metsulfuron-methyl and in particular Appendices I and II thereof, as finalised in the COMMISSION STAFF WORKING DOCUMENT (SANTE/10319/2015 Rev 3) on 11 December 2015 shall be taken into account. In this overall assessment:

Member States may pay particular attention to the:

On the basis of the proposed and supported uses (as listed in Appendix II), the following issues have been identified as requiring particular and short term attention from all Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:
- the protection of consumers,
- the protection of groundwater,
- the protection of non-target terrestrial plants

Subsequent to the EU review of metsulfuron-methyl an evaluation of all uses has been made to establish EU MRLs **(***Commission Directive 617/2014 of 3 June 2014 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ethoxysulfuron, metsulfuron-methyl, nicosulfuron, prosulfuron, rimsulfuron, sulfosulfuron and thifensulfuron-methyl in or on certain products*). The evaluation reviewed all the data relevant to establishing MRLs for all supported uses and considered the dietary risk assessments appropriate for all EU member states utilising the EFSA model. The MRLs for metsulfuron-methyl are published in Annex III of Regulation (EC) No 396/2005. In this document the GAPs applied for will be compared with the critical GAPs used to set the EU MRL. A justification will be presented to show that the GAPs applied for at National level are covered by the critical EU GAPs for MRL setting (point 8.3).

In this summary all crops and application parameters applied for, for the National registration of TOTO 75 SG, including climatic condition (zonal) parameters are within the use parameters assessed for EU MRLs for metsulfuron-methyl. The supporting data including residue trials generated under comparable climatic conditions were comprehensively discussed in the corresponding EU MRL evaluation for metsulfuron methyl (*Commission Directive 617/2014 of 3 June 2014 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ethoxysulfuron, metsulfuron-methyl, nicosulfuron, prosulfuron, rimsulfuron, sulfosulfuron and thifensulfuron-methyl in or on certain products*) where all study references and conclusions can be found.
It can be concluded that no further evaluation is required for National registration.
Appendix 1 of this document contains the list of references included in this document for support of the evaluation.

The Commission Implementing Regulation for thifensulfuron methyl 2016/1424 of 25 August 2016 provides specific provisions under Part B which need to be considered by the applicant in the preparation of their renewal of authorisation and by the MS prior to granting a renewal of authorisation.

For the implementation of the uniform principles of Annex VI, the conclusions of the review report on the metsulfuron-methyl and in particular Appendices I and II thereof, as finalised in the COMMISSION STAFF WORKING DOCUMENT (SANTE/10150/2016 rev. 2) 12 July 2016 shall be taken into account. In this overall assessment:

Member States may pay particular attention to the:

On the basis of the proposed and supported uses (as listed in Appendix II), the following issues have been identified as requiring particular and short term attention from all Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:
- the protection of groundwater,
- the protection of non-target plants and aquatic organisms.

Subsequent to the EU review of thifensulfuron-methyl an evaluation of all uses has been made to establish EU MRLs **(***Commission Directive 617/2014 of 3 June 2014 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ethoxysulfuron, metsulfuron-methyl, nicosulfuron, prosulfuron, rimsulfuron, sulfosulfuron and thifensulfuron-methyl in or on certain products*). The evaluation reviewed all the data relevant to establishing MRLs for all supported uses and considered the dietary risk assessments appropriate for all EU member states utilising the EFSA model. The MRLs for thifensulfuron-methyl are published in Annex III of Regulation (EC) No 396/2005. In this document the GAPs applied for will be compared with the critical GAPs used to set the EU MRL. A justification will be presented to show that the GAPs applied for at National level are covered by the critical EU GAPs for MRL setting (point 8.3).

In this summary all crops and application parameters applied for, for the National registration of TOTO 75 SG, including climatic condition (zonal) parameters are within the use parameters assessed for EU MRLs for thifensulfuron-methyl. The supporting data including residue trials generated under comparable climatic conditions were comprehensively discussed in the corresponding EU MRL evaluation for thifensulfuron-methyl. (*Commission Directive 617/2014 of 3 June 2014 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ethoxysulfuron, metsulfuron-methyl, nicosulfuron, prosulfuron, rimsulfuron, sulfosulfuron and thifensulfuron-methyl in or on certain products*) where all study references and conclusions can be found.
It can be concluded that no further evaluation is required for National registration.
Appendix 1 of this document contains the list of references included in this document for support of the evaluation.

Metsulfuron - methyl
Thifensulfuron – methyl
Proposed ‘representative formulation’ during the Annex I of the Directive 91/414/EEG inclusion: WG.

IIIA 8.1 Stability of Residues

The stability of residues for the active substances metsulfuron-methyl and thifensulfuron-methyl were reviewed during the Annex I inclusion process (Annex II Section 4 Point 6.1) and no further data is required.

IIIA 8.1.1 Stability of residues during storage of samples

The stability of residues for the active substances were reviewed during the Annex I inclusion process (Annex II Section 4 Point 6.1) and no further data is required.
Recovery values or procedural recoveries obtained by the measurement of fortified specimens as part of the analysis of samples from supervised field trials and in the validation of these analytical methods were acceptable (70 – 120%). These recoveries demonstrate the stability of metsulfuron – methyl and thifensulfuron – methyl.
Conclusion:
There is no need to evaluate any new data.

According to EFSA Journal 2015;13(7):4201 stability of thifensulfuron-methyl was proved in wheat grain after 42 months storage at -20 °C and in corn after 24 months storage at -20 °C. According to EFSA Journal 2015;13(1):3936 stability of metsulfuron-methyl was proved in wheat grain, straw and forage after 12 months storage at -20 °C.

Study Comments: IIIA 8.1.1/01	Provided data are sufficient to support the proposed use. Comment for Thifensulfuron: Metabolite IN-A4098 is provisionally included in the residue definition for risk assessment for plant commodities (pending the outcome of the confirmatory data requirement on genotoxic potential). Storage stability data addressing this metabolite is not required at this stage. Storage stability data for IN-L9225 is reqiured for grown specifically as animal feed (a forage crop). The application does not apply to this case.	
Agreed endpoint: IIIA 8.1.1/01	Thifensulfuron and Metsulfuron-methyl Residue trials are valid in relation to storage stability data. No additional tests are required.	

IIIA 8.1.2 Stability of residues in sample extracts

The stability of residues for the active substances were reviewed during the Annex I inclusion process (Annex II Section 4 Point 6.1) and no further data is required.

Study Comments: IIIA 8.1.2/01	

Agreed endpoint: IIIA 8.1.2/01	No additional tests are required.

IIIA 8.2 Supplementary studies on metabolism in plants or livestock

Studies were reviewed at EU level for the Annex I inclusion.
The data evaluated during the Annex I inclusion of the active substances metsulfuron-methyl and thifensulfuron-methyl are sufficient to describe the behaviour of the formulated product, and no further studies are required.

Metsulfuron - methyl

The metabolic fate of metsulfuron - methyl was investigated in barley and wheat crops grown and treated with phenyl labelled metsulfuron - methyl under field conditions (35g/ha in the tiller stage). Metabolism studies in wheat were also conducted under greenhouse conditions using both phenyl label and triazine label forms of metsulfuron - methyl (35 and 70 g as/ha, at 3-5 leaf stage). There were no significant residues of metsulfuron - methyl or its transformation products (>0.01 mg/kg) in mature barley and wheat grain. Metsulfuron - methyl was metabolized by either hydroxylation of the phenyl ring and subsequent conjugations with glucose or cleavage of the sulfonylurea bridge.

Thifensulfuron – methyl

The metabolism of thifensulfuron - methyl and the identification of residues were studied in field grown wheat and corn with labelled active substance. The elimination of thifensulfuron methyl in wheat was rapid (DT50 estimated to 2 days). There were no significant residues of thifensulfuron - methyl or its metabolites (< 0.01 ppm) in mature field wheat grain, two months after treatment (74-80 g a.s./ha) at the 5 leave stage. Mature forage and straw total residues were 0.80 to 0.45 ppm for the thiophene and triazine labelled test substances. The main degradation products were thifensulfuron acid (< 0.04 ppm), 2-acid-3-sulfonamide (< 0.06 ppm) and triazine urea (< 0.02 ppm) in mature wheat. The unextracted residues found in plants are believed to result in ^{14}C incorporation into natural plant sugars. The metabolic fate of thifensulfuron - methyl in field wheat and corn was adequately described and the major compounds found in plants were the same as those detected in rat metabolism studies.

Livestock metabolism

Metsulfuron - methyl

Metabolism studies were performed in goat. Metsulfuron - methyl was well absorbed and residues were eliminated as intact parent compound primarily in the urine. Very low levels of radioactive residues (0.009 mg/kg, 0,3% of daily dose) representing mostly intact parent compound were present in the milk. Insignificant concentratons (<0.01 mg/kg) of radioactive residues were found in body organs including liver and kidneys and in tissues.
There were no detectable residues (>0.01 mg/kg) of metsulfuron - methyl on poultry feed items, therefore, no poultry studies were conducted.

Thifensulfuron – methyl

The metabolism of thifensulfuron - methyl were studied in lactating goat. There were no detectable residues (>0.01 mg/kg) of thifensulfuron - methyl on poultry feed items, therefore, no poultry studies were conducted.
Dosed radioactivity was efficiently absorbed from the gastro intestinal tract and voided from the lactating goats. Excretion occurred mainly via urine (53 to 64%) and also in the faeces (28 to 33%).

0.4 to 0.7% of the dose were eliminated in milk. The composition of radioactivity in the urine and faeces indicated that intact thifensulfuron - methyl was the major radiolabelled compound, comprising 72-88% of the total radioactivity in the urine samples and 60-81% of the total radioactivity in the faeces samples. Milk was a minor excretion route and thifensulfuron - methyl was excreted mainly in unchanged form. Metabolism in lactating goat was minimal and radioactivity did not accumulate in the tissue. Total residue levels were highest in the kidneys (0.16 ppm). The excretion routes and the metabolic pathways of thifensulfuron - methyl in goat were very similar to those encountered in rat.

Conclusion:

There is no need to evaluate any new data.

According to EFSA Journal 2015;13(1):3936 metabolism of metsulfuron-methyl was investigated upon foliar application oilseeds (linseed), using 14C-phenyl and 14C-triazine labelled metsulfuron-methyl. Information reported regarding the metabolism in cereals (barley, wheat) was considered insufficient by the peer review. a data gap was identified for sufficient information on cereal metabolism data with metsulfuron-methyl. The residue definition for enforcement of MRLs in cereals is currently set as parent metsulfuron-methyl only,

As for cereals being a relevant feed item, metabolism data were submitted with metsulfuron-methyl in goat and hen. However, in terms of the representative uses and the provisional residue definition for cereals as metsulfuron-methyl alone the estimated livestock exposure did not exceed the trigger for requiring such studies. The livestock residue assessment is however pending the availability of required plant metabolism data, and the finalisation of the assessment in terms of the relevant residue in food and feed commodities for dietary risk assessment.

The risk assessment definition is not finalised. It is, however, to be submitted on the EU level.

Thifensulfuron-methyl

According to EFSA Journal 2015;13(7):4201 metabolism of thifensulfuron-methyl in wheat, maize and soybean was similar, yielding the same degradation compounds. Most of the radioactivity was recovered in the leaves. Based on the available data in plants, the residue definition for risk assessment for fodder crops is proposed as sum of thifensulfuron-methyl and thifensulfuron acid (IN-L9225), expressed as thifensulfuron-methyl, and provisionally IN-A4098 to be considered separately pending the toxicological profile of this compound to be fully addressed. The residue definition for risk assessment for other plant commodities (food commodities) is proposed as thifensulfuron-methyl and provisionally IN-A4098 to be considered separately pending on the toxicological profile of this compound. The plant residue definition for monitoring is proposed as thifensulfuron-methyl only, since fodder crops are currently not affected by MRL setting. Metabolism data were available for two primary crop groups (cereals and pulses), and following current guidance it is not possible to set a general residue definition.

Livestock metabolism was studied with thifensulfuron-methyl in goat and hen. Based on these data and assuming a similar behaviour of the thifensulfuron acid (IN-L9225) in the animals, the residue definition for risk assessment in livestock matrices was derived as sum of thifensulfuron-methyl and thifensulfuron acid (IN-L9225), expressed as thifensulfuron-methyl, and provisionally IN-A4098 to be considered separately pending on the toxicological profile of this compound. IN-A4098 also appeared as a livestock metabolite of thifensulfuron-methyl, and therefore a livestock exposure assessment for IN-A4098

residues in feeding stuffs is to be conducted to estimate the actual residue levels of INA4098 in animal commodities from both internal and external exposure to IN-A4098.

The risk assessment definition is not finalised with regard to metabolites IN-A4098 and IN-B5528. The consumer exposure assessment is moreover pending further clarification on the toxicological properties of IN-W8268 and INA5546. It is, however, to be submitted on the EU level.

Study Comments: IIIA 8.2/01	The intended uses are covered by the available metabolism studies reported in the EU.	
Agreed endpoint: IIIA 8.2/01	<u>Thifensulfuron-methyl (EFSA Journal 2015;13(7):4201):</u> Plant residue definition for monitoring Thifensulfuron-methyl (parent) (EFSA 2015) Although currently no EU MRLs are set for feed commodities, for possible future applicability it is proposed for animal feed items (grass / alfalfa): Sum of thifensulfuron-methyl and thifensulfuron acid (IN-L9225), expressed as thifensulfuron-methyl Plant residue definition for risk assessment For oilseeds and cereals: thifensulfuron-methyl and provisionally IN A4098 (EFSA, 2015) For Animal feed items (grass / alfalfa): Sum of thifensulfuron-methyl and thifensulfuron acid (IN-L9225), expressed as thifensulfuron-methyl and provisionally triazine amine (IN-A4098) Animal residue definition for monitoring Thifensulfuron-methyl (parent) (EFSA 2015) Animal residue definition for risk assessment Sum of thifensulfuron-methyl and thifensulfu-ron acid (IN-L9225), expressed as thifensulfuron-methyl and provisionally triazine amine (IN-A4098) (EFSA 2015) <u>Metsulfuron - methyl (EFSA Journal 2015;13(1):3936):</u> Plant residue definition for monitoring: Metsulfuron-methyl (parent) Plant residue definition for risk assessment: provisionally Metsulfuron-methyl (parent), pending submission of sufficient metabolism data in cereals and in rotational crops Monitoring residue definition for animals: metsulfuron methyl (parent). Risk assessment residue definition for animals (proposed): metsulfuron-methyl (parent), triazine amine; finalization pending plant residue definition and respective livestock exposure estimates.	

IIIA 8.3 Supplementary residue trials (supervised field trials)

Table 8.3-1: Summary of the critical GAP for the proposed uses for TOTO 75

Crop	Outdoor/ Protected	Growth stage	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g ai/ha)	Water (L/ha)	
Winter wheat	outdoor	21-31	1	N/A	[Met]: 6 [Thifen]: 61.4	200-300	N/A

Table 8.3-2: Summary of critical GAPs used for setting the EU MRL

Crop	Outdoor/ Protected	Growth stage	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g ai/ha)	Water (L/ha)	
Winter wheat	outdoor	12-39	1	N/A	[Met]: 6 [Thifen]:61.4	100-400	N/A

Table 8.3-2.01: Summary of critical GAPs used for setting the EU MRL

Crop	Outdoor/ Protected	Growth stage	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g ai/ha)	Water (L/ha)	
Winter wheat	outdoor	21-39	1	N/A	6.1 [Met] 61.4 [Thifen]	50-400	N/A

IIIA 8.3.1 Crop 1 (wheat)

IIIA 8.3.1 Crop 1 (wheat)

Metsulfuron – methyl
Thifensulfuron – methyl

Uses and conditions of use of metsulfuron - methyl and thifensulfuron - methyl on wheat are covered by residue data submitted in the Annex IIA dossier for metsulfuron - methyl and thifensulfuron - methyl. Supplementary residue trials:

New trials conducted with TOTO 75

Report:	KIIIA1 8.3.1/01, Cross Reference to **KIIIA1 5.3.1/01 Wójcik M., Winiarska K., Zmijowska A. 2008**
Title:	TOTO 75 WG Determination of residues of metsulfuron methyl and thifensulfuron methyl in wheat grain
Document No:	Study code C/05/08 Institute of Industrial Organic Chemistry, Branch Pszczyna, ul. Doswiadczalna 27, 43-200 Pszczyna, Poland
Guidelines:	**GLP, OECD 1997 and SOP /C/133**
GLP	**Yes**

In 2 trials in which TOTO 75 was applied to winter wheat using the critical GAP as proposed in Poland, the residues of metsulfuron - methyl and thifensulfuron - methyl were determined after harvest in wheat grain. The residues of metsulfuron - methyl and thifensulfuron - methyl were less than Limit of Quantification of 0.05 mg/kg.

Conclusion:

There is no need to evaluate any new data.

New trials conducted with TOTO 75

The scheme of treatment of wheat with Toto 75 SG is presented below, in table 8.3.1-1.

Table 8.3.1-1 Summary of the residue trials for winter wheat.

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment			Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzed	Growth stage at sampling (BBCH)	Residues (mg/kg) Tifensulfuron-methyl Metsulfuron-methyl IN-A4098	PHI (days)	Details on trial
	(a)	(b)	g prod./ha	Water (L/ha)	g prod./hL	(c)	(d)		(d)		(e)	(f)
103141104/ Groß-Zimmern, in Darmstadt-Dieburg/Germany/ Northern Zone 2015	Winter wheat / -	1. 19.10.~~2014~~ 2015 2. – 3. 23.07.2015 4. 23.07.2015	TOTO 75 SG- 90 g / ha Asystent+ - 100 ml/ha	300	30	09.04.2015	BBCH 89	2 g, straw	89	T: <LOD M: <LOD	-	
								10 g, grains	89	T: <LOD M: <LOD		
RF-B8109/ Groß-Zimmern, in Darmstadt-Dieburg/Germany/ Northern Zone 2015	Winter wheat/-	1. 14.04.2014 2. – 3. 09.04.2015- 23.07.2015 4. 09.04.2015-	TOTO 75 SG- 90 g / ha Asystent+ - 100 ml/ha	300	30	09.04.2015	BBCH 89	10 g, plant	29-31	T: 2.871 M: 0.314	7	
								10 g, plant	32	T: 0.032 M: <LOQ		

		23.07.2015						10 g, plant	47-57	T: <LOQ M: LOD		
								10 g, plant	65-69	T: <LOQ M: <LOD		
								2 g, straw	89	T: <LOD M: <LOD		
								10 g, heads	89	T: <LOD M: <LOD		
B8109/ 99-122 Gora Swietej Malgorzaty, Morakow, Lodzkie, Poland/ Northern Zone **2018**	Winter wheat/BANDEROLA	1. 10.10.2017 2. – 3. 07.05.2018-09.08.2018 4. 24/07/2018-06.09.2018	TOTO 75 SG- 90 g / ha (61.38 g tifensulfuron-methyl/ha + 6.12 g metsulfuron-methyl/ha) Asystent+ - 100 ml/ha	300	30	07.05.2018	BBCH 89	5 g, plant	32	T: 1.724 M: 0.272 I: 0.022	-	
								5 g, plant	69	T: <LOD M: <LOD I: <LOD		
								5 g, plant	73-75	T: <LOD M: <LOD I: <LOD		

								5 g, plant	83	T: <LOD M: <LOD I: <LOD		
								5 g, grain	89	T: <LOD M: <LOD I: <LOD		
								2.5 g, straw	89	T: <LOD M: <LOD I: <LOD		
B7040 PL1/62-704 Kawęczyn, Marianów, Wielkopolskie, Poland/ Northern Zone **2017**	Winter wheat/ SKAGEN	1. 28.10.2016 2. – 3. 01.05.2017-03.08.2017 4. 09/08/2017	TOTO 75 SG- 90 g / ha (61.4 g tifensulfuron-methyl/ha + 6.1 g metsulfuron-methyl/ha) Asystent+ - 100 ml/ha	300	6.00	01.05.2017	BBCH 89	5 g, plant	30-31	T: 1.24 M: 0.303 I: 0.028	-	
								5 g, plant	37-39	T: <LOQ M: <LOD I: <LOD		

								5 g, plant	65	T: <LOD M: <LOD I: <LOD		
								5 g, plant	75-77	T: <LOD M: <LOD I: <LOD		
								5 g, grain	89	T: <LOD M: <LOD I: <LOD		
								2.5 g, straw	89	T: <LOD M: <LOD I: <LOD		
B7040 PL2/62-704 Kawęczyn, Marianów, Wielkopolskie, Poland/ Northern	Winter wheat/ Julius	1. 28.10.2016 2. – 3. 16.05.2017-	TOTO 75 SG-90 g / ha (61.4 g tifensulfuron-methyl/ha + 6.1 g metsulfuron-	300	6.00	16.05.2017	BBCH 89	5 g, plant	30-31	T: 0.841 M: 0.198 I: 0.022	-	

Zone **2017**		01.08.2017 4. 09/08/2017	methyl/ha) Asystent+ - 100 ml/ha					5 g, plant	45-47	T: <LOD M: <LOD I: <LOD		
								5 g, plant	69-71	T: <LOD M: <LOD I: <LOD		
								5 g, plant	77	T: <LOD M: <LOD I: <LOD		
								2.5 g, straw	89	T: <LOD M: <LOD I: <LOQ		
								5 g, grain	89	T: <LOD M: <LOD I: <LOD		

Report:	KIIIA1 8.3.1/01, Dr. Matthias Eichler, Stefanie Schabio, Silke Hermann
Title:	TOTO 75 SG: Field Residue Decline Study on Wheat Commodities in Central Europe
Document No:	ibacon GmbH, Arheilger Weg 17 64380 Rossdorf Germany Project No: **Project 103141104**
Guidelines:	**GLP compliant study based on SANCO 7525/VI/95 rev.9 2011, SANCO 7029/VI/95, SANCO/10329/2002, SANCO/3029/99 rev.4, 2000 and OECD 2009 Test No. 509**
GLP	**Yes**

Summary of new trials:

The test item TOTO 75 SG was studied on an arable field to quantify the decline and the magnitude of residues of Thifensulfuron methyl and Metsulfuron methyl in Wheat commodities following the application according to the critical good agricultural practice.
Two trials (one test item and one control trial) were settled. The study was designed to reflect the worst case use pattern that leads to the highest possible residues.
The study based on SANCO 7525/VI/95 rev.9 2011, SANCO 7029/VI/95 rev.5 1997, SANCO/10329/2002, SANCO/3029/99 rev.4, 2000 and OECD 2009 Test No. 509.
The trial was placed in Groß-Zimmern, in Darmstadt-Dieburg/Germany. The test item was applied once in April 2015, as a spray application with a rate of of 90 g TOTO 75 SG /ha and 100 mL adjuvant/ha.
For the trial five samplings were conducted. Two samples per plot (one for analysis, one as retain sample) per sampling. Each mixed sample consists of 12 subsamples taken from 12 different areas. The wheat samples were taken manually at different growth stages of the crop. The determination of the BBCH stage and the height of the plants were conducted at each sampling date. There were no visible differences between the TOTO 75 SG treated and untreated trial.

Materials and Methods

PROTOCOL

Test material	**2 winter wheat grain and straw samples**
Analytical standard	**Thifensulfuron-methyl, Dr. Ehrenstorfer, Germany, Batch No: 41031, Expiry Date: January 26, 2019** **Metsulfuron-methyl, Dr. Ehrenstorfer, Germany, Batch No: 30829, Expiry Date: August 29, 2019**
Method	**LC-MS/MS**
Column	**Gemini 3µ C18 110A (150 * 3 mm)**
HPLC Conditions:	**Column: Gemini 3µ C18 110A (150 * 3 mm)** **Mobile Phase:** Eluent A: HPLC-grade water + 0.05 % acetic acid Eluent B: Methanol + 0.05 % acetic acid **Isocratic Mode:** 20 % Eluent A / 80 % Eluent B Flow Rate: 0.3 mL/min Injection Volume: 10 µL Oven Temperature: 40 °C
LC-MS/MS Conditions:	**Ion Source:** Electrospray, positive **Ion Source:** 4500

	Temperature: 600 °C **Mass Transitions:** 388 amu to 167 amu (quantifier, Thifensulfuron-methyl) 388 amu to 141 amu (qualifier, Thifensulfuron-methyl) 382 amu to 167 amu (quantifier, Metsulfuron-methyl) 382 amu to 141 amu (quantifier, Metsulfuron-methyl)
Concentration range	**0.1 to 10 µg Thifensulfuron-methyl/L** **0.1 to 10 µg Metsulfuron-methyl /L**

Parameter for Validation of the Chromatographic Method

Test substance	**Thifensulfuron-methyl**	**Metsulfuron-methyl**
Interference	Interferences from solvent blank, i.e. control matrix, were not detected.	Interferences from solvent blank, i.e. control matrix, were not detected.
Calibration Range	0.1 to 10 µg Thifensulfuron-methyl/L	0.1 to 10 µg Metsulfuron-methyl /L
Linearity of Response:	Correlation of peak area of different standard solutions with their corresponding concentrations, using a linear regression	Correlation of peak area of different standard solutions with their corresponding concentrations, using a linear regression.
Regression Coefficient r: **Typical Calibration Curve:**	0.9999 for quantifier y = 330672 * x + 8747	0.9998 for quantifier y = 405346 * x + 11740
Limit of Detection:	0.011 µg Thifensulfuron-methyl/L corresponding to 0.00022 mg Thifensulfuron-methyl/kg	0.0034 µg Metsulfuron-methyl /L corresponding to 0.000068 mg Metsulfuron-methyl /kg
Limit of Quantification:	10 µg Thifensulfuron-methyl/kg The LOQ is defined as the mean nominal concentration of the lowest validated concentration level.	10 µg Metsulfuron-methyl /kg plant The LOQ is defined as the mean nominal concentration of the lowest validated concentration level
Accuracy of the Analytical Method:	**Mean recovery rate of Thifensulfuron-methyl in the fortified plant samples - quantifier:** 10 µg Thifensulfuron-methyl/kg plant: 84 % (n = 5; RSD = 6 %) 100 µg Thifensulfuron-methyl/kg plant: 88 % (n = 5; RSD = 7 %) Overall mean recovery: 86 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified** plant samples - qualifier:	**Mean recovery rate of Metsulfuron-methyl in the fortified plant samples - quantifier:** 10 µg Metsulfuron-methyl /kg plant: 86 % (n = 5; RSD = 6 %) 100 µg Metsulfuron-methyl /kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 87 % (n = 10; RSD = 6 %) **Mean recovery rate of Metsulfuron-methyl in the fortified plant samples - qualifier:**

	10 µg Thifensulfuron-methyl/kg plant: 85 % (n = 5; RSD = 7 %) 100 µg Thifensulfuron-methyl/kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 87 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified grains samples - quantifier:** 10 µg Thifensulfuron-methyl/kg grains: 84 % (n = 5; RSD = 4 %) 100 µg Thifensulfuron-methyl/kg grains: 89 % (n = 5; RSD = 5 %) Overall mean recovery: 87 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified grains samples - qualifier:** 10 µg Thifensulfuron-methyl/kg grains: 94 % (n = 5; RSD = 4 %) 100 µg Thifensulfuron-methyl/kg grains: 98 % (n = 5; RSD = 4 %) Overall mean recovery: 96 % (n = 10; RSD = 6 %)	10 µg Metsulfuron-methyl /kg plant: 86 % (n = 5; RSD = 6 %) 100 µg Metsulfuron-methyl /kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 88 % (n = 10; RSD = 6 %) **Mean recovery rate of Metsulfuron-methyl in the fortified grains samples - quantifier:** 10 µg Metsulfuron-methyl/kg grains: 84 % (n = 5; RSD = 4 %) 100 µg Metsulfuron-methyl/kg grains: 91 % (n = 5; RSD = 3 %) Overall mean recovery: 87 % (n = 10; RSD = 5 %) **Mean recovery rate of Metsulfuron-methyl in the fortified grains samples - qualifier:** 10 µg Metsulfuron-methyl/kg grains: 98 % (n = 5; RSD = 5 %) 100 µg Metsulfuron-methyl/kg grains: 100 % (n = 5; RSD = 3 %) Overall mean recovery: 99 % (n = 10; RSD = 4 %)
Precision of the Analytical Method:	Relative standard deviation: 7 % for plants and grains.	Relative standard deviation: 6 % for plants and 5 % for grains.
Storage Stability:	**Stability of Thifensulfuron-methyl in plant samples - quantifier:** 86 µg Thifensulfuron-methyl/kg plant: 79 % (n = 2; RSD = 8 %) **Stability of Thifensulfuron-methyl in plant samples - qualifier:** 86 µg Thifensulfuron-methyl/kg plant: 81 % (n = 2; RSD = 7 %)	**Stability of Metsulfuron-methyl in plant samples - quantifier:** 87 µg Metsulfuron-methyl/kg plant: 83 % (n = 2; RSD = 6 %) **Stability of Metsulfuron-methyl in plant samples - qualifier:** 87 µg Metsulfuron-methyl/kg plant: 83 % (n = 2; RSD = 5 %)
Repeatability of Injection:	The standard deviation obtained from a five-fold injection of two single calibration standards was max. 3.3 %.	The standard deviation obtained from a five-fold injection of two single calibration standards was max. 4.2 %.

Application of the Test Item

Application Date: April 09, 2015

Table 1. Concentration of the Test Item Spraying Dilution

	Water Volume [L/ha]	Concentration of Spraying Dilution [g/L]		Concentration of Spraying Dilution (g in 5000 mL)		Target Volume / plot (L)
		TOTO 75 SG	Asystent+	TOTO 75 SG	Asystent+	
Application	300	0.3	0.34	1.5	1.7	3.0

Application of the Test Item:	The application was carried out according to critical Good Agricultural Practice (cGAP) for each experimental plot during daytime, with standard field spraying equipment. The test item was sprayed onto the wheat plant at BBCH 30 using an adapted plot sprayer.
Application of the Control:	The control was left untreated.
Application Equipment:	Movable plot sprayer for field application; type "*PSG-System 4*" (Fa. Schachtner Gerätetechnik, 71640 Ludwigsburg, Germany), with an extension tube including 5 spraying nozzles (Lechler IDK 120-04; distance between nozzles: 50 cm) operating with compressed air and a boom width of 250 cm. Distance between the nozzles and soil was approx. 50 cm. The plot was sprayed by four passes of the plot sprayer.
Verification of Application:	The sprayer was calibrated before application in order to ensure the exact amount of spray application. The calibration was conducted by measuring the spray volume per time per nozzle at a fixed pressure. This procedure was repeated 3 times to ensure that the application rate was 300 L/ha ± 10 %. A visual check demonstrated that no nozzles were leaking or blocked. A calibrated volumetric flow instrument gave the exact amount of the actual application. The results of the application data as well as the verification data is documented in the raw data.
Spraying Pressure:	2.0 bar;
Distance Between Nozzle and Soil:	Approximately 50 cm
Water Amount in this Study:	300 L tap water/ha with max. deviation of ±10 %. The spraying solution preparation had a volume of 5 L to ensure sufficient spray solution for the plot plus a reserve.

Deviation from Target [%]:

	plot I ($100m^2$)
Test Item*	+1.0

	* Deviation from the Target [%] based on a calibrated volumetric flow instrument which gave the exact amount of the actual application for each plot.
Documentation:	Application details are stored in the raw data
Climatic Conditions during the Application:	Air temperature: min: 18.3°C; max: 18.5°C Soil temperature: 13.0°C Relative humidity: min: 47.5 %; max: 48.3% Wind Velocity: min: 0.4 m/s; max: 1.7 m/s
Spraying Solution:	A specimen (approx. 20 mL) of the spray solution preparation from the application was taken for the test item and stored frozen (≤ -20°C) after transfer to ibacon.

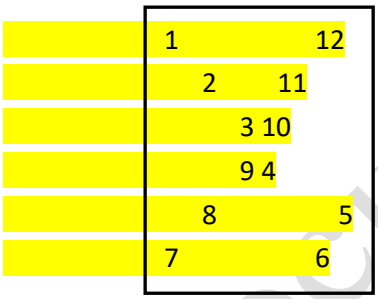
The application of 90 g/ha TOTO 75 SG and 100 mL/ha adjuvant was at BBCH 30 and the control was left untreated.

After the application has been carried out, samplings of plant material were used to determine the magnitude and decline of residues in Wheat Commudities.

The duration of the test was approximately four months from application in April to harvest in July (because of the weather conditions harvest was earlier than expected).

Replication:	1 plot for the decline trail and 1 control trail.
Size of the Plots:	100 m² for the decline trail and for the control trail with at least with 3 m distance between each plot
Exposure Time:	Approximately 4 months (from April 2015 to July 2015)
	1st Sampling (within 3 hours after application) April 09, 2015
	2nd Sampling 20 Days after application: April 29, 2015
	3rd Sampling 42 Days after application: May 21, 2015
	4th Sampling 61 Days after application: June 09, 2015
	5th Sampling 105 Days after application (Harvest): July 23, 2015

Wheat Collection

Number of Samples per Plot/Treatment:	Two mixed samples per plot (one for analysis, one as retain sample) per sampling. Each mixed sample consists of 12 subsamples taken from 12 different areas.
Sampling Method:	Wheat samples were taken manually at different growth stages of the crop. The material for field samples was selected systematically from each plot along an "X"-pattern.  In order to avoid contamination samples from control plot was taken prior to the samples from test item treated plot.
Retain Samples:	A second set of samples was taken in the same way as the other samples on each sampling date as retain samples.
Sampling Dates:	The whole plant (grain and straw) sample should weighed ca. 1 kg per plot for the main and the retain sample. - At harvest: The mixed grain sample weighed ca. 1 kg and the mixed straw sample weighed ca. 0.5 kg. The control plot was shared with the simultaneously running field residue decline study (ibacon study no. 103142104).
Interim Storage:	Directly after sampling, each mixed specimen was transferred into a suitable labelled container (plastic bags) and stored in a shady and dry place. Temperature conditions were recorded using a tiny tag datalogger.
Labelling:	Each specimen was uniquely identified with at least study number, treatment group and day of sampling.
Plant Height:	The plant height was recorded at each sampling date.

BBCH Scale:

The phenological growth stages of each plot were recorded at each sampling date using the BBCH-identification key for Wheat (Witzenberger et al., 1989; Lancashire et al., 1991).

Sampling	BBCH Scale	Plant height [cm]
1st Sampling (within 3 hours after application)	29 – 31 (mean 30)	15
2nd Sampling 20 Days after application:	32	36 - 50
3rd Sampling 42 Days after application:	47 - 57	60 - 87
4th Sampling 61 Days after application:	65 - 69	100 - 120
5th Sampling 105 Days after application (Harvest):	89	55 - 80

Summary of results:

day after application	matrix	control trial: total sample amount [g]	control trial: concentration analysed Thifensulfuron-methyl [mg a.i./kg]	control trial: concentration analysed Metsulfuron-methyl [mg a.i./kg]	decline trial: total sample amount [g]	decline trial: concentration analysed Thifensulfuron-methyl [mg a.i./kg]	decline trial: concentration analysed Metsulfuron-methyl [mg a.i./kg]
0	plant	1125.65	< LOD	< LOD	111.09	2.871	0.314
20	plant	1093.74	< LOD	< LOD	2619.90	0.032	< LOQ
42	plant	1571.01	< LOD	< LOD	1214.82	< LOQ	< LOD
61	plant	1931.00	< LOD	< LOD	2107.47	< LOQ	< LOD
(harvest) 105	straw	763.63	< LOD	< LOD	755.50	< LOD	< LOD
(harvest) 105	heads	1226.83	< LOD	< LOD	1480.02	< LOD	< LOD

LOQ: Limit of Quantification = 0.01 mg Thifensulfuron-methyl/kg
LOD = Limit of Detection = 0.011 µg/L corresponding to 0.00022 mg Thifensulfuron-methyl /kg
LOQ: Limit of Quantification = 0.01 mg Metsulfuron-methyl/kg
LOD = Limit of Detection = 0.0034 µg/L corresponding to 0.000068 mg Metsulfuron-methyl /kg

There were no residues detectable in the control samples at any time of sampling. Residues of both active ingredients, Thifensulfuron-methyl and Metsulfuron-methyl, were found in samples taken on the day of application from the decline plot, but on day 42 after application they were already below the limit of quantification or limit of detection, respectively.

There were no detectable levels of residues in the grain and straw specimens taken at harvest.

New trials conducted with TOTO 75

Report:	KIIIA1 8.3.1/01, Dr. Matthias Eichler, Stefanie Schabio, Silke Hermann
Title:	TOTO 75 SG: Field Residue Study on Wheat Commodities in Central Europe
Document No:	ibacon GmbH, Arheilger Weg 17 64380 Rossdorf Germany Project No: Project 103142104
Guidelines:	**GLP compliant study based on SANCO 7525/VI/95 rev.9 2011, SANCO 7029/VI/95, SANCO/10329/2002, SANCO/3029/99 rev.4, 2000 and OECD 2009 Test No. 509**
GLP	**Yes**

Summary of new trials:

The test item TOTO 75 SG was studied on an arable field to quantify the magnitude of residues of Thifensulfuron methyl and Metsulfuron methyl in Wheat commodities following the application according to the critical good agricultural practice.

Two trials (one test item and one control trial) were settled. The study was designed to reflect the worst case use pattern that leads to the highest possible residues.

The study based on SANCO 7525/VI/95 rev.9 2011, SANCO 7029/VI/95 rev.5 1997, SANCO/10329/2002, SANCO/3029/99 rev.4, 2000 and OECD 2009 Test No. 509.

The trial was placed in Groß-Zimmern, in Darmstadt-Dieburg/Germany. The test item was applied once in April 2015, as a spray application with a rate of 90 g TOTO 75 SG /ha and 100 mL adjuvant/ha.

For the trial one harvest sampling was conducted with two mixed samples per plot (one for analysis, one as retain sample) in the control and test item trial. Each mixed sample consists of 12 subsamples taken from 12 different areas. The wheat samples were taken manually at harvest. The determination of the BBCH stage and the height of the plants were conducted. There were no visible differences between the TOTO 75 SG treated and untreated trial.

Materials and Methods

PROTOCOL

Test material	**2 winter wheat grain and straw samples**
Analytical standard	**Thifensulfuron-methyl, Dr. Ehrenstorfer, Germany, Batch No: 41031, Expiry Date: January 26, 2019** **Metsulfuron-methyl, Dr. Ehrenstorfer, Germany, Batch No: 30829, Expiry Date: August 29, 2019**
Method	**LC-MS/MS**
Column	**Gemini 3µ C18 110A (150 * 3 mm)**
HPLC Conditions:	**Column: Gemini 3µ C18 110A (150 * 3 mm)** **Mobile Phase:** Eluent A: HPLC-grade water + 0.05 % acetic acid Eluent B: Methanol + 0.05 % acetic acid **Isocratic Mode:** 20 % Eluent A / 80 % Eluent B Flow Rate: 0.3 mL/min Injection Volume: 10 µL Oven Temperature: 40 °C
LC-MS/MS Conditions:	**Ion Source:** Electrospray, positive **Ion Source:** 4500 **Temperature:** 600 °C **Mass Transitions:** 388 amu to 167 amu (quantifier, Thifensulfuron-methyl) 388 amu to 141 amu (qualifier, Thifensulfuron-methyl) 382 amu to 167 amu (quantifier, Metsulfuron-methyl) 382 amu to 141 amu (quantifier, Metsulfuron-methyl)
Concentration range	**0.1 to 10 µg Thifensulfuron-methyl/L** **0.1 to 10 µg Metsulfuron-methyl /L**

Parameter for Validation of the Chromatographic Method

Test substance	**Thifensulfuron-methyl**	**Metsulfuron-methyl**
Interference	Interferences from solvent blank, i.e. control matrix, were not detected.	Interferences from solvent blank, i.e. control matrix, were not detected.
Calibration Range	0.1 to 10 µg Thifensulfuron-methyl/L	0.1 to 10 µg Metsulfuron-methyl /L
Linearity of Response:	Correlation of peak area of different standard solutions with their corresponding concentrations, using a linear regression	Correlation of peak area of different standard solutions with their corresponding concentrations, using a linear regression.
Regression Coefficient r: **Typical Calibration Curve:**	0.9999 for quantifier y = 330672 * x + 8747	0.9998 for quantifier y = 405346 * x + 11740
Limit of Detection:	0.011 µg Thifensulfuron-methyl/L corresponding to 0.00022 mg Thifensulfuron-methyl/kg	0.0034 µg Metsulfuron-methyl /L corresponding to 0.000068 mg Metsulfuron-methyl /kg
Limit of Quantification:	10 µg Thifensulfuron-methyl/kg The LOQ is defined as the mean nominal concentration of the lowest validated concentration level.	10 µg Metsulfuron-methyl /kg plant The LOQ is defined as the mean nominal concentration of the lowest validated concentration level
Accuracy of the Analytical Method:	**Mean recovery rate of Thifensulfuron-methyl in the fortified plant samples - quantifier:** 10 µg Thifensulfuron-methyl/kg plant: 84 % (n = 5; RSD = 6 %) 100 µg Thifensulfuron-methyl/kg plant: 88 % (n = 5; RSD = 7 %) Overall mean recovery: 86 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified** plant samples - qualifier: 10 µg Thifensulfuron-methyl/kg plant: 85 % (n = 5; RSD = 7 %) 100 µg Thifensulfuron-methyl/kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 87 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified grains samples - quantifier:** 10 µg Thifensulfuron-methyl/kg	**Mean recovery rate of Metsulfuron-methyl in the fortified plant samples - quantifier:** 10 µg Metsulfuron-methyl /kg plant: 86 % (n = 5; RSD = 6 %) 100 µg Metsulfuron-methyl /kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 87 % (n = 10; RSD = 6 %) **Mean recovery rate of Metsulfuron-methyl in the fortified plant samples - qualifier:** 10 µg Metsulfuron-methyl /kg plant: 86 % (n = 5; RSD = 6 %) 100 µg Metsulfuron-methyl /kg plant: 89 % (n = 5; RSD = 6 %) Overall mean recovery: 88 % (n = 10; RSD = 6 %) **Mean recovery rate of Metsulfuron-methyl in the fortified grains samples - quantifier:** 10 µg Metsulfuron-methyl/kg grains: 84 % (n = 5; RSD = 4 %)

	grains: 84 % (n = 5; RSD = 4 %) 100 µg Thifensulfuron-methyl/kg grains: 89 % (n = 5; RSD = 5 %) Overall mean recovery: 87 % (n = 10; RSD = 7 %) **Mean recovery rate of Thifensulfuron-methyl in the fortified grains samples - qualifier:** 10 µg Thifensulfuron-methyl/kg grains: 94 % (n = 5; RSD = 4 %) 100 µg Thifensulfuron-methyl/kg grains: 98 % (n = 5; RSD = 4 %) Overall mean recovery: 96 % (n = 10; RSD = 6 %)	100 µg Metsulfuron-methyl/kg grains: 91 % (n = 5; RSD = 3 %) Overall mean recovery: 87 % (n = 10; RSD = 5 %) **Mean recovery rate of Metsulfuron-methyl in the fortified grains samples - qualifier:** 10 µg Metsulfuron-methyl/kg grains: 98 % (n = 5; RSD = 5 %) 100 µg Metsulfuron-methyl/kg grains: 100 % (n = 5; RSD = 3 %) Overall mean recovery: 99 % (n = 10; RSD = 4 %)
Precision of the Analytical Method:	Relative standard deviation: 7 % for plants and grains.	Relative standard deviation: 6 % for plants and 5 % for grains.
Storage Stability:	**Stability of Thifensulfuron-methyl in plant samples - quantifier:** 86 µg Thifensulfuron-methyl/kg plant: 79 % (n = 2; RSD = 8 %) **Stability of Thifensulfuron-methyl in plant samples - qualifier:** 86 µg Thifensulfuron-methyl/kg plant: 81 % (n = 2; RSD = 7 %)	**Stability of Metsulfuron-methyl in plant samples - quantifier:** 87 µg Metsulfuron-methyl/kg plant: 83 % (n = 2; RSD = 6 %) **Stability of Metsulfuron-methyl in plant samples - qualifier:** 87 µg Metsulfuron-methyl/kg plant: 83 % (n = 2; RSD = 5 %)
Repeatability of Injection:	The standard deviation obtained from a five-fold injection of two single calibration standards was max. 3.3 %.	The standard deviation obtained from a five-fold injection of two single calibration standards was max. 4.2 %.

Application of the Test Item

Application Date: April 09, 2015

Table 2. Concentration of the Test Item Spraying Dilution

	Water Volume [L/ha]	Concentration of Spraying Dilution [g/L]		Concentration of Spraying Dilution (g in 5000 mL)		Target Volume / plot (L)
		TOTO 75 SG	Asystent+	TOTO 75 SG	Asystent+	
Application	300	0.3	0.34	1.5	1.7	3.0

Application

Application of the Test Item:	The application was carried out according to critical Good Agricultural Practice (cGAP) for each experimental plot during daytime, with standard field spraying equipment. The test item was sprayed onto the soil surface using an adapted plot sprayer.
Application of the Control:	The control was left untreated.
Application Equipment:	Movable plot sprayer for field application; type "*PSG-System 4*" (Fa. Schachtner Gerätetechnik, 71640 Ludwigsburg, Germany), with an extension tube including 5 spraying nozzles (Lechler IDK 120-04; distance between nozzles: 50 cm) operating with compressed air and a boom width of 250 cm. Distance between the nozzles and soil was approx. 50 cm. The plot was sprayed by four passes of the plot sprayer.
Verification of Application:	The sprayer was calibrated before application in order to ensure the exact amount of spray application. The calibration was conducted by measuring the spray volume per time per nozzle at a fixed pressure. This procedure was repeated 3 times to ensure that the application rate was 300 L/ha ± 10 %. A visual check demonstrated that no nozzles were leaking or blocked. A calibrated volumetric flow instrument gave the exact amount of the actual application. The results of the application data as well as the verification data is documented in the raw data.
Spraying Pressure:	2.0 bar;
Distance Between Nozzle and Soil:	Approximately 50 cm
Water Amount in this Study:	300 L tap water/ha with max. deviation of ±10 %. The spraying solution preparation had a volume of 5 L to ensure sufficient spray solution for the plot plus a reserve.
Deviation from Target [%]:	

	plot I ($100 m^2$)
Test Item*	+2.7

* Deviation from the Target [%] based on a calibrated volumetric flow instrument which gave the exact amount of the actual application for each plot.

Documentation:	Application details are stored in the raw data
Climatic Conditions during the Application:	Air temperature: min: 18.3°C; max: 18.5°C Soil temperature: 13.0°C Relative humidity: min: 47.5 %; max: 48.3% Wind Velocity: min: 0.4 m/s; max: 1.7 m/s

Spraying Solution:	A specimen (approx. 20 mL) of the spray solution preparation from the application was taken for the test item and stored frozen (≤ -20°C) after transfer to ibacon.

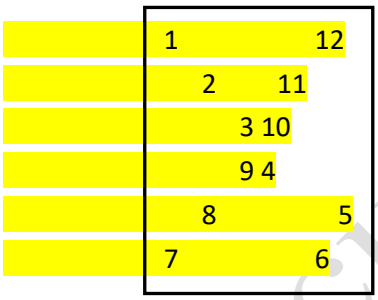
Course of the Test

The application of 90 g/ha TOTO 75 SG and 100 mL/ha adjuvant was at BBCH 30 and the control was left untreated.

The duration of the test was approximately four months from application in April to harvest in July (because of the weather conditions harvest was earlier than expected).

Replication:	1 plot for the harvest trail and 1 control trail.
Size of the Plots:	100 m² for the harvest trial and for the control trial with at least with 3 m distance between each plot
Exposure Time:	Approximately 4 months (from April 2015 to July 2015)
	Harvest Sampling 105 Days after application July 23, 2015

Wheat Collection

Number of Samples per Plot/Treatment:	Two mixed samples per plot (one for analysis, one as retain sample) per sampling. Each mixed sample consists of 12 subsamples taken from 12 different areas.
Sampling Method:	Wheat samples were taken manually at harvest. The material for field samples was selected systematically from each plot along an "X"-pattern.  In order to avoid contamination samples from control plot was taken prior to the samples from test item treated plot.
Retain Samples:	A second set of samples was taken in the same way as the other samples on each sampling date as residue samples.
Sampling Date:	The mixed grain sample weighed ca. 1 kg and the mixed straw sample weighed ca. 0.5 kg. The control plot was shared with the simultaneously running field residue decline study (ibacon study no. 103141104).
Interim Storage:	Directly after sampling, each mixed specimen was transferred into a suitable labelled container (plastic bags) and stored in a shady and dry place. Temperature conditions were recorded using a tiny tag datalogger.
Labelling:	Each specimen was uniquely identified with at least study number, treatment group and day of sampling.
Plant Height:	The plant height was recorded the day of sampling.

BBCH Scale:	The phenological growth stages of each plot were recorded at each sampling date using the BBCH-identification key for Wheat (Witzenberger et al., 1989; Lancashire et al., 1991).		
	Sampling	BBCH Scale	Plant height [cm]
	Date of application	29 – 31 (mean 30)	15
	Harvest Sampling 105 Days after application ():	89	55 - 80

Summary of results:

day after application	matrix	harvest trial: total sample amount [g]	harvest trial: concentration analysed Thifensulfuron-methyl [mg a.i./kg]	harvest trial: concentration analysed Metsulfuron-methyl [mg a.i./kg]
(harvest) 105	straw	817.45	< LOD	< LOD
(harvest) 105	heads	1101.10	< LOD	< LOD

LOQ: Limit of Quantification = 0.01 mg Thifensulfuron-methyl/kg
LOD = Limit of Detection = 0.011 µg/L corresponding to 0.00022 mg Thifensulfuron-methyl /kg
LOQ: Limit of Quantification = 0.01 mg Metsulfuron-methyl/kg
LOD = Limit of Detection = 0.0034 µg/L corresponding to 0.000068 mg Metsulfuron-methyl /kg

The analytical method was validated according to SANCO guideline 3029/99. All validity criteria were considered fulfilled.

There were no detectable levels of residues in the grain and straw specimens taken at harvest.

Study No. B7040

Study title: Generation of Field Specimens for the determination of Thifensulfuron methyl and Metsulfuron methyl Residues in Winter Wheat Following Foliar application with TOTO 75 SG under Field Conditions in Poland in 2017

Final report No. R B7040

Author: Mrs Corinne ERTUS

GLP: Yes

The objective of the study was to generate specimens of winter wheat raw agricultural commodity after one foliar application of the formulated product TOTO 75 SG (682 g thifensulfuron methyl/kg, 68 g metsulfuron methyl/kg), at the rate of 0.09 kg/ha.

The study consisted of one single phase: the field phase.

The study was conducted under field conditions at 2 sites in Poland. The trials were sampled frequently to monitor the decline of residues shortly after the last treatment and at harvest.

In each trial one plot was treated once with TOTO 75 SG at the application rate of 0.09 kg/ha (0.0614 kg thifensulfuron methyl/ha, 0.0061 kg metsulfuron methyl/ha). The application was made at BBCH 30-31 (as close as possible of BBCH 31).

One plot remained untreated.

Plot	Test Item	App. No.	Target timing	Application Rate of the Formulated Product	Application Rate of the active substance	Spray volume
U	Untreated	-	-	-	-	-
T	TOTO 75 SG + Asystent **	T1	BBCH 30-31*	90 g / ha	Thifensulfuron-Me: 0.0614 kg / ha Metsulfuron-Me: 0.0061 kg / ha	300 L/ha (±10%)

* As close as possible of BBCH 31

** Adjuvant rate: 0.1 L/ha

In each trial (trial no B7040 PL1 and B7040 PL2) sampling was performed just after application, then at 20 (±1), 42 (±1), 61 (±1) and at BBCH 89 normal harvest (at maturity of the grain).

Samples generated during this study were sent for analysis to FOOD SAFETY LABORATORY.

List of specimens sampled

Field Sample No.*	Sampling date	DALA	Growth stage (BBCH)	Matrix	Number of units / zones	Specimen size (kg)	Sampling to freezing time
B7040 PL1 / U0 / A	01/05/2017	0	30-31	Whole plant	>12/12	1.050	4h15
B7040 PL1 / U0 / R	01/05/2017	0	30-31	Whole plant	>12/12	1.062	4h15
B7040 PL1 / T0 / A	01/05/2017	0	30-31	Whole plant	>12/12	1.042	1h30
B7040 PL1 / T0 / R	01/05/2017	0	30-31	Whole plant	>12/12	1.044	1h30
B7040 PL1 / U20 / A	22/05/2017	21	37-39	Whole plant	>12/12	1.832	2h30
B7040 PL1 / U20 / R	22/05/2017	21	37-39	Whole plant	>12/12	1.794	2h30
B7040 PL1 / T20 / A	22/05/2017	21	37-39	Whole plant	>12/12	1.884	1h55
B7040 PL1 / T20 / R	22/05/2017	21	37-39	Whole plant	>12/12	1.952	1h55
B7040 PL1 / U42 / A	12/06/2017	42	65	Whole plant	>12/12	1.566	1h55
B7040 PL1 / U42 / R	12/06/2017	42	65	Whole plant	>12/12	1.666	1h55
B7040 PL1 / T42 / A	12/06/2017	42	65	Whole plant	>12/12	1.644	1h35
B7040 PL1 / T42 / R	12/06/2017	42	65	Whole plant	>12/12	1.594	1h35
B7040 PL1 / U61 / A	30/06/2017	60	75-77	Whole plant	>12/12	2.182	1h55
B7040 PL1 / U61 / R	30/06/2017	60	75-77	Whole plant	>12/12	2.142	1h55
B7040 PL1 / T61 / A	30/06/2017	60	75-77	Whole plant	>12/12	2.026	1h25
B7040 PL1 / T61 / R	30/06/2017	60	75-77	Whole plant	>12/12	2.112	1h25
B7040 PL1 / UHg / A	03/08/2017	94	89	Grain	>12/12	1.426	3h15
B7040 PL1 / UHg / R	03/08/2017	94	89	Grain	>12/12	1.416	3h15
B7040 PL1 / UHs / A	03/08/2017	94	89	Straw	>12/12	1.010	3h15
B7040 PL1 / UHs / R	03/08/2017	94	89	Straw	>12/12	0.944**	3h15
B7040 PL1 / THg / A	03/08/2017	94	89	Grain	>12/12	1.430	2h11
B7040 PL1 / THg / R	03/08/2017	94	89	Grain	>12/12	1.438	2h11
B7040 PL1 / THs / A	03/08/2017	94	89	Straw	>12/12	0.882**	2h11
B7040 PL1 / THs / R	03/08/2017	94	89	Straw	>12/12	0.846**	2h11

Field Sample No.*	Sampling date	DALA	Growth stage (BBCH)	Matrix	Number of units / zones	Specimen size (kg)	Sampling to freezing time
B7040 PL2 / U0 / A	16/05/2017	0	30-31	Whole plant	>12/12	1.012	2h15
B7040 PL2 / U0 / R	16/05/2017	0	30-31	Whole plant	>12/12	1.048	2h15
B7040 PL2 / T0 / A	16/05/2017	0	30-31	Whole plant	>12/12	1.276	0h50
B7040 PL2 / T0 / R	16/05/2017	0	30-31	Whole plant	>12/12	1.318	0h50
B7040 PL2 / U20 / A	05/06/2017	20	45-47	Whole plant	>12/12	1.626	2h20
B7040 PL2 / U20 / R	05/06/2017	20	45-47	Whole plant	>12/12	1.716	2h20
B7040 PL2 / T20 / A	05/06/2017	20	45-47	Whole plant	>12/12	1.438	2h05
B7040 PL2 / T20 / R	05/06/2017	20	45-47	Whole plant	>12/12	1.500	2h05
B7040 PL2 / U42 / A	27/06/2017	42	69-71	Whole plant	>12/12	1.504	1h05
B7040 PL2 / U42 / R	27/06/2017	42	69-71	Whole plant	>12/12	1.526	1h05
B7040 PL2 / T42 / A	27/06/2017	42	69-71	Whole plant	>12/12	1.514	0h35
B7040 PL2 / T42 / R	27/06/2017	42	69-71	Whole plant	>12/12	1.634	0h35
B7040 PL2 / U61 / A	15/07/2017	60	77	Whole plant	>12/12	2.484	0h55
B7040 PL2 / U61 / R	15/07/2017	60	77	Whole plant	>12/12	2.182	0h55
B7040 PL2 / T61 / A	15/07/2017	60	77	Whole plant	>12/12	2.196	0h40
B7040 PL2 / T61 / R	15/07/2017	60	77	Whole plant	>12/12	2.198	0h40
B7040 PL2 / UHg / A	01/08/2017	77	89	Grain	>12/12	1.104	1h45
B7040 PL2 / UHg / R	01/08/2017	77	89	Grain	>12/12	1.090	1h45
B7040 PL2 / UHs / A	01/08/2017	77	89	Straw	>12/12	0.762**	1h45
B7040 PL2 / UHs / R	01/08/2017	77	89	Straw	>12/12	0.732**	1h45
B7040 PL2 / THg / A	01/08/2017	77	89	Grain	>12/12	1.138	0h40
B7040 PL2 / THg / R	01/08/2017	77	89	Grain	>12/12	1.128	0h40
B7040 PL2 / THs / A	01/08/2017	77	89	Straw	>12/12	0.940**	0h40
B7040 PL2 / THs / R	01/08/2017	77	89	Straw	>12/12	0.982**	0h40

Analytical part were performed in Food Safety Laboratory, results are presented in the report summarized below:

Study Code/No.: ZBBZ-2017/01/DPL/1

Study Title: Determination of Thifensulfuron-methyl and Metsulfuron-methyl Residues in Winter Wheat Samples After Application of "TOTO 75 SG"

Guidelines: SANCO/3029/99 rev. 4, SANCO/825/00 rev. 8.1

Study Director: Piotr Sikorski

GLP: Yes

The objective of this study was to determine the decline and the magnitude of residues of Thifensulfuron-methyl and Metsulfuron-methyl in winter wheat plants, straw and grain taken from the field trial following application of TOTO 75 SG.

The general principles of the analytical procedure were based on the normalized method EN 15662:2008. In brief, samples of winter wheat plants, straw and grain were extracted with acetonitrile after addition of water. After addition of a buffer-salt mixture containing magnesium sulfate, sodium chloride and sodium citrate the extract was shaken. Following centrifugation, an aliquot of the upper acetonitrile phase was diluted with water and injected into the LC-MS/MS.

Selectivity and Confirmation of Residue Identity

Quantification was performed by use of highly selective liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Two selected ion mass transitions were evaluated in order to demonstrate that the method achieves a high level of selectivity. The retention times of analytes in extracts corresponds to that of the calibration standards with a tolerance of < ± 0.1 min. Confirmation ion ratios for Thifensulfuron-methyl and Metsulfuron-methyl in all samples were within ± 30 % of the average found for the standards.

No significant interference above 30 % of LOQ was detected in any of the reagent blanks or control specimen extracts for winter wheat plants, straw and grain matrices, so that a highly level of selectivity was demonstrated and an additional confirmatory method is not necessary.

Matrix Effects

Matrix effects on the detection of Thifensulfuron-methyl and Metsulfuron-methyl vary between ion mass transitions. Matrix effects on the detection of Thifensulfuron-methyl for quantitative ion mass transition (388.2→167.3) in extracts of winter wheat plants, straw and grain were greater than 20% and thus considered significant, according to SANCO guidelines. Matrix effects on the detection of Metsulfuron-methyl for quantitative ion mass transition (382.2→167.1) in extracts of winter wheat plants and grain except for straw were greater than 20% and thus considered significant, according to SANCO guidelines. Matrix-matched standards were used for quantification.

Linearity

The linearity of the detector response for Thifensulfuron-methyl and Metsulfuron-methyl were demonstrated by single determination of matrix-matched calibration standards at eight concentration levels ranging from 0.00025 µg/mL to 0.5 µg/mL for winter wheat plants and grain and from 0.0001 µg/mL to 0.25 µg/mL for straw. These ranges corresponds from 0.0025 mg/kg to 5 mg/kg for winter wheat plants and grain and from 0.002 mg/kg to 5 mg/kg for winter wheat straw thus covering the range from no more than 30% of the LOQ and at least + 20 % of the highest analyte concentration level detected in samples.

The calibration curves obtained for both ion mass transitions of target analytes and matrices were linear with the coefficients of correlation (R) greater than 0.99. Linear regression was performed with 1/x weighting.

Stability of Analytes in Extracts

The stability of analyte in extracts was not tested specifically. Recoveries of the fortified samples within the acceptable range of 70-110% obtained with calibration solutions and the use of bracketing standards to insure integrity of the analytical sequence sufficiently demonstrate the stability.

Accuracy and Precision

The mean recovery values at the fortification levels of 0.01 mg/kg and 0.1 mg/kg for both ion mass transitions were all in the range 70 – 110 % and thus comply with the standard acceptance criteria of the guidance documents SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4. All precision values at the fortification levels of 0.01 mg/kg and 0.1 mg/kg for both ion mass transitions were < 20%. Mean recovery and precision results for both ion mass transitions Metsulfuron-methyl are shown in Table below.

Analyte	Matrix	Fortification Level (mg/kg)	Mean Recovery (%)	RSD (%)	n	Overall Mean Recovery (%)	Overall RSD (%)
Metsulfuron-methyl	Quantification Ion Mass Transition 382.2→167.1						
	Winter wheat (plants)	0.01*	94	3.6	5	94	2.5
		0.1	94	1.0	5		
	Winter wheat (straw)	0.01*	97	2.1	5	96	2.0
		0.1	95	0.9	5		
	Winter wheat (grain)	0.01*	87	5.2	5	89	4.5
		0.1	91	3.0	5		
	Confirmation Ion Mass Transition 382.2→141.1						
	Winter wheat (plants)	0.01*	99	4.3	5	97	3.7
		0.1	95	1.0	5		
	Winter wheat (straw)	0.01*	90	7.8	5	94	6.8
		0.1	98	2.5	5		
	Winter wheat (grain)	0.01*	94	6.8	5	94	4.7
		0.1	94	1.6	5		

*-Limit of quantification, defined by the lowest validated fortification level

Limit of Quantification (LOQ) and Limit of Detection (LOD)

The limit of quantification (LOQ) is the lowest validated fortification level and was thus successfully established at 0.01 mg/kg for both ion mass transitions of Metsulfuron-methyl in winter wheat plants, straw and grain matrices.

The limits of detection (LOD) for Metsulfuron-methyl were set at 0.0025 mg/kg for winter wheat plants and grain and at 0.002 mg/kg for winter wheat straw, which is < 30% of the LOQ.

Results obtained for the analysis of winter wheat plants, straw and grain

Field Trial Sample Code	Type	Sampling DALA	Variant	Lab. Sample ID	Total Residues [mg/kg]	
					Thifensulfuron-methyl	Metsulfuron-methyl
B7040 PL1/U0/A	Plant	0	Untreated	17/01/DPL/1/1	< LOD	< LOD
B7040 PL1/T0/A	Plant		Treated	17/01/DPL/1/2	**1.24**	**0.303**
B7040 PL1/U20/A	Plant	20	Untreated	17/01/DPL/1/3	< LOD	< LOD
B7040 PL1/T20/A	Plant		Treated	17/01/DPL/1/4	**< LOQ**	< LOD
B7040 PL1/U42/A	Plant	42	Untreated	17/01/DPL/1/5	< LOD	< LOD
B7040 PL1/T42/A	Plant		Treated	17/01/DPL/1/6	<LOD	< LOD
B7040 PL1/U61/A	Plant	61	Untreated	17/01/DPL/1/7	< LOD	< LOD
B7040 PL1/T61/A	Plant		Treated	17/01/DPL/1/8	< LOD	< LOD
B7040 PL1/UHs/A	Straw	Harvest	Untreated	17/01/DPL/1/9	< LOD	< LOD
B7040 PL1/THs/A	Straw		Treated	17/01/DPL/1/10	< LOD	< LOD
B7040 PL1/UHg/A	Grain	Harvest	Untreated	17/01/DPL/1/11	< LOD	< LOD
B7040 PL1/THg/A	Grain		Treated	17/01/DPL/1/12	< LOD	< LOD
B7040 PL2/U0/A	Plant	0	Untreated	17/01/DPL/1/13	< LOD	< LOD
B7040 PL2/T0/A	Plant		Treated	17/01/DPL/1/14	**0.841**	**0.198**
B7040 PL2/U20/A	Plant	20	Untreated	17/01/DPL/1/15	< LOD	< LOD
B7040 PL2/T20/A	Plant		Treated	17/01/DPL/1/16	< LOD	< LOD
B7040 PL2/U42/A	Plant	42	Untreated	17/01/DPL/1/17	< LOD	< LOD
B7040 PL2/T42/A	Plant		Treated	17/01/DPL/1/18	< LOD	< LOD
B7040 PL2/U61/A	Plant	61	Untreated	17/01/DPL/1/19	< LOD	< LOD
B7040 PL2/T61/A	Plant		Treated	17/01/DPL/1/20	< LOD	< LOD
B7040 PL2/UHs/A	Straw	Harvest	Untreated	17/01/DPL/1/21	< LOD	< LOD
B7040 PL2/THs/A	Straw		Treated	17/01/DPL/1/22	< LOD	< LOD
B7040 PL2/UHg/A	Grain	Harvest	Untreated	17/01/DPL/1/23	< LOD	< LOD
B7040 PL2/THg/A	Grain		Treated	17/01/DPL/1/24	< LOD	< LOD

LOD: Limit of Detection = 0.0025 mg/kg (for winter wheat plants and grain), 0.002 mg/kg (for winter wheat straw)
LOQ: Limit of Quantification = 0.01 mg/kg
DALA: Days After Last Application

Conclusions

The method was shown to be highly selective, as it includes two parent-daughter ion mas transitions for Thifensulfuron-methyl and Metsulfuron-methyl, and it yields accurate and repeatable results. The limit of quantification (LOQ) was established at 0.01 mg/kg for target analytes, interfering signals in control specimens were negligible, and thus the limit of detection (LOD) is 0.0025 mg/kg for winter wheat plants and grain and 0.002 mg/kg for winter wheat straw.

It is conclude that method fulfils the requirements as defined in EC Guidance documents on residue analytical methods (SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4) and is, applicable as enforcement and data generation method for determination of Thifensulfuron-methyl and Metsulfuron-methyl in winter wheat plants, straw and grain after application of TOTO 75 SG.

Residues of active ingredients Thifensulfuron-methyl and Metsulfuron-methyl were not detectable in the control samples at any time of sampling.

Metsulfuron-methyl were found in plant samples taken from the decline plots on the day of application, but on day 42 after application were below the limit of detection.

The levels of Metsulfuron-methyl residues were not detectable in the winter wheat straw and grain specimens taken at harvest.

Study Code/No.: ZBBZ-2017/18/DPL/1

Study Title: Determination of the Residues of Metabolite IN-A4098 in Winter Wheat Samples After Application of "TOTO 75 SG"

Guidelines: SANCO/3029/99 rev. 4, SANCO/825/00 rev. 8.1

Study Director: Piotr Sikorski

GLP: Yes

The objective of this study was to determine magnitude of the residues of metabolite IN-A4098 in winter wheat plants, straw and grain matrices taken from the field trial following application of TOTO 75 SG. The general principles of the analytical procedure were based on the normalized method EN 15662:2008. In brief, samples of winter wheat plants, straw and grain were extracted with acetonitrile after addition of water. After addition of a buffer-salt mixture containing magnesium sulfate, sodium chloride and sodium citrate the extract was shaken. Following centrifugation, an aliquot of the upper acetonitrile phase was diluted with water and injected into the LC-MS/MS.

Selectivity and Confirmation of Residue Identity

Quantification was performed by use of highly selective liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Two selected ion mass transitions were evaluated in order to demonstrate that the method achieves a high level of selectivity. The retention times of target analyte in extracts corresponds to that of the calibration standards with a tolerance of < ± 0.1 min. Confirmation ion ratio for IN-A4098 in all samples were within ± 30 % of the average found for the standards.

No significant interference above 30 % of LOQ was detected in any of the reagent blanks or control specimen extracts for winter wheat plants, straw and grain matrices, so that a highly level of selectivity was demonstrated and an additional confirmatory method is not necessary.

Matrix Effects

Matrix effects on the detection of IN-A4098 in extracts of winter wheat plants, straw and grain was lesser than 20% and thus considered insignificant, according to SANCO guidelines. However matrix-matched standards were used for quantification.

Linearity

The linearity of the detector response for IN-A4098 was demonstrated by single determination of matrix-matched calibration standards at eight concentration levels ranging from 0.00025 µg/mL to 0.5 µg/mL for winter wheat plants and grain and from 0.0001 µg/mL to 0.25 µg/mL for straw. These ranges corresponds from 0.0025 mg/kg to 5 mg/kg for winter wheat plants and grain and from 0.002 mg/kg to 5 mg/kg for winter wheat straw thus covering the range from no more than 30% of the LOQ and at least + 20 % of the highest analyte concentration level detected in samples.

The calibration curves obtained for both ion mass transitions of target analyte and matrices were linear with the coefficients of correlation (R) greater than 0.99.

Stability of Analyte in Extracts

The stability of analyte in extracts was not tested specifically. Recoveries of the fortified samples within the acceptable range of 70-110% obtained with calibration solutions and the use of bracketing standards to insure integrity of the analytical sequence sufficiently demonstrate the stability.

Accuracy and Precision

The mean recovery values at the fortification levels of 0.01 mg/kg and 0.1 mg/kg for both ion mass transitions were all in the range 70 – 110 % and thus comply with the standard acceptance criteria of the guidance document SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4. All precision values at the fortification levels of 0.01 mg/kg and 0.1 mg/kg for both ion mass transitions were < 20%.

Mean recovery and precision results for both ion mass transitions of IN-A4098 are shown in Table below.

Analyte	Matrix	Fortification Level (mg/kg)	Mean Recovery (%)	RSD (%)	n	Overall Mean Recovery (%)	Overall RSD (%)
IN-A4098	Quantification Ion Mass Transition 141.2→57.1						
	Winter wheat (plants)	0.01*	83	1.4	5	84	1.8
		0.1	85	0.6	5		
	Winter wheat (straw)	0.01*	77	3.3	5	77	2.8
		0.1	78	2.1	5		
	Winter wheat (grain)	0.01*	80	2.1	5	81	3.1
		0.1	82	3.0	5		
	Confirmation Ion Mass Transition 141.2→58.1						
	Winter wheat (plants)	0.01*	83	2.5	5	84	2.4
		0.1	86	0.3	5		
	Winter wheat (straw)	0.01*	77	2.9	5	77	2.8
		0.1	78	2.5	5		
	Winter wheat (grain)	0.01*	81	3.4	5	82	3.0
		0.1	82	2.8	5		

*-Limit of quantification, defined by the lowest validated fortification level

Limit of Quantification (LOQ) and Limit of Detection (LOD)

The limit of quantification (LOQ) is the lowest validated fortification level and was thus successfully established at 0.01 mg/kg for both ion mass transitions of IN-A4098 in winter wheat plants, straw and grain matrices.

The limit of detection (LOD) for IN-A4098 was set at 0.0025 mg/kg for winter wheat plants and grain and 0.002 mg/kg for winter wheat straw, which is < 30% of the LOQ.

Results obtained for the analysis of winter wheat plants, straw and grain

Field Trial Sample Code	Type	Sampling DALA	Variant	Lab. Sample ID	Total Residues [mg/kg]
					IN-A4098
B7040 PL1/U0/A	Plant	0	Untreated	17/18/DPL/1/1	< LOD
B7040 PL1/T0/A	Plant		Treated	17/18/DPL/1/2	**0.028**
B7040 PL1/U20/A	Plant	20	Untreated	17/18/DPL/1/3	< LOD
B7040 PL1/T20/A	Plant		Treated	17/18/DPL/1/4	< LOD
B7040 PL1/U42/A	Plant	42	Untreated	17/18/DPL/1/5	< LOD
B7040 PL1/T42/A	Plant		Treated	17/18/DPL/1/6	< LOD
B7040 PL1/U61/A	Plant	61	Untreated	17/18/DPL/1/7	< LOD
B7040 PL1/T61/A	Plant		Treated	17/18/DPL/1/8	< LOD
B7040 PL1/UHs/A	Straw	Harvest	Untreated	17/18/DPL/1/9	< LOD
B7040 PL1/THs/A	Straw		Treated	17/18/DPL/1/10	< LOD
B7040 PL1/UHg/A	Grain	Harvest	Untreated	17/18/DPL/1/11	< LOD
B7040 PL1/THg/A	Grain		Treated	17/18/DPL/1/12	< LOD
B7040 PL2/U0/A	Plant	0	Untreated	17/18/DPL/1/13	< LOD
B7040 PL2/T0/A	Plant		Treated	17/18/DPL/1/14	**0.022**
B7040 PL2/U20/A	Plant	20	Untreated	17/18/DPL/1/15	< LOD
B7040 PL2/T20/A	Plant		Treated	17/18/DPL/1/16	< LOD
B7040 PL2/U42/A	Plant	42	Untreated	17/18/DPL/1/17	< LOD
B7040 PL2/T42/A	Plant		Treated	17/18/DPL/1/18	< LOD
B7040 PL2/U61/A	Plant	61	Untreated	17/18/DPL/1/19	< LOD
B7040 PL2/T61/A	Plant		Treated	17/18/DPL/1/20	< LOD
B7040 PL2/UHs/A	Straw	Harvest	Untreated	17/18/DPL/1/21	< LOD
B7040 PL2/THs/A	Straw		Treated	17/18/DPL/1/22	**< LOQ**
B7040 PL2/UHg/A	Grain	Harvest	Untreated	17/18/DPL/1/23	< LOD
B7040 PL2/THg/A	Grain		Treated	17/18/DPL/1/24	< LOD

LOD: Limit of Detection = 0.0025 mg/kg (for winter wheat plants and grain), 0.002 mg/kg (for winter wheat straw)
LOQ: Limit of Quantification = 0.01 mg/kg
DALA: Days After Last Application

Conclusions

The method was shown to be highly selective, as it includes two parent-daughter ion mas transitions for IN-A4098, and it yields accurate and repeatable results. The limit of quantification (LOQ) was established at 0.01 mg/kg for target analyte, interfering signals in control specimens were negligible, and thus the limit of detection (LOD) is 0.0025 mg/kg for winter wheat plants and grain and 0.002 mg/kg for winter wheat straw.

It is conclude that method fulfils the requirements as defined in EC Guidance documents on residue analytical methods (SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4 and is, applicable as enforcement and data generation method for determination of IN-A4098 in winter wheat plants, straw and grain after application of TOTO 75 SG.

Residues of metabolite IN-A4098 were not detectable in the control (untreated) samples at any time of sampling.

IN-A4098 was found in plant samples taken from the decline plots on the day of application, but on day 20 after application was below the limit of detection.

IN-A4098 residues were found below limit of quantification in straw sample taken at harvest and were not detectable in the winter wheat grain specimens.

Conclusion:

In none of the 4 field trials, metsulfuron-methyl and thifensulfuron methyl residues were found above the limit of quantification. Also presented studies (two trials) showing no residues of metabolite IN-4098 above the limit of quantification.. Considering this, no residues of metsulfuron-methyl and its metabolite IN-A4098 and thifensulfuron methyl should be expected after the TOTO 75 SG has been used.

Study No. B78109

Study title: Generation of Field Specimens for the determination of Thifensulfuron-methyl, Metsulfuron-methyl and their metabolites Residues in Winter Wheat Following Foliar application with TOTO 75 SG under Field Conditions in Poland in 2018

Final report No. R B8109

Author: Mrs Corinne ERTUS

GLP: Yes

The objective of the study was to generate specimens of winter wheat raw agricultural commodity after one foliar application of the formulated product TOTO 75 SG (682 g thifensulfuron-methyl/kg, 68 g metsulfuron-methyl/kg), at the rate of 0.09 kg/ha.

The study consisted of one phase: the field phase. The study was conducted under field conditions at 1 site in Poland. The trial was sampled frequently to monitor the decline of residues shortly after the treatment and at harvest.

One plot was treated once with TOTO 75 SG at the application rate of 0.09 kg/ha (61.38 g thifensulfuron-methyl/ha, 6.12 g metsulfuron-methyl/ha). The application was made at BBCH 32.

One plot remained untreated..

Plot	Test Item	App. No.	Target timing	Application Rate of the Formulated	Application Rate of the active substance	Spray volume

				Product		
U	Untreated	-	-	-	-	-
T	TOTO 75 SG + Asystent *	T1	BBCH 32	90 g / ha	Thifensulfuron-Methyl: 61.38 g / ha Metsulfuron-Methyl: 6.12 g / ha	300 L/ha (±10%)

* Adjuvant rate: 0.1 L/ha

Sampling was performed just after application, then at 21, 42, 58 days after application and at normal harvest, at maturity of the grain (BBCH 89).

Samples generated during this study were sent for analysis to Food Safety Laboratory.

List of specimens sampled

Field Sample No.*	Sampling date	DAA	Growth stage (BBCH)	Matrix	Number of units / zones	Specimen size (kg)	Sampling to freezing time
B8109 PL1 / U0 / A	07/05/2018	0	32	Whole plant	>12 / 12	1.334	2h40
B8109 PL1 / U0 / R	07/05/2018	0	32	Whole plant	>12 / 12	1.290	2h40
B8109 PL1 / T0 / A	07/05/2018	0	32	Whole plant	>12 / 12	1.212	1h00
B8109 PL1 / T0 / R	07/05/2018	0	32	Whole plant	>12 / 12	1.212	1h00
B8109 PL1 / U20 / A	28/05/2018	21	69	Whole plant	>12 / 12	1.664	1h45
B8109 PL1 / U20 / R	28/05/2018	21	69	Whole plant	>12 / 12	1.734	1h45
B8109 PL1 / T20 / A	28/05/2018	21	69	Whole plant	>12 / 12	1.438	1h25
B8109 PL1 / T20 / R	28/05/2018	21	69	Whole plant	>12 / 12	1.580	1h25
B8109 PL1 / U42 / A	18/06/2018	42	73-75	Whole plant	>12 / 12	1.670	1h45
B8109 PL1 / U42 / R	18/06/2018	42	73-75	Whole plant	>12 / 12	1.756	1h45
B8109 PL1 / T42 / A	18/06/2018	42	73-75	Whole plant	>12 / 12	1.648	1h20
B8109 PL1 / T42 / R	18/06/2018	42	73-75	Whole plant	>12 / 12	1.778	1h20
B8109 PL1 / U61 / A	04/07/2018	58	83	Whole plant	>12 / 12	1.828	1h00
B8109 PL1 / U61 / R	04/07/2018	58	83	Whole plant	>12 / 12	1.804	1h00
B8109 PL1 / T61 / A	04/07/2018	58	83	Whole plant	>12 / 12	1.606	0h55
B8109 PL1 / T61 / R	04/07/2018	58	83	Whole plant	>12 / 12	1.630	0h55
B8109 PL1 / UHg / A	09/08/2018	94	89	Grain	>12 / 12	1.218	3h35
B8109 PL1 / UHg / R	09/08/2018	94	89	Grain	>12 / 12	1.220	3h35
B8109 PL1 / UHs / A	09/08/2018	94	89	Straw	>12 / 12	1.076	3h35
B8109 PL1 / UHs / R	09/08/2018	94	89	Straw	>12 / 12	1.050	3h35
B8109 PL1 / THg / A	09/08/2018	94	89	Grain	>12 / 12	1.182	2h10
B8109 PL1 / THg / R	09/08/2018	94	89	Grain	>12 / 12	1.178	2h10
B8109 PL1 / THs / A	09/08/2018	94	89	Straw	>12 / 12	1.042	2h10
B8109 PL1 / THs / R	09/08/2018	94	89	Straw	>12 / 12	1.044	2h10

*..... / A: Specimen for analysis
/ R: Spare specimen
DAA: days after application

Analytical part were performed in Food Safety Laboratory, results are presented in the report summarized below:

Study Code/No.: ZBBZ-2018/12/DPL/1

Study Title: DETERMINATION OF THIFENSULFURON-METHYL, METSULFURON-METHYL AND IN-A4098 RESIDUES IN WINTER WHEAT SAMPLES FOLLOWING FOLIAR APPLICATION WITH ”TOTO 75 SG” UNDER FIELD CONDITIONS IN POLAND IN 2018

Guidelines: Regulation (EC) No 1107/2009 of the European Parliament and of the Council

of 21-Oct-2009 concerning the placing of plant protection products on the market and

repealing council Directives 79/117/EEC and 91/414/EC

Guideline 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009

EU Guidance Document SANCO/3029/99 rev. 4

EU Guidance Document SANCO/825/00 rev. 8.1

Study Director: Anna Markowicz

GLP: Yes

The objective of this study was to determine the decline and the magnitude of residues of Thifensulfuron-methyl, Metsulfuron-methyl and their metabolite IN-A4098 in winter wheat plants, straw and grain taken from the field trial following application of TOTO 75 SG. To achieve the objective appropriate analytical method for determination of target analytes in plant material was validated in accordance to the guidance documents SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4 of the European Commission and to meet residue regulatory requirements. The validation data were presented in the Final Report No. ZBBZ-2018/12/DPL/1 and Final Report No. ZBBZ-2017/18/DPL/1. Validated limit of quantification is 0.01 mg/kg.

The general principles of the analytical procedure were based on the normalized method EN 15662:2008. In brief, samples of winter wheat plants, straw and grain were extracted with acetonitrile after addition of water. After addition of a buffer-salt mixture containing magnesium sulfate, sodium chloride and sodium citrate the extract was shaken. Following centrifugation, an aliquot of the upper acetonitrile phase was diluted with water and injected into the LC-MS/MS..

Selectivity and Confirmation of Residue Identity

Quantification was performed by use of highly selective liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Two selected ion mass transitions were evaluated in order to demonstrate that the method achieves a high level of selectivity. The retention times of analytes in extracts corresponds to that of the calibration standards with a tolerance of < ± 0.1 min. Confirmation ion ratios for Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 in all samples were within ± 30 % of the average found for the standards..

Matrix Effects

Determination was performed using matrix-matched calibration standards.

Linearity

The linearity of the detector response for Thifensulfuron-methyl and Metsulfuron-methyl were demonstrated by single determination of matrix-matched calibration standards at eight concentration levels ranging from 0.00025 µg/mL to 0.5 µg/mL for winter wheat plants and grain and from 0.0001 µg/mL to 0.25 µg/mL for straw. These ranges corresponds from 0.0025 mg/kg

to 5 mg/kg for winter wheat plants and grain and from 0.002 mg/kg to 5 mg/kg for winter wheat straw thus covering the range from no more than 30% of the LOQ and at least + 20 % of the highest analyte concentration level detected in samples.

The calibration curves obtained for both ion mass transitions of target analytes and matrices were linear with the coefficients of correlation (R) greater than 0.99. Linear regression was performed with 1/x weighting.

Stability of Analytes in Extracts

The stability of analyte in extracts was not tested specifically. Recoveries of the fortified samples within the acceptable range of 70-110% obtained with calibration solutions and the use of bracketing standards to insure integrity of the analytical sequence sufficiently demonstrate the stability.

Accuracy and Precision

Accuracy was determined by fortification of control samples with known amounts of the reference item and subsequent determination of the recoveries when applying the extraction procedure. Precision was determined by repeatability (relative standard deviation – RSD).

The mean recovery values at the fortification level of 0.01 mg/kg for both ion mass transitions of analytes were all in the range 70 – 110 % and thus comply with the standard acceptance criteria of the guidance documents SANCO/825/00, rev. 8.1. [1] and SANCO/3029/99, rev. 4 [2]. All precision values at the fortification level of 0.01 mg/kg for both ion mass transitions of analytes were < 20%. Mean recovery and precision results for both ion mass transitions Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 (Quality Control) are shown in Table below.

Analyte	Matrix	Fortification Level (mg/kg)	Mean Recovery (%)	RSD (%)	n
Thifensulfuron-methyl	Quantification Ion Mass Transition 388.1→167.3				
	Winter wheat (plants)	0.01	96	4.9	3
	Quantification Ion Mass Transition 388.1→141.3				
	Winter wheat (straw)	0.01	97	8.9	3
	Quantification Ion Mass Transition 388.1→167.3				
	Winter wheat (grain)	0.01	94	3.8	3
	Confirmation Ion Mass Transition 388.1→141.3				
	Winter wheat (plants)	0.01	100	3.2	3
	Confirmation Ion Mass Transition 388.1→167.3				
	Winter wheat (straw)	0.01	97	10.0	3
	Confirmation Ion Mass Transition 388.1→141.3				
	Winter wheat (grain)	0.01	101	5.7	3

Analyte	Matrix	Fortification Level (mg/kg)	Mean Recovery (%)	RSD (%)	n
Metsulfuron-methyl	Quantification Ion Mass Transition 382.1→167.1				
	Winter wheat (plants)	0.01	96	2.6	3
	Winter wheat (straw)	0.01	91	0.9	3
	Winter wheat (grain)	0.01	94	7.8	3
	Confirmation Ion Mass Transition 382.1→141.1				
	Winter wheat (plants)	0.01	96	0.6	3
	Winter wheat (straw)	0.01	95	5.7	3
	Winter wheat (grain)	0.01	93	5.7	3
IN-A4098	Quantification Ion Mass Transition 141.1→57.1				
	Winter wheat (plants)	0.01	79	1.1	3
	Winter wheat (straw)	0.01	71	3.5	3
	Winter wheat (grain)	0.01	77	5.6	3
	Confirmation Ion Mass Transition 141.1→58.1				
	Winter wheat (plants)	0.01	78	2.7	3
	Winter wheat (straw)	0.01	71	2.3	3
	Winter wheat (grain)	0.01	77	4.5	3

Results obtained for the analysis of winter wheat plants, straw and grain

Field Trial Sample Code	Type	Sampling DAA*	Plot	Lab. Sample ID	Total Residues [mg/kg]		
					Thifensulfuron-methyl	Metsulfuron-methyl	IN-A4098
B8109 PL1/U0/A	Plant	0	U**	18/12/DPL/1/1	< LOD	< LOD	< LOD
B8109 PL1/T0/A	Plant		T***	18/12/DPL/1/2	1.724	0.272	0.022
B8109 PL1/U20/A	Plant	21	U	18/12/DPL/1/3	< LOD	< LOD	< LOD
B8109 PL1/T20/A	Plant		T	18/12/DPL/1/4	< LOD	< LOD	< LOD
B8109 PL1/U42/A	Plant	42	U	18/12/DPL/1/5	< LOD	< LOD	< LOD
B8109 PL1/T42/A	Plant		T	18/12/DPL/1/6	< LOD	< LOD	< LOD
B8109 PL1/U61/A	Plant	58	U	18/12/DPL/1/7	< LOD	< LOD	< LOD
B8109 PL1/T61/A	Plant		T	18/12/DPL/1/8	< LOD	< LOD	< LOD
B8109 PL1/UHg/A	Grain	94	U	18/12/DPL/1/9	< LOD	< LOD	< LOD
B8109 PL1/UHs/A	Grain		T	18/12/DPL/1/10	< LOD	< LOD	< LOD
B8109 PL1/THg/A	Straw	94	U	18/12/DPL/1/11	< LOD	< LOD	< LOD
B8109 PL1/THs/A	Straw		T	18/12/DPL/1/12	< LOD	< LOD	< LOD

LOD: Limit of Detection - 0.0025 mg/kg (for winter wheat plants and grain), 0.002 mg/kg (for winter wheat straw)
LOQ: Limit of Quantification = 0.01 mg/kg
*DAA – Days after application
**Untreated
***Treated

Conclusions

The method was shown to be highly selective, as it includes two parent-daughter ion mass transitions for Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 and it yields accurate and repeatable results. The limit of quantification (LOQ) was established at 0.01 mg/kg for target analytes, interfering signals in control specimens were negligible, and thus the limit of detection (LOD) is 0.0025 mg/kg for winter wheat plants and grain and 0.002 mg/kg for winter wheat straw.

It is conclude that method fulfils the requirements as defined in EC Guidance documents on residue analytical methods (SANCO/825/00, rev. 8.1. and SANCO/3029/99, rev. 4) and is, applicable as enforcement and data generation method for determination of Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 in winter wheat plant, straw and grain after application of TOTO 75 SG.

Residues of active ingredients Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 were not detectable in the control samples at any time of sampling. Thifensulfuron-methyl, Metsulfuron-methyl and IN-A4098 were found in plant sample taken from the decline plots on the day of application, but on day 21 after application were below the limit of detection. The levels of Thifensulfuron-methyl and Metsulfuron-methyl residues were not detectable in the winter wheat straw and grain specimens taken at harvest.

Residues of thifensulfuron methyl and metsulfuron methyl in winter cereals after treatment with Toto 75 SG according to proposed GAP are below MRL of 0.01 mg/kg both for thifensulfuron methyl and metsulfuron methyl.

Study Comments: IIIA 8.2/01	The applicant has submitted new trials data to support the proposed GAP. Studies are accepted. One trial in Germany (2015), two trials in Poland (2017) and one trial in Poland (2018): Application rate (winter wheat): 90 g TOTO 75 SG /ha (6 g a.s./ha) and 100 mL adjuvant/ha; BBCH: 30-31 Results: 4 x <0.01 mg/kg (thifensulfuron methyl) 2 x <0.01 mg/kg (metabolite IN-A40978) 4 x <0.01 mg/kg (metsulfuron methyl) There is sufficient residues trials to cover the proposed uses on wheat.
Agreed endpoint: IIIA 8.2/01	All residues are below MRLs for thifensulfuron methyl and metsulfuron methyl set at 0.01 mg/kg (Reg. (EU) No 617/2014)

IIIA 8.4 Supplementary Livestock Feeding Studies

Data/information on livestock feeding studies were reviewed during the Annex I inclusion process and was considered to be acceptable and no further data have been generated.

Both for thifensulfuron methyl and metsulfuron methyl there are no expected intakes by livestock 0.1 mg/kg diet and metabolism studies indicate no potential level of residues ≥ 0.01 mg/kg in edible tissues.

Comment:
Information provided is accepted

IIIA 8.5 Supplementary Studies on Industrial Processing and/or Household Preparation

Metsulfuron - methyl

Thifensulfuron – methyl

Data/informations on livestock feeding studies were reviewed during the Annex I inclusion process and were considered to be acceptable and no further data have been generated.

Metsulfuron - methyl and thifensulfuron - methyl are used on grain cereal crops. There were no residues in grain at harvest, and low levels of one metabolite of metsulfuron - methyl in forage samples where

exaggerated (8 x N) treatment rates were used. Metsulfuron - methyl and thifensulfuron - methyl feeding studies in ruminants are not needed since exposure through feed items would be negligible. There is no expectation of residues of poultry being exposed to metsulfuron - methyl and thifensulfuron - methyl through diet.

Conclusion:
There is no need to evaluate any new data.

Processing factors are not necessary both for thifensulfuron methyl as metsulfuron methyl.

Comment:
Information provided is accepted

IIIA 8.5.4.2 Potable waters

This is not an EC data requirement/ not required by Directive 91/414/EEC.

IIIA 8.5.4.3 Irrigated crops

This is not an EC data requirement/ not required by Directive 91/414/EEC.

IIIA 8.6 Supplementary Studies for Residues in Representative Succeeding Crops

Metsulfuron - methyl
Thifensulfuron – methyl
The data requirement is not relevant for metsulfuron - methyl and thifensulfuron - methyl. There were no residues at harvest in residue trials.
Data/informations on processing studies were reviewed during the Annex I inclusion of the metsulfuron - methyl and thifensulfuron - methyl and were considered to be acceptable. No further studies have been performed.

Thifensulfuron-methyl:
Radiolabelled residues were found not to accumulate in rotational crops (beets, peas and sunflowers) grown in soil treated 30 and 120 days earlier with Thifensulfuron-methyl [thiophene-2- 14C]. In mature crop samples, the level of radiolabelled residues was found to be < 0.01 mg/kg

Metsulfuron-methyl:
In mature crop samples, the level of radiolabelled residues was found to be < 0.01 mg/kg in sugar beet, cereal grain or oilseed. Not significant, provided the relevant residue will be metsulfuron-methyl alone.

Comment:

Information provided is accepted

It is proposed a restriction that in case of necessity for termination of plantation treated with TOTO 75 SG because of crops damages caused by frost, diseases or insects, do not use plant protection products containing metsulfuron methyl for succeeding crops in this vegetation season.

~~**IIIA 8.5.1 Nature of residues**~~

~~There is no need to evaluate any new data.~~

~~**IIIA 8.5.2 Distribution of the residue in peel/pulp**~~

~~There is no need to evaluate any new data.~~

~~**IIIA 8.5.3 Balance studies on a core set of representative processes**~~

~~There is no need to evaluate any new data.~~

~~**IIIA 8.5.4 Follow-up studies; potable waters; irrigated crops**~~

~~**IIIA 8.5.4.1 Follow-up studies to determine concentration or dilution factors**~~

~~There is no need to evaluate any new data.~~

~~**IIIA 8.5.4.2 Potable waters**~~

~~This is not an EC data requirement/ not required by Directive 91/414/EEC.~~

~~**IIIA 8.5.4.3 Irrigated crops**~~

~~This is not an EC data requirement/ not required by Directive 91/414/EEC.~~

IIIA 8.7 Proposed Residue Definition and Maximum Residue Levels

IIIA 8.7.1 Proposed residue definition

The EU residue definitions (monitoring and risk assessment):
Metsulfuron - methyl
Thifensulfuron – methyl
Commission Regulation (EC) No 149/2008 *of 29 January 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council by establishing Annexes II, III and IV setting maximum residue levels for products covered by Annex I thereto (Text with EEA relevance (1.3.2008., L 58/1).*

Thifensulfuron-methyl
Plant residue definition for monitoring: For oilseeds and cereals (weed-control use): Thifensulfuron-methyl (parent only)
Plant residue definition for risk assessment: For oilseeds and cereals (weed-control use): Thifensulfuron-methyl and provisionally triazine amine (IN-A4098)
Animal residue definition for monitoring: Thifensulfuron-methyl (parent only)
Animal residue definition for risk assessment: Sum of thifensulfuron-methyl and thifensulfuron acid (IN-L9225), expressed as thifensulfuronmethyl and provisionally triazine amine (INA4098)

Metsulfuron-methyl
Plant residue definition for monitoring: Metsulfuron-methyl (parent)
Plant residue definition for risk assessment: Provisonally Metsulfuron-methyl (parent)
Animal residue definition for monitoring: Metsulfuron-methyl (parent)
Animal residue definition for risk assessment: Metsulfuron-methyl (parent), triazine amine; finalisation pending plant residue definition and respective livestock exposure estimates

IIIA 8.7.2 Proposed maximum residue levels (MRLs)

MRLs are set at European Level and the review is performed by EFSA. The EU MRLs for the crops for which this dossier are submitted are summarised in Table 8.7.2-1.

~~**Table 8.7.2-1: EU MRLs set for the uses of metsulfuron-methyl**~~

~~Crop~~	~~EU MRL (mg/kg)~~	~~Proposed EU MRL (mg/kg)~~	~~STMR (mg/kg)~~	~~HR (mg/kg)~~
~~Winter wheat grain~~	~~[Met] 0.5 mg/kg [Thifen] 0.05 mg/kg~~	~~[Met] 0.5 mg/kg [Thifen] 0.05 mg/kg~~	~~Not necessary~~	~~Not necessary~~

Current MRLs, according to Commission Regulation (EU) No 617/2014 of 3 June 2014 are presented in table below:

Crop/ food of animal origin	EU MRL thifensulfuron methyl (mg/kg)	EU MRL metsulfuron methyl (mg/kg)
Wheat (spelt, triticale)	0.01*	0.01*
Rye	0.01*	0.01*

*- limit of quantification

IIIA 8.8 Proposed Pre-Harvest Intervals, Re-Entry or Withholding Periods

IIIA 8.8.1 Pre-harvest interval (in days) for each relevant crop

IIIA 8.8.2 Re-entry period (in days) for livestock, to areas to be grazed

Re-entry periods is not relevant.

IIIA 8.8.3 Re-entry period for man to crops, buildings or spaces treated

The probability of risk for workers exposed to residues on the crop after treatment is low and does not justify the establishment of re-entry periods.

Proposed re-entry period (before the spray solution has dried on the plants): 1 day

IIIA 8.8.4 Withholding period (in days) for animal feedingstuffs

Withholding periods for animal feedingstuffs is not relevant.

IIIA 8.8.5 Waiting period before sowing or planting crop to be protected

No such period is required for sowing or planting of winter wheat.

IIIA 8.8.6 Waiting period between application and handling treated products

Post-harvest treatment is not relevant.

IIIA 8.8.7 Waiting period (in days) before sowing or planting succeeding crops

Waiting period (in days) before sowing or planting succeeding crops is not relevant.

It is proposed a restriction that in case of necessity for termination of plantation treated with TOTO 75 SG because of crops damages caused by frost, diseases or insects, do not use plant protection products containing metsulfuron methyl for succeeding crops in this vegetation season.

Comment:
Information provided is accepted

IIIA 8.9 Other/Special Studies

Not relevant.

IIIA 8.10 Estimation of Exposure Through Diet and Other Means

The ADI and ARfD for metsulfuron-methyl contained in *TOTO 75* are summarised in the table below.

~~End Point~~	~~Value~~	~~Study~~	~~Safety factor~~	~~Reference~~
~~Acceptable Daily Intake (ADI)~~	~~0.22 mg/kg bw/d~~	~~e.g. 2-year study in rats, supported by the~~ ~~e.g. 1-year study in dogs~~	~~100~~	~~EFSA Scientific Report 2007~~
~~Acute Reference Dose (ARfD)~~	~~Not allocated - Not necessary~~	~~e.g. 28-day to 1-year study in dogs~~	~~100~~	~~EFSA Scientific Report 2007~~

End-points for metsulfuron-methyl were updated in EFSA Journal 2015;13(1):3936. The updated values ADI and ARfD for metsulfuron-methyl are summarised in the table below.

End-Point	Value	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.22 mg/kg bw/d	Rat, 2-year study	100	EFSA Journal 2015;13(1):3936
Acute Reference Dose (ARfD)	0.25 mg/kg bw	Rabbit developmental study	100	EFSA Journal 2015;13(1):3936

The ADI and ARfD for thifensulfuron-methyl contained in *TOTO 75* are summarised in the table below.

~~End Point~~	~~Value~~	~~Study~~	~~Safety factor~~	~~Reference~~
~~Acceptable Daily Intake (ADI)~~	~~0.01 mg/kg bw/d~~	~~24 month toxicity and carcinogenicity study in rat (NOEL=1.3 mg/kg)~~	~~100~~	~~DAR B.5.10.9~~
~~Acute Reference Dose (ARfD)~~	~~Not allocated - Not necessary~~	~~e.g. 90-day to 1-year study in dogs~~	~~100~~	~~DAR B 5.3.3 and 5~~

End-points for thifensulfuron-methyl were updated in EFSA Journal 2015;13(7):4201.

End-Point	Value	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.01 mg/kg bw/d	2-yr rat study	100	EFSA Journal 2015;13(7):4201
Acute Reference Dose (ARfD)	2 mg/kg bw	Rat developmental toxicity study	100	EFSA Journal 2015;13(7):4201

IIIA 8.10.1 TMDI calculations

TOTO 75 SG is intended only for use in winter wheat applying GAP contained within the critical EU GAP used for setting EU MRL and TMDI. Therefore no additional calculations using the EFSA model are necessary for TMDI.

Metsulfuron - methyl

The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is less than 1 % of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

Thifensulfuron – methyl

The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is 3 % of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

Due to the fact, that end-points in point 8.10 were updated, additional calculations have been performed. Results are presented below:

8.10.1.01/ PRIMO rev.3.1 Metsulfuron methyl

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Thifensulfuron-methyl

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0.22	ARfD (mg/kg bw):	0.25
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2015	Year of evaluation:	2015

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
0.0%	DK child	0.10	0.0%	Rye	0.0%	Wheat				
0.0%	GEMS/Food G06	0.07	0.0%	Wheat	0.0%	Rye				
0.0%	IT toddler	0.07	0.0%	Wheat		Grapefruits				
0.0%	RO general	0.05	0.0%	Wheat		Grapefruits				
0.0%	DE child	0.05	0.0%	Wheat	0.0%	Rye				
0.0%	GEMS/Food G15	0.05	0.0%	Wheat	0.0%	Rye				
0.0%	GEMS/Food G08	0.05	0.0%	Wheat	0.0%	Rye				
0.0%	FR child 3 15 yr	0.05	0.0%	Wheat	0.0%	Rye				
0.0%	ES child	0.04	0.0%	Wheat		Grapefruits				
0.0%	NL toddler	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	NL child	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	GEMS/Food G07	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	IT adult	0.04	0.0%	Wheat		Grapefruits				
0.0%	PT general	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	GEMS/Food G10	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	UK toddler	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	GEMS/Food G11	0.04	0.0%	Wheat	0.0%	Rye				
0.0%	SE general	0.03	0.0%	Wheat	0.0%	Rye				
0.0%	FR toddler 2 3 yr	0.03	0.0%	Wheat	0.0%	Rye				
0.0%	DE women 14-50 yr	0.03	0.0%	Wheat	0.0%	Rye				
0.0%	UK infant	0.03	0.0%	Wheat		Grapefruits				
0.0%	DE general	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	IE adult	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	ES adult	0.02	0.0%	Wheat		Grapefruits				
0.0%	FR adult	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	LT adult	0.02	0.0%	Rye	0.0%	Wheat				
0.0%	UK vegetarian	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	NL general	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	FI 3 yr	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	UK adult	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	DK adult	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	FI 6 yr	0.02	0.0%	Wheat	0.0%	Rye				
0.0%	IE child	0.01	0.0%	Wheat		Grapefruits				
0.0%	FI adult	0.01	0.0%	Rye	0.0%	Wheat				
0.0%	FR infant	0.01	0.0%	Wheat	0.0%	Rye				
	Column7			Grapefruits		Grapefruits				

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

Acute risk assessment /children | **Acute risk assessment / adults / general population**

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

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

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI				IESTI			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.06%	Wheat	0.01 / 0.01	0.14	0.03%	Wheat	0.01 / 0.01	0.08
0.03%	Rye	0.01 / 0.01	0.06	0.02%	Rye	0.01 / 0.01	0.05

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI				IESTI			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.0%	Wheat / milling (flour)	0.01 / 0.01	0.12	0.0%	Wheat / bread/pizza	0.01 / 0.01	0.04
0.0%	Wheat / milling (wholemea	0.01 / 0.01	0.06	0.02%	Wheat / pasta	0.01 / 0.01	0.04
0.0%	Rye / boiled	0.01 / 0.01	0.04	0.01%	Wheat / bread	0.01 / 0.01	0.03
0.0%	Rye / milling (wholemeal)-l	0.01 / 0.01	0.04	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!

Expand/collapse list

Maximum TMDI is <0.0% ADI (DK child). The highest ARfD/ADI is 0.06%.

Thifensulfuron-methyl

8.10.1.02/ PRIMO rev.3.1 Thifensulfuron methyl

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Thifensulfuron-methyl

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0.01	ARfD (mg/kg bw):	2
Source of ADI:	EFSA	Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
1.0%	DK child	0.10	0.6%	Rye	0.4%	Wheat				
0.7%	GEMS/Food G06	0.07	0.7%	Wheat	0.0%	Rye				
0.7%	IT toddler	0.07	0.7%	Wheat		Grapefruits				
0.5%	RO general	0.05	0.5%	Wheat		Grapefruits				
0.5%	DE child	0.05	0.4%	Wheat	0.1%	Rye				
0.5%	GEMS/Food G15	0.05	0.5%	Wheat	0.0%	Rye				
0.5%	GEMS/Food G08	0.05	0.4%	Wheat	0.1%	Rye				
0.5%	FR child 3 15 yr	0.05	0.5%	Wheat	0.0%	Rye				
0.4%	ES child	0.04	0.4%	Wheat		Grapefruits				
0.4%	NL toddler	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	NL child	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	GEMS/Food G07	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	IT adult	0.04	0.4%	Wheat		Grapefruits				
0.4%	PT general	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	GEMS/Food G10	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	UK toddler	0.04	0.4%	Wheat	0.0%	Rye				
0.4%	GEMS/Food G11	0.04	0.4%	Wheat	0.0%	Rye				
0.3%	SE general	0.03	0.3%	Wheat	0.0%	Rye				
0.3%	FR toddler 2 3 yr	0.03	0.3%	Wheat	0.0%	Rye				
0.3%	DE women 14-50 yr	0.03	0.2%	Wheat	0.0%	Rye				
0.3%	UK infant	0.03	0.3%	Wheat		Grapefruits				
0.2%	DE general	0.02	0.2%	Wheat	0.1%	Rye				
0.2%	IE adult	0.02	0.2%	Wheat	0.0%	Rye				
0.2%	ES adult	0.02	0.2%	Wheat		Grapefruits				
0.2%	FR adult	0.02	0.2%	Wheat	0.0%	Rye				
0.2%	LT adult	0.02	0.1%	Rye	0.1%	Wheat				
0.2%	UK vegetarian	0.02	0.2%	Wheat	0.0%	Rye				
0.2%	NL general	0.02	0.2%	Wheat	0.0%	Rye				
0.2%	FI 3 yr	0.02	0.1%	Wheat	0.1%	Rye				
0.2%	UK adult	0.02	0.2%	Wheat	0.0%	Rye				
0.2%	DK adult	0.02	0.1%	Wheat	0.1%	Rye				
0.2%	FI 6 yr	0.02	0.1%	Wheat	0.1%	Rye				
0.1%	IE child	0.01	0.1%	Wheat		Grapefruits				
0.1%	FI adult	0.01	0.1%	Rye	0.0%	Wheat				
0.1%	FR infant	0.01	0.1%	Wheat	0.0%	Rye				
	Column7			Grapefruits		Grapefruits				

Conclusion:

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of Thifensulfuron-methyl is unlikely to present a public health concern.

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

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

Show results for all crops

Unprocessed commodities

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.01%	Wheat	0.01 / 0.01	0.14	0.00%	Wheat	0.01 / 0.01	0.08
0.00%	Rye	0.01 / 0.01	0.06	0.00%	Rye	0.01 / 0.01	0.05
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

Processed commodities

Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	**Results for adults** No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.0%	Wheat / milling (flour)	0.01 / 0.01	0.12	0.0%	Wheat / bread/pizza	0.01 / 0.01	0.04
0.0%	Wheat / milling (wholemea	0.01 / 0.01	0.06	0.00%	Wheat / pasta	0.01 / 0.01	0.04
0.0%	Rye / boiled	0.01 / 0.01	0.04	0.00%	Wheat / bread	0.01 / 0.01	0.03
0.0%	Rye / milling (wholemeal)-l	0.01 / 0.01	0.04	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
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#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!

Maximum TMDI is 1.0% ADI (DK child)). The highest ARfD/ADI is 0.01%.

IIIA 8.10.2 NEDI calculations

Not necessary.

Conclusion:
Long-term dietary exposure assessments showing adequate safety margins to consumers from the proposed uses.

IIIA 8.10.3 NESTI calculations

~~Not necessary~~. See point 8.10.1.01 and 8.10.1.02

IIIA 8.11 Summary and Evaluation of Residue Behaviour

TOTO 75 SG contain a mixture of metsulfuron - methyl which was included into Annex I of Directive 91/414 by Commission Directive 2000/49/EC of 26 July 2000 and thifensulfuron - methyl included in Annex I Directive 91/414 by Commission Directive 2001/99/EC of 20 November 2001. The SANCO report for metsulfuron - methyl (SANCO/7593/VI/97-final 14 August 2000, and SCP/METSU/002-Final 5 April 2000), and SANCO report for thifensulfuron - methyl (SANCO/7577/VI/97-final 12 December 2001) provide the relevant review information or a reference used in the evaluation.

TOTO 75 SGis intended only for use in winter wheat applying GAP contained within the critical EU GAP used for setting EU MRL.
The residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health.
Since application of TOTO 75 SGis made at an early stage in the crop's development, it is not necessary to establish Preharvest Interval (PHI) in days. Residue levels decline to below the Limit of Quantification at harvest.

Residues of metsulfuron methyl after treatment of TOTO 75 SG in accordance with the proposed label – instruction for use in the protection of winter wheat, winter triticale and winter rye do not pose a health risk to humans and animals.

Conclusion:
The residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health.

zRMS comments:

Sufficient trials on wheat are available to support the proposed uses. The residue data are valid with regard to storage stability data

All residues are below MRLs for thifensulfuron methyl and metsulfuron methyl set at 0.01 mg/kg (Reg. (EU) No 617/2014).

Extrapolation to rye and triticale is possible (SANCO 7525/VI/95_rev 10.3).

Residues of metsulfuron methyl after treatment of TOTO 75 SG in accordance with the proposed label – instruction for use in the protection of winter wheat, winter triticale and winter rye do not pose a health risk to humans and animals.

The proposed uses of thifensulfuron methyl and metsulfuron methyl in the formulation TOTO 75/ TYTAN 75/ HERKULES 75 do not represent unacceptable chronic risks for the consumer.

There is no risk to the consumer if used together with adjuvant PARTNER or ASYSTENT according to the GAP.

There is no risk to the consumer if used in Tank Mix with Galaper (fluroksypyr) 250 EC according to the GAP.

Appendix 1: List of data submitted in support of the evaluation

Annex point	Author	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or Unpublished	Data protection claimed Y/N	Owner
IIIA 8.3.1/01	Wojcik. M.	2008	TOTO 75 WG Determination of residues of metsulfuron methyl and thifensulfuron methyl in wheat grain Study code C/05/08 Institute of Industrial Organic Chemistry, Branch Pszczyna, ul. Doswiadczalna 27, 43-200 Pszczyna, Poland Report to GLP Unpublished ⇨ KIIIA 5.3.1/01	N	Chemirol
IIIA 8.3.1/01	Dr. Matthias Eichler Stefanie Schabio Silke Hermann	2015	TOTO 75 SG: Field Residue Decline Study on Wheat Commodities in Central Europe IBACON GmbH Arheilger Weg 17 64380 Rossdorf Germany Study Project: 103141104 GLP Unpublished	Y	Chemirol
IIIA 8.3.1/02	Dr. Matthias Eichler Stefanie Schabio Silke Hermann	2015	TOTO 75 SG: Field Residue Study on Wheat Commodities in Central Europe IBACON GmbH Arheilger Weg 17 64380 Rossdorf Germany Study Project: 103141204 GLP Unpublished	Y	Chemirol

Annex point	Author	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or Unpublished	Data protection claimed Y/N	Owner
IIIA 8.3.1/03	Ertus, C.	2017	Generation of Field Specimens for the determination of Thifensulfuron methyl and Metsulfuron methyl Residues in Winter Wheat Following Foliar application with TOTO 75 SG under Field Conditions in Poland in 2017 ANADIAG Study number: B7040 GLP Unpublished	Y	Chemirol
IIIA 8.3.1/04	Sikorski, P.	2018	DETERMINATION OF THIFENSULFURON-METHYL AND METSULFURON-METHYL RESIDUES IN WINTER WHEAT SAMPLES AFTER APPLICATION OF “TOTO 75 SG” Food Safety Laboratory Research Institute of Horticulture 18 Pomologiczna Street 96-100 Skierniewice POLAND Study Code ZBBZ-2017/01/DPL/1 GLP Unpublished	Y	Chemirol

Annex point	Author	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or Unpublished	Data protection claimed Y/N	Owner
IIIA 8.3.1/05	Sikorski, P.	2017	DETERMINATION OF THE RESIDUES OF METABOLITE IN-A4098 IN WINTER WHEAT SAMPLES AFTER APPLICATION OF "TOTO 75 SG" Food Safety Laboratory Research Institute of Horticulture 18 Pomologiczna Street 96-100 Skierniewice POLAND Study Code ZBBZ-2017/18/DPL/1 GLP Unpublished	Y	Chemirol
IIIA 8.3.1/06	Ertus, C.	2018	Generation of Field Specimens for the determination of Thifensulfuron-methyl, Metsulfuron-methyl and their metabolites Residues in Winter Wheat Following Foliar application with TOTO 75 SG under Field Conditions in Poland in 2018 ANADIAG 16, rue Ampère 67500 HAGUENAU France Study number: B8109 GLP Unpublished	Y	Chemirol

Annex point	Author	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or Unpublished	Data protection claimed Y/N	Owner
IIIA 8.3.1/07	Markowicz, A.	2019	DETERMINATION OF THIFENSULFURON-METHYL, METSULFURON-METHYL AND IN-A4098 RESIDUES IN WINTER WHEAT SAMPLES FOLLOWING FOLIAR APPLICATION WITH "TOTO 75 SG" UNDER FIELD CONDITIONS IN POLAND IN 2018" Food Safety Laboratory Research Institute of Horticulture 18 Pomologiczna Street 96-100 Skierniewice POLAND Study Code ZBBZ-2018/12/DPL/1 GLP Unpublished	Y	Chemirol
IIIA 8.10.1.01/	K.Stefanska	2017	**PRIMO rev.2 Metsulfuron methyl** No-GLP Unpublished	N	Chemirol
IIIA 8.10.1.01/	K.Stefanska	2017	**PRIMO rev.2 Metsulfuron methyl** No-GLP Unpublished	N	Chemirol

Appendix 2 – Product uses (Critical GAP)

Crop and/or situation	**Member State or Country**	**Product name**	**F G or I**	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment**			**PHI** (days)	**Remarks:**
					Type	Conc.	method	growth	number	interval between applications (min)	kg as/hL	water L/ha	kg as/ha		
(a)			(b)	(c)	(d-f)	of as (i)	kind (f-h)	stage & season (j)	min max (k)		min max	min max	min max	(l)	(m)
TRZAW	**PL**	**TOTO 75**	**F**	**weeds**	**SG**	Thifensulfuron-methyl 682 g/kg + metsulfuron-methyl 68 g/kg	Spry mediu m	BBCH 12-15 BBCH 22-29	1	Not applicablr	thifensulfuron-methyl= 0,0205-0,0307 Metsulfuron-methyl = 0,00203-0,00305	200-300	Thifensulfuron-methyl = 0,0614 + metsulfuron-methyl = 0,0061	N/A	

Remarks:

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

PPP (product name/code): TOTO / TYTAN / HERKULES

Active substance(s) (name and content, g/L or g/kg): Metsulfuron-methyl and Thifensulfuron-methyl

Formulation type: SG

Field of use: cereals

Zone(s): central

Appendix B - details of all intended national GAPs within the zone

1	2	3	4	5	6	7	8	9	10	11	12	13	14
Use-	**Member**	**Crop and/**	**F**	**Pests or Group of**	**Application**				**Application rate**			**PHI**	**Remarks:**

No.	state(s)	or situation (crop destination / purpose of crop)	G or I	pests controlled (additionally: developmental stages of the pest or pest group)	Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	kg or L product / ha a) max. rate per appl. b) max. total rate per crop/season	g or kg as/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min / max	(days)	e.g. g safener/synergist per ha
1													
2													
3													
4													
Field uses													
1	PL, SK	Winter wheat	F	weeds	spray medium	PL: BBCH 21-31 SK: BBCH 22-31	1	N/A	a) 0,09 b) 0,09	a) thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g b) thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g	200-300	N/A	PL: plus adiuvant ASYSTENT+90 EC in dose 0,1l/ha
2	PL, SK	Winter triticale	F	Weeds	spray medium	BBCH 21 -31	1	N/A	a) 0,09 b) 0,09	a) thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g b)			PL: plus adiuvant PARTNER+ in dose 0,5 l/ha SK – extention of registration is currently pending

										thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g			
3	PL, SK	Winter rye	F	Weeds	spray medium	BBCH 21 -31	1	N/A	a) 0,09 b) 0,09	a) thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g b) thifensulfuron methyl 61,4 g + metsulfuron methyl 6,1 g			PL: plus adiuvant PARTNER+ in dose 0,5 l/ha SK – extention of registration is currently pending
4	PL, SK	Winter rye	F	Weeds	spray medium	BBCH 21 -31	1	N/A	a) 0,07 b) 0,07	a) thifensulfuron methyl 47,7 g + metsulfuron methyl 4,8 g b) thifensulfuron methyl 47,7 g + metsulfuron methyl 4,8 g			SK – extention of registration is currently pending: Tank Mix with Galaper (fluroksypyr) 250 EC in dose 0,25 l of product /ha PL: Tank Mix with Galaper (fluroksypyr) 250 EC in dose 0,25 l of product /ha + adiuvant Partner+ in dose 0,5

													l/ha
5	PL, SK	Winter triticale	F	Weeds	spray medium	BBCH 21 -31	1	N/A	a) 0,07 b) 0,07	a) thifensulfuron methyl 47,7 g + metsulfuron methyl 4,8 g b) thifensulfuron methyl 47,7 g + metsulfuron methyl 4,8 g			SK – extention of registration is currently pending: Tank Mix with Galaper (fluroksypyr) 250 EC in dose 0,25 l of product /ha PL: Tank Mix with Galaper (fluroksypyr) 250 EC in dose 0,25 l of product /ha + adiuvant Partner+ in dose 0,5 l/ha
EU-wide uses (use on sowing seed, in greenhouses (or other closed places of plant production), as post-harvest treatment or for treatment of empty storage rooms)													
3	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-	-
Minor uses according to article 51													
5	-	-	-	-	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-	-