FINAL REGISTRATION REPORT

Part B

Section 3

Efficacy Data and Information

Concise summary

Product code: TOTO 75 SG / Tytan 75 SG / Herkules 75 SG

Chemical active substance:

Thifensulfuron-methyl 682 g/kg

Metsulfuron-methyl 68 g/kg

Central Zonal Rapporteur Member State: zRMS

NATIONAL ADDENDUM Poland

(renewal of authorization)

Applicant: Innvigo Sp. z o.o.

Submission date: 11/2020

MS Finalisation date: 27/11/2020; October 2022

Version history

When	What
November 2020	ZRMs evaluated submitted dRR.
October 2022	Final Registration Report

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3 Efficacy Data and Information (including Value Data) on the Plant Protection Product (KCP 6)

Please research to core dossier.

Transformation of the dRR (applicant version) into the RR (zRMS version)

The process chosen by the zRMS to transform the dRR into a RR should be explained. Options are to rewrite the document (with track change or not) or to use commenting boxes such as the following

Comments of zRMS:	This is the version of dRR submitted by the applicant. The grey commenting boxes were used by the zRMS. They were usually placed at the end of each chapter.

3.1 Summary and conclusions of zRMS on Section 3: Efficacy (KCP 6)

Please research to core dossier.

Abstract

zRMS provided main conclusions on each use. Overall summaries are not necessary here, because they were provided at the end of each chapter of the dRR.

Table 3.1-1: Acceptability of intended uses (and respective fall-back GAPs, if applicable)

Please research to core dossier.

Comments of zRMS:	In accordance with the Article 43 of Regulation (EC) No 1107/2009, the already submitted data will not be re-evaluated because the conclusions of previous assessments are still considered valid in the case of no significant change of the GAP table.

3.2 Efficacy data (KCP 6)

Please research to core dossier.

Comments of zRMS:	All necessary information's were provided above by Applicant. This document summarises the information related to the efficacy of the plant protection product – TOTO 75 SG/ Tytan 75 SG / Herkules 75 SG. **The data presented in this dossier fully support the renewal under Article 43 of TOTO 75 SG / Tytan 75 SG / Herkules 75 SG for the control of weeds in cereals in Poland. However, in our opinion cMS should decide if presented documentation is sufficient for re-registered product, according to attached Zonal GAP (in first core dossier) and copies of permits.**

3.3 Information on the occurrence or possible occurrence of the development of resistance (KCP 6.3)

Summary and Conclusions

In accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009, Article 43 and the EPPO PP1 1/213(4) methodology, an updated risk assessment of weed resistance to TOTO 75 SG / Herkules 75 SG / Tytan 75 SG was prepared.

According to information available on the website www.weedscience.org, which is the property of Inter-national Survey of Herbicide Resistant Weeds /HRAC/, ~~tribenuron~~ thifensulfuron-methyl is included in the group B – Inhibition of acetolactate synthase ALS. This is active substance control a lot of dicots weeds species. According to the HRAC, many cases of resistance to this chemical group have been reported. World-wide, 149 cases of resistance to thifensulfuron-methyl and methsulfuron-methyl (table 3.4-2) have been reported. In Poland so far, only 1 case of resistance in weeds have been recorded.

Mode of Action

According to the classification Herbicide Resistance Action Committee (HRAC) thifensulfuron methyl and metsulfuron-methyl are among the HRAC Group B - ALS inhibitors. Substances belonging to this group inhibit the action of ALS enzyme that is essential for the biosynthesis of amino acids: leucine, isoleucine and valine. These amino acids play a key role in the development of protein and are necessary for the formation of new plant cells. After the application of these substances are rapidly taken by both the above-ground parts and by the roots, and then move to the meristematic tissue, which inhibit cell division, which leads to halt further growth and development of susceptible weeds. The first symptoms of herbicide are visible after a few days, a dying weeds after 2-4 weeks of application.

Mechanism(s) of resistance

The occurrence of a resistant plant is a result of two major phenomena: 1) DNA mutations which underpin the natural variability of organisms, and 2) Selection by constant use of the same mode-of-action herbicides. There are two major types of herbicide resistance. Target site resistance is

usually based on a single gene mutation, which encodes the enzyme that is the herbicide's target. Substitutions in the aminoacid sequence alter the protein structure in a way which prevents the inhibitor molecule to bind with the enzyme [*according to: Krysiak M., Gawroński S., Kierzek R., Adamczewski K. 2011. Molecular basis of blackgrass (Alopecurus mysuroides Huds.) resistance to sulfonylurea herbicides*].

According to Table 1, in the weeds targeted by the product control, the most common mutation is the replacement of the proline codon with a codon other amino acid (mutation Pro 197). Also Ala 122, Asp 376, Trp 574 are mutations that induce mechanism of resistance to ALS inhibitors.

Table 1. Amino acid substitutes which give herbicide resistance to ALS inhibitors and which have been identified in selected herbicide-resistant weed populations. Intentionally selected (i.e. laboratory selected) are not included in this table [Tranel, P.J., Wright, T.R, and Heap, I.M. Mutations in herbicide-resistant weeds to ALS inhibitors. Online http://www.weedscience.com. 11/26/2020].

Substitute	Species	TP	SU	PTB	IMI	SCT	Year
Ala 122							
Val	*Apera spica-venti*	ND	R	ND	ND	S	2011
Pro 197							
Thr	*Apera spica-venti*	r	R	ND	ND	r	2011
Asn	*Apera spica-venti*	r	R	ND	ND	r	2011
Ser	*Apera spica-venti*	ND	R	ND	ND	r	2011
Ala	*Apera spica-venti*	ND	R	ND	ND	ND	2013
His	*Papaver rhoeas*	S	R	ND	r	ND	2004
Thr	*Papaver rhoeas*	r	R	r	r	ND	2004
Ser	*Papaver rhoeas*	r	R	r	r	ND	2004
Leu	*Thlaspi arvense*	S	R	ND	r	ND	2007
Arg	*Papaver rhoeas*	r	R	r	r	ND	2009
Leu	*Papaver rhoeas*	S	R	ND	R	ND	2009
Ala	*Papaver rhoeas*	r	R	r	r	ND	2009
Gln	*Stellaria media*	S	R	ND	ND	ND	2010
Ser	*Capsella bursa-pastoris*	ND	R	ND	ND	ND	2011
Leu	*Galium aparine*	r	R	r	r	r	2016
Thr	*Galium aparine*	ND	R	ND	ND	ND	2016
Ser	*Galium aparine*	r	r	r	r	r	2019
His	*Galium aparine*	r	r	r	r	r	2019
Asp 376							
Glu	*Galium aparine*	r	r	r	r	r	2019
Trp 574							

Met	Apera spica-venti	ND	R	ND	ND	ND	2013
Leu	*Papaver rhoeas*	ND	R	ND	ND	ND	2011
Gly	*Galium aparine*	ND	R	ND	ND	ND	2011
Leu	*Galium aparine*	r	r	r	r	r	2019

*R – high resistance; r - moderate resistance; S – susceptible biotype; ND – not determined

Evidence of resistance

According to the HRAC website www.weedscience.org, 164 cases of resistance to ALS inhibitors have been reported worldwide, including a total of 149 cases of thifensulfuron-methyl and metsulfuron-methyl (Table 2).

Among the species that have developed mechanisms of resistance to these herbicides are also weeds that are the subject of Toto 75 SG / Herkules 75 SG. Resistance occurred in *Brassica rapa* (1), *Matricaria chammomila* (2), *Tripleurospermum inodorum* (1), *Stellaria media* (15), *Papaver rhoeas* (5), *Galium* sp. (4), *Thlaspi arvense* (3), *Capsella bursa-pastoris* (3).

In Poland, so far, only 1 case of resistance occurrence in *Avena fatua* was reported in 2011.

Table 2. Selected cases of occurrence of resistance to ALS inhibitors in weeds [www.weedscience.org].

Year	Species	Country	MOAs	Actives	Situations
2012	Brassica rapa (=B. campestris)	Argentina	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9)	imazapyr, metsulfuron-methyl, diclosulam, glyphosate	Soybean, Wheat
2019	Apera spica-venti	Belgium	ALS inhibitors (B/2)	foramsulfuron, iodosulfuron-methyl-sodium, and mesosulfuron-methyl	Wheat
2012	Matricaria recutita (= M. chamomilla)	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
2013	Stellaria media	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
2014	Papaver rhoeas	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl, florasulam	Wheat
1988	Stellaria media	Canada	ALS inhibitors (B/2)	imazamethabenz-methyl, thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, ethametsulfuron-methyl, sulfometuron-methyl	Cereals, Wheat
1996	Galium spurium	Canada	ALS inhibitors (B/2), Synthetic Auxins (O/4)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl, triasulfuron, sulfometuron-methyl, quinclorac	Cereals, Wheat, Canola
2001	Thlaspi arvense	Canada	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, metsulfuron-methyl, ethametsulfuron-methyl	Spring Barley, Wheat, Canola, Peas

2011	Capsella bursa-pastoris	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
2008	Thlaspi arvense	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
2008	Galium spurium	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Canola
2008	Stellaria media	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Peas
2005	Stellaria media	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
2006	Galium spurium	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
2008	Capsella bursa-pastoris	Canada	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, imazamox	Wheat
2009	Thlaspi arvense	Canada	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
2007	Papaver rhoeas	France	ALS inhibitors (B/2)	metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Wheat
2010	Tripleurospermum perforatum (=T. inodorum)	France	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
2012	Stellaria media	France	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, florasulam, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Wheat
2016	Papaver rhoeas	France	ALS inhibitors (B/2), Synthetic Auxins (O/4)	metsulfuron-methyl, MCPA, 2,4-D, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Cereals
2011	Stellaria media	Germany	ALS inhibitors (B/2)	thifensulfuron-methyl, amidosulfuron, triflusulfuron-methyl, tribenuron-methyl, nicosulfuron, imazamox, florasulam, iodosulfuron-methyl-sodium, tritosulfuron, mesosulfuron-methyl, pyroxsulam	Spring Barley, Wheat, Rapeseed
1998	Papaver rhoeas	Greece	ALS inhibitors (B/2)	pyrithiobac-sodium, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, triasulfuron, imazamox, florasulam	Winter wheat
1996	Stellaria media	Ireland	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals

2002	Stellaria media	Norway	ALS inhibitors (B/2)	tribenuron-methyl, metsulfuron-methyl, iodosulfuron-methyl-sodium	Cereals
2012	Matricaria recutita (= M. chamomilla)	Norway	ALS inhibitors (B/2)	tribenuron-methyl, metsulfuron-methyl	Wheat, Winter barley
2011	Avena fatua	**Poland**	ACCase inhibitors (A/1), ALS inhibitors (B/2)	fenoxaprop-P-ethyl, metsulfuron-methyl, sulfometuron-methyl, iodosulfuron-methyl-sodium, pinoxaden, propoxycarbazone-sodium	Spring Barley, Spring wheat
2002	Stellaria media	South Africa	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, triasulfuron	Cereals
2008	Galium aparine	Turkey	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, triasulfuron, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Winter wheat
2000	Stellaria media	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl, florasulam	Cereals
2001	Papaver rhoeas	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
2002	Tripleurospermum perforatum (=T. inodorum)	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
2012	Stellaria media	United States	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
2013	Stellaria media	United States	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, flucarbazone-sodium	Wheat
2009	Stellaria media	United States	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, mesosulfuron-methyl	Wheat
2010	Stellaria media	United States	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl, pyroxsulam	Alfalfa, Spring Barley, Wheat
2008	Stellaria media	United States	ALS inhibitors (B/2)	thifensulfuron-methyl	Wheat

Cross-Resistance

Weeds resistant to thifensulfuron-methyl and methylfuron-methyl are very likely to be at risk of resistance to all substances belonging to the ALS inhibitor group. Cross-resistance may therefore apply to other substances in the groups (table 1) such as sulfonylurea, imidazolin, triazolopyrimidine, pyrimidinylthiobenzoates, sulfonylaminocarbonyltriazolinone.

Sensitivity-data

No special studies have been conducted to determine the sensitivity of weeds within the population.

According to efficacy studies, species susceptible and moderately susceptible to Toto 75 SG / Hercules 75 SG / / Tytan 75 SG include *Centaurea cyanus*, *Viola arvensis*, *Stellaria media*, *Lamium purpureum*, *Papaver rhoeas*, *Tripleurospermum inodorum*, *Apera spica-venti*, *Myosotis arvensis*, *Veronica triphyllos*, *Galium aparine*, *Brassica napus* (self-sown plant), *Capsella bursa-pastoris*, *Thlaspi arvense*, *Veronica hederifolia* and *Veronica persica*.

In modern agriculture, most farmers rely on herbicides for weed control. The intensive use of herbicides in crops has led to the development of herbicide resistance in numerous weeds worldwide. In Belgium, farmers have encountered problems with controlling populations of Alopecurus myosuroides, Matricaria recutita, Stellaria media and Popover rhoeas in some wheat fields with the conventionally used acetolactate synthase (ALS)-inhibiting herbicides. Dose response assays were conducted in the greenhouse to test the sensitivity of these populations to the key ALS-inhibiting herbicides mesosulfuron-methyl + iodosulfuron-methyl for A. myosuroides and metsulfuron-methyl and florasulam for M. recutita, S. media and P. rhoeas. The ED_{90}- and ED_{50}-values (effective dose for resp. 90% and 50% biomass reduction) were compared with those of sensitive reference populations and the resistance index (RI) was calculated. High levels of resistance were detected forA. myosuroides (RI: 24.3) after treatment with mesosulfuron-methyl and for M. recutita (RI: 36.4 to 49.5), S. media (RI > 20) and P. rhoeas (RI: 23.6) after treatment with metsulfuron-methyl. However, the metsulfuron-methyl resistant populations of M. recutita and S. media were sufficiently controlled with florasulam at the maximum authorised field dose. This was not the case for P. rhoeas. The metsulfuron-methyl resistant P. rhoeas population were also high-level resistant against florasulam (RI: 29.5). Integrated weed management practices (crop rotation, herbicide mixing, ...) should be applied to reduce the selection pressure for resistant weeds [according to information available on the website www.ncbi.nlm.nih.gov/pubmed/27145589].

Use pattern

Toto 75 SG / Hercules 75 SG / Tytan 75 SG should be applied once a season, in winter wheat, winter triticale and winter life, in spring from BBCH 21 to BBCH 31. The optimal effective dose is 70-90 g/ha.

Resistance risk assessment of unrestricted use patterns

Tifensulfuron-methyl and metsulfuron-methyl belong to the group of ALS inhibitors, particularly exposed to the risk of resistance. In addition, the product is used to protect cereals, in which substances from this group are most commonly used and the most cases of resistance occurrence are recorded.

Toto 75 SG / Hercules 75 SG / Tytan 75 SG, when used without restrictions, could significantly induce the mechanism of resistance in weeds. In particular, the risk could be increased if substances with the same mechanism of action were applied several times per season or ALS inhibitors were used in follow-up crops.

Rationally performed, one-time treatment during the season, due to its high effectiveness against the controlled weeds is not burdened with a high risk of resistance occurrence.

Acceptability of the resistance risk

The presented risk of resistance is very high. Therefore, the existing restriction and guidelines on the label must be maintained. The presented risk of resistance is very high. Therefore, the existing restriction and guidelines on the label must be maintained. Using the preparation once a season with the rotation of herbicides in subsequent years minimises the risk of resistance occurrence and makes it acceptable.

Management strategy

Resistance management strategies developed in relation to the risks involved lead to the following recommendations:

a) use the product only once per season,
b) avoid annual use of substances from the ALS inhibitor group in the same field,
c) use the correct crop rotation,
d) use herbicide doses to ensure effective weed control,
e) follow the recommendations on the label.

Monitoring, reporting and reaction to changes in performance and implementation of the management strategy

The existing provisions on the label on reducing the risk of resistance should be maintained. This is the right way to give guidance to product users.

Any suspicion of weed resistance in agricultural practice may be reported by users to the manufacturer of the product.

Comments of zRMS:	Resistance is the naturally-occurring inheritable ability of some weed biotypes within a given weed population to survive an herbicide treatment that should, under normal use conditions, effectively control weed population. The major reason herbicides are selective against weeds in crops is because crop plants are able to metabolize the herbicide to a non-toxic form. The basis for herbicide selectivity relies on enzymatic systems present in the plant's normal metabolic processes. There are several processes in plants which can lead to resistance (target site alterations, enhanced metabolism, changes in uptake and translocation). **Immunity risk assessments should be presented in accordance with the standard: EPPO PP1 PP 1/213 (4) resistance risk analysis. Applicant properly presents the risk of resistance**. Below, we present the performed risk assessment of resistance development. For TOTO 75 SG / Tytan 75 SG / Herkules 75 SG being a mixture of two products (thifensulfuron-methyl and metsulfuron-methyl), the following anti-resistance use recommendations are therefore valid: • **Thifensulfuron-methyl** is an herbicide, which acts by inhibition of acetolactate synthase. It belongs to HRAC group B. In terms of mode of action, thifensulfuron-methyl act as inhibitors of acetolactate synthase ALS, (acetohydroxyacid synthase AHAS). It is the sulfonylurea urea class, classified as B herbicides according to HRAC-system and classified as 2 in the WSSA-System, hereafter referred to as Class B/2. Class B/2 contains five different chemical classes. The sulfonylureas are the largest chemical class within this group. There are mainly three groups of amino acid synthesis inhibitors commonly used as herbicides: the sulfonylureas, the imidazolinones, and amino acid derivative herbi-

cide families. Sulfonylurea herbicides inhibit the production of three essential branch-chain amino acids by inhibiting one key plant enzyme. This key plant enzyme is called acetolactate synthase (ALS) or acetohydroxy acid synthase (AHAS). In general, injury symptoms due to the use of herbicides with this mode of action are slow to develop (one to two weeks) and include stunting or delayed plant growth, leading to eventual death of the plant. Herbicides in the sulfonylurea family can be taken up through plant foliage and roots and are mobile in both the xylem and phloem.

Group B/2 herbicides bind to the substrate binding site of the acetolactate synthase (ALS) enzyme, thus preventing the production of essential amino acids, and without these amino acids, the plant eventually dies. The mechanism of resistance found against sulfonylureas is a so-called target site mechanism. Target site resistance is caused by a mutation on the enzyme at the site where the herbicide molecule binds, thus stopping the plant's normal biochemical processes.

Resistance against B/2 herbicides is known for various species. In the database of www.weedscience.org, 85 cases of resistance against thifensulfuron-methyl are momentarily documented.

Table: Overview of the resistance cases for thifensulfuron-methyl

#	Year	Species	Country	MOAs	Actives	Situations
1	1988	*Stellaria media*	Canada (Alberta)	ALS inhibitors (B/2)	imazamethabenz-methyl, thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, ethametsulfuron-methyl, sulfometuron-methyl	Cereals, Wheat
2	1989	*Kochia scoparia*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl	Spring Barley, Wheat
3	1996	*Galium spurium*	Canada (Alberta)	ALS inhibitors (B/2), Synthetic Auxins (O/4)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl, triasulfuron, sulfometuron-methyl, quinclorac	Cereals, Wheat, Canola
4	1996	*Sonchus asper*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl	Spring Barley, Pastures
5	2001	*Thlaspi arvense*	Canada (Alberta)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, metsulfuron-methyl, ethametsulfuron-methyl	Spring Barley, Wheat, Canola, Peas
6	2006	*Galeopsis tetrahit*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Cereals
7	2007	*Polygonum convolvulus (=Fallopia convolvulus)*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl, florasulam	Wheat, Peas
8	2007	*Salsola tragus*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
9	2011	*Capsella bursa-pastoris*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
10	2012	*Kochia scoparia*	Canada (Alberta)	ALS inhibitors (B/2), EPSP synthase inhibi-	thifensulfuron-methyl, tribenuron-methyl, glyphosate	Spring Barley, Wheat

				tors (G/9)		
11	2012	*Vaccaria hispanica*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl	Wheat
12	2017	*Kochia scoparia*	Canada (Alberta)	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9), Synthetic Auxins (O/4)	thifensulfuron-methyl, tribenuron-methyl, glyphosate, dicamba	Corn (maize), Lentils, Wheat, Canola, Peas, Winter barley, Fallow
13	1988	*Kochia scoparia*	Canada (Manitoba)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron	Spring Barley, Industrial sites, Wheat
14	2008	*Thlaspi arvense*	Canada (Manitoba)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
15	2008	*Galium spurium*	Canada (Manitoba)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Canola
16	2008	*Stellaria media*	Canada (Manitoba)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Peas
17	2008	*Amaranthus powellii*	Canada (Manitoba)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat, Beans
18	2009	*Polygonum lapathifolium*	Canada (Manitoba)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
19	2014	*Kochia scoparia*	Canada (Manitoba)	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9)	thifensulfuron-methyl, tribenuron-methyl, glyphosate	Corn (maize), Soybean
20	1998	*Amaranthus powellii*	Canada (Ontario)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl	Corn (maize), Cropland, Soybean
21	1998	*Amaranthus retroflexus*	Canada (Ontario)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl	Corn (maize), Cropland, Soybean
22	2001	*Chenopodium album*	Canada (Ontario)	ALS inhibitors (B/2)	thifensulfuron-methyl	Soybean
23	2008	*Chenopodium album*	Canada (Quebec)	ALS inhibitors (B/2)	thifensulfuron-methyl	Soybean
24	1988	*Kochia scoparia*	Canada (Saskatchewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Cropland, Wheat
25	2002	*Sinapis arvensis*	Canada (Saskatchewan)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, ethametsulfuron-methyl	Cereals, Canola
26	2005	*Stellaria media*	Canada (Saskatchewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
27	2006	*Galium spurium*	Canada (Saskatchewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
28	2008	*Capsella bursa-pastoris*	Canada (Saskatchewan)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, imazamox	Wheat

	29	2009	*Thlaspi arvense*	Canada (Saskatch-ewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
	30	2009	*Chenopodium album*	Canada (Saskatch-ewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Spring Barley, Wheat
	31	2010	*Amaranthus retroflexus*	Canada (Saskatch-ewan)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
	32	2012	*Kochia scoparia*	Canada (Saskatch-ewan)	ALS inhibitors (B/2), EPSP synthase inhibi-tors (G/9)	thifensulfuron-methyl, tribenuron-methyl, glyphosate	Spring Barley, Wheat, Canola
	33	2015	*Kochia scoparia*	Canada (Saskatch-ewan)	ALS inhibitors (B/2), Synthetic Auxins (O/4)	thifensulfuron-methyl, tribenuron-methyl, dicamba, fluroxypyr	Spring wheat
	34	1996	*Kochia scoparia*	Czech Republic	ALS inhibitors (B/2), Photosys-tem II inhibitors (C1/5)	imazapyr, sulfosulfuron, thifensulfuron-methyl, chlorsulfuron, triflusulfu-ron-methyl, tribenuron-methyl, prosulfuron, metsulfuron-methyl, nicosulfuron, rimsulfuron, atrazine	Railways, Roadsides
	35	2012	*Stellaria media*	France	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, florasulam, iodosulfuron-methyl-sodium, mesosul-furon-methyl	Wheat
	36	2017	*Rumex obtusifo-lius*	France	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, florasulam	Wheat
	37	2011	*Stellaria media*	Germany	ALS inhibitors (B/2)	thifensulfuron-methyl, amidosulfuron, triflusul-furon-methyl, tribenuron-methyl, nicosulfuron, imazamox, florasulam, iodosulfuron-methyl-sodium, tritosulfuron, mesosulfuron-methyl, pyroxsulam	Spring Barley, Wheat, Rapeseed
	38	1998	*Papaver rhoeas*	Greece	ALS inhibitors (B/2)	pyrithiobac-sodium, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, triasulfuron, imazamox, florasulam	Winter wheat
	39	2003	*Amaranthus retroflexus*	Italy	ALS inhibitors (B/2)	imazethapyr, thifensulfu-ron-methyl, nicosulfuron, oxasulfuron, imazamox	Soybean
	40	2004	*Alopecurus aequalis*	Japan	ALS inhibitors (B/2), Microtu-bule inhibitors (K1/3)	thifensulfuron-methyl, trifluralin	Spring Barley, Wheat
	41	2006	*Alopecurus aequalis*	Japan	ALS inhibitors (B/2)	thifensulfuron-methyl	Wheat
	42	2010	*Ranunculus acris*	New Zea-land	ALS inhibitors (B/2), Synthetic Auxins (O/4)	thifensulfuron-methyl, flumetsulam, MCPA	Pastures
	43	2010	*Ranunculus acris*	New Zea-land	ALS inhibitors (B/2)	thifensulfuron-methyl, flumetsulam	Pastures
	44	2014	*Lolium perenne*	New Zea-	ALS inhibitors	thifensulfuron-methyl,	Wheat

				land	(B/2)	chlorsulfuron, tribenuron-methyl, iodosulfuron-methyl-sodium, pyroxsulam	
	45	1997	*Raphanus raphanistrum*	South Africa	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron, iodosulfuron-methyl-sodium	Spring Barley, Wheat
	46	2002	*Stellaria media*	South Africa	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, triasulfuron	Cereals
	47	2008	*Sinapis arvensis*	Turkey	ALS inhibitors (B/2), Synthetic Auxins (O/4)	thifensulfuron-methyl, tribenuron-methyl, triasulfuron, dicamba, propoxycarbazone-sodium	Wheat
	48	2008	*Galium aparine*	Turkey	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, triasulfuron, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Winter wheat
	49	2008	*Bifora radians*	Turkey	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, triasulfuron, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Winter wheat
	50	2016	*Sonchus asper*	United Kingdom	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, imazamox	Wheat
	51	2010	*Conyza canadensis*	United States (Delaware)	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9)	thifensulfuron-methyl, tribenuron-methyl, glyphosate	Soybean, Wheat
	52	2012	*Stellaria media*	United States (Delaware)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl	Wheat
	53	1987	*Lactuca serriola*	United States (Idaho)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron	Cereals, Lentils, Wheat, Canola, Peas, Chickpea
	54	1997	*Anthemis cotula*	United States (Idaho)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl	Cereals, Lentils, Wheat, Canola, Peas, Chickpea
	55	1993	*Amaranthus tuberculatus (=A. rudis)*	United States (Illinois)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorimuron-ethyl	Corn (maize), Soybean
	56	1996	*Amaranthus tuberculatus (=A. rudis)*	United States (Illinois)	ALS inhibitors (B/2), Photosystem II inhibitors (C1/5)	imazethapyr, thifensulfuron-methyl, flumetsulam, atrazine	Corn (maize), Cropland, Soybean
	57	2002	*Amaranthus tuberculatus (=A. rudis)*	United States (Illinois)	ALS inhibitors (B/2), Photosystem II inhibitors	thifensulfuron-methyl, atrazine, fomesafen, lactofen, acifluorfen-	Corn (maize), Cropland,

					(C1/5), PPO inhibitors (E/14)	sodium, imazamox	Soybean
	58	2009	*Amaranthus tuberculatus (=A. rudis)*	United States (Iowa)	ALS inhibitors (B/2), HPPD inhibitors (F2/27), Photosystem II inhibitors (C1/5)	thifensulfuron-methyl, rimsulfuron, atrazine, mesotrione, tembotrione, topramezone	Seed corn
	59	2011	*Amaranthus tuberculatus (=A. rudis)*	United States (Iowa)	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9), HPPD inhibitors (F2/27), Photosystem II inhibitors (C1/5)	imazamethabenz-methyl, thifensulfuron-methyl, chlorimuron-ethyl, atrazine, isoxaflutole, glyphosate, mesotrione	Corn (maize), Soybean
	60	1995	*Amaranthus tuberculatus (=A. rudis)*	United States (Kansas)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl	Alfalfa, Corn (maize), Soybean, Sorghum
	61	2001	*Amaranthus tuberculatus (=A. rudis)*	United States (Kansas)	ALS inhibitors (B/2), PPO inhibitors (E/14)	imazethapyr, thifensulfuron-methyl, chlorimuron-ethyl, fomesafen, lactofen, acifluorfen-sodium	Soybean
	62	2009	*Amaranthus palmeri*	United States (Kansas)	ALS inhibitors (B/2), HPPD inhibitors (F2/27), Photosystem II inhibitors (C1/5)	thifensulfuron-methyl, atrazine, mesotrione, pyrasulfotole, tembotrione, topramezone	Corn (maize), Sorghum
	63	2011	*Conyza canadensis*	United States (Kansas)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, rimsulfuron, iodosulfuron-methyl-sodium, thiencarbazone-methyl	Corn (maize), Cotton, Soybean, Wheat
	64	1992	*Amaranthus hybridus (syn: quitensis)*	United States (Kentucky)	ALS inhibitors (B/2)	imazethapyr, imazaquin, thifensulfuron-methyl, chlorimuron-ethyl, nicosulfuron, primisulfuron-methyl, flumetsulam	Soybean
	65	2013	*Stellaria media*	United States (Kentucky)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, flucarbazone-sodium	Wheat
	66	2009	*Stellaria media*	United States (Maryland)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, mesosulfuron-methyl	Wheat
	67	2000	*Amaranthus tuberculatus (=A. rudis)*	United States (Michigan)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorimuron-ethyl	Soybean
	68	2001	*Chenopodium album*	United States (Michigan)	ALS inhibitors (B/2)	thifensulfuron-methyl, imazamox	Soybean
	69	2002	*Amaranthus hybridus (syn: quitensis)*	United States (Michigan)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorimuron-ethyl, imazamox	Soybean
	70	1994	*Kochia scoparia*	United States	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, tribenuron-	Cropland, Wheat

				(Minneso-ta)		methyl	
	71	1994	*Amaranthus tuberculatus (=A. rudis)*	United States (Minneso-ta)	ALS inhibitors (B/2)	imazethapyr, thifensulfu-ron-methyl	Soybean
	72	2007	*Amaranthus tuberculatus (=A. rudis)*	United States (Minneso-ta)	ALS inhibitors (B/2), EPSP synthase inhibi-tors (G/9)	imazapyr, thifensulfuron-methyl, glyphosate	Soybean
	73	1994	*Amaranthus tuberculatus (=A. rudis)*	United States (Missouri)	ALS inhibitors (B/2)	imazethapyr, imazaquin, thifensulfuron-methyl, chlorimuron-ethyl, prosulfuron, nicosulfuron, halosulfuron-methyl, primisulfuron-methyl, flumetsulam, imazamox	Corn (maize), Cotton, Soybean
	74	2013	*Kochia scoparia*	United States (Montana)	ALS inhibitors (B/2), EPSP synthase inhibi-tors (G/9)	thifensulfuron-methyl, tribenuron-methyl, met-sulfuron-methyl, glypho-sate	Wheat
	75	1999	*Sinapis arvensis*	United States (North Dakota)	ALS inhibitors (B/2)	imazethapyr, thifensulfu-ron-methyl, cloransulam-methyl	Soybean
	76	1996	*Amaranthus tuberculatus (=A. rudis)*	United States (Ohio)	ALS inhibitors (B/2)	imazethapyr, thifensulfu-ron-methyl, chlorimuron-ethyl	Soybean
	77	2001	*Chenopodium album*	United States (Ohio)	ALS inhibitors (B/2)	thifensulfuron-methyl	Soybean
	78	2001	*Amaranthus hybridus (syn: quitensis)*	United States (Ohio)	ALS inhibitors (B/2)	thifensulfuron-methyl, flumetsulam	Soybean
	79	1998	*Amaranthus retroflexus*	United States (Pennsyl-vania)	ALS inhibitors (B/2), Photosys-tem II inhibitors (C1/5)	imazethapyr, imazaquin, thifensulfuron-methyl, chlorimuron-ethyl, primi-sulfuron-methyl, cloran-sulam-methyl, atrazine, imazamox	Corn (maize), Soybean, Tomatoes
	80	2010	*Stellaria media*	United States (Pennsyl-vania)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl, pyrox-sulam	Alfalfa, Spring Barley, Wheat
	81	2010	*Amaranthus palmeri*	United States (South Carolina)	ALS inhibitors (B/2), EPSP synthase inhibi-tors (G/9)	pyrithiobac-sodium, thifensulfuron-methyl, glyphosate, trifloxysulfu-ron-sodium	Corn (maize), Cotton, Soybean
	82	2008	*Stellaria media*	United States (Virginia)	ALS inhibitors (B/2)	thifensulfuron-methyl	Wheat
	83	2000	*Sonchus asper*	United States (Washing-ton)	ALS inhibitors (B/2)	thifensulfuron-methyl, imazamox	Lentils, Wheat
	84	2010	*Anthemis cotula*	United States (Washing-ton)	ALS inhibitors (B/2)	imazethapyr, thifensulfu-ron-methyl, tribenuron-methyl, cloransulam-methyl	Spring Barley, Wheat
	85	2014	*Amaranthus palmeri*	United States	ALS inhibitors (B/2), HPPD	imazethapyr, thifensulfu-ron-methyl, tembotrione	Corn (maize)

			(Wiscon-sin)	inhibitors (F2/27)		

As reviewed by Saari *et al.* (1994), there are now many biotypes within at least 15 weed species (especially *Kochia scoparia* and *Lolium rigidum*) which have developed resistance to ALS-inhibiting herbicides. Since ALS inhibiting herbicides were introduced, they have mainly been targeted at broad-leaved weeds. Targeting has mainly been through selection with sulfonylurea herbicides (presumably because they have been in commercial use for the longest period). In the vast majority of cases of resistance following selection with sulfonylurea herbicides, the resistance mechanism is a change in the target site enzyme ALS (reviewed by Saari et al., 1994). In most cases, the sulfonylurea-resistant biotypes with resistant ALS enzyme exhibit varying levels of target site cross-resistance to the chemically dissimilar, but ALS-inhibiting, imidazolinone and/or triazolopyrimidine herbicides (Hall and Devine, 1990; Christopher *et al.*, 1992; Saari *et al.*, 1990; 1992; 1994).

There are several multiple resistances reported within the group sulfonylureas, but only *Kochia scoparia* is affected with the chemicals focused on in this report.

According to HRAC, sensitivity monitoring was carried out in Austria, France, Spain, Portugal, Italy, Germany and Australia in commercial fields. Other information in context of sensitivity data is reported on: https://hracglobal.com/files/Monitoring-and-Mitigation-of-Herbicide-Resistance.pdf

As sulfonylureas, actives belong to a HRAC group with a high resistance risk. Several dicotyledonous weeds species have been reported with resistance to ALS inhibitors worldwide and also in Europe. Most of these were found to be resistant to sulfonylureas. **The inherent risk of thifensulfuron-methyl has to be classified as high.**

Resistance may be a result of repeated use of the same herbicide, or several herbicides with the same mode of action and is often associated with crop monoculture as well as reduced cultivation practices. For instance, increasing infestations of *Alopecurus myosuroides* and *Apera spica-venti* is associated with continuous winter cereal production, minimal cultivation and/or direct drilling. Furthermore, seeds of *A. myosuroides* and *A. spica-venti* are spread widely in the field through modern harvesting equipment.

The principle of crop rotation as a resistance management tool is to avoid successive crops in the same field which require herbicides with the same mode of action for control of the same weed species.

Cultural (or non-chemical) weed control methods do not exert a chemical selection pressure and assist greatly in reducing the soil seed bank. Cultural techniques must be incorporated into the general agronomy of the crop and other weed control strategies.

The use of chemical mixtures to prevent resistance: Mixtures can be a useful tool in managing or preventing the establishment of resistant weeds.
For chemical mixtures to be effective, they should include active ingredients which both give high levels of control of the target weed, AND include active ingredients with different modes of action.

- **Metsulfuron-methyl** is a sulfonylurea compound, classified in the HRAC mode of action group B (ALS inhibitors) for which the mode of action involves inhibition of the enzyme acetolactate synthase (ALS)

Metsulfuron-methyl is well known and already approved for use in Europe. It belongs to the chemical group of sulfonylureas and result in inhibition of the plant

enzyme acetolactate synthase (ALS). Due to this primary mode of action, it is classified as HRAC group B herbicides.

Resistance to ALS inhibitors can be caused by an insensitive target enzyme or by metabolic processes. Regarding dicotyledonous weed species, mainly target site resistance mechanisms have been detected. Different mutations have been detected on the ALS gene of resistant weed species and seven amino acids have been identified whose exchange may result in resistance towards ALS inhibitors. Different mutations have been detected on the ALS gene of resistant weed species and seven amino acids have been identified whose exchange may result in resistance towards ALS inhibitors, with the inherence mode of the mutation is dominant/semi dominant. The mechanisms of resistance to ALS inhibitors in various broad-leaved weed species have been relatively widely studied and reported. The first reported case of resistance in Europe was in *Stellaria media* in 1991 (Kudsk et al., 1995), with the resistant biotype arising in Denmark in a field treated with either chlorsulfuron or metsulfuron-methyl for eight successive years.

Resistance of metsulfuron-methyl has been reported for 80 weed species cases worldwide. Numbers of recorded cases of resistance to HRAC B herbicides and numbers of broad-leaved weed species with developed resistance to are relatively high**. The risk of resistance arising from the use of metsulfuron-methyl is therefore considered to be high.**

Table. Overview of the resistance cases for metsulfuron-methyl

#	Year	Species	Country	MOAs	Actives	Situations
1	2008	*Raphanus sativus*	Argentina	ALS inhibitors (B/2)	imazethapyr, imazapyr, bispyribac-sodium, chlorimuron-ethyl, metsulfuron-methyl, diclosulam, flumetsulam, imazamox, iodosulfuron-methyl-sodium, flucarbazone-sodium	Wheat, Sunflower, Canola
2	2012	*Brassica rapa (=B. campestris)*	Argentina	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9)	imazapyr, metsulfuron-methyl, diclosulam, glyphosate	Soybean, Wheat
3	2013	*Hirschfeldia incana*	Argentina	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat, Winter barley
4	2016	*Hirschfeldia incana*	Argentina	ALS inhibitors (B/2), Synthetic Auxins (O/4)	metsulfuron-methyl, 2,4-D	Wheat
5	1985	*Lolium rigidum*	Australia (New South Wales)	ACCase inhibitors (A/1), ALS inhibitors (B/2), Microtubule inhibitors (K1/3)	haloxyfop-methyl, diclofop-methyl, fluazifop-P-butyl, quizalofop-P-ethyl, sethoxydim, tralkoxydim, chlorsulfuron, metsulfuron-methyl, triasulfuron, trifluralin	Spring Barley, Lentils, Wheat, Lupins, Canola, Peas, Chickpea, Faba beans
6	2004	*Raphanus raphanistrum*	Australia (New South Wales)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, triasulfuron	Cereals
7	1982	*Lolium rigidum*	Australia (South Australia)	ACCase inhibitors (A/1), ALS inhibitors (B/2), DOXP inhibitors (F4/13), Lipid Inhibitors (N/8), Long chain fatty acid inhibitors (K3/15), Microtubule inhibitors (K1/3), Mitosis inhibitors (K2/23)	diclofop-methyl, fluazifop-P-butyl, quizalofop-P-ethyl, sethoxydim, tralkoxydim, imazapyr, chlorsulfuron, metsulfuron-methyl, triasulfuron, clomazone, ethalfluralin, trifluralin, chlorpropham, metolachlor, triallate	Spring Barley, Wheat
8	1990	*Sisymbrium orientale*	Australia (South Aus-	ALS inhibitors (B/2)	imazethapyr, chlorsulfuron, metsulfuron-methyl, triasul-	Spring Barley, Wheat

				tralia)		furon, metosulam	
	9	1994	*Lactuca serriola*	Australia (South Australia)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, triasulfuron, flumetsulam, metosulam	Spring Barley, Roadsides, Wheat, Canola
	10	2004	*Pentzia suffruticosa*	Australia (South Australia)	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
	11	2005	*Sisymbrium orientale*	Australia (South Australia)	ALS inhibitors (B/2), Synthetic Auxins (O/4)	imazethapyr, metsulfuron-methyl, metosulam, MCPA, 2,4-D	Cereals
	12	1984	*Lolium rigidum*	Australia (Victoria)	ACCase inhibitors (A/1), ALS inhibitors (B/2), Microtubule inhibitors (K1/3)	diclofop-methyl, fluazifop-P-butyl, quizalofop-P-ethyl, sethoxydim, chlorsulfuron, metsulfuron-methyl, trifluralin	Spring Barley, Pastures, Wheat
	13	2009	*Lactuca serriola*	Australia (Victoria)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Spring Barley, Wheat
	14	1984	*Lolium rigidum*	Australia (Western Australia)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Spring Barley, Cropland, Wheat
	15	2012	*Matricaria recutita (= M. chamomilla)*	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
	16	2013	*Stellaria media*	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
	17	2014	*Papaver rhoeas*	Belgium	ALS inhibitors (B/2)	metsulfuron-methyl, florasulam	Wheat
	18	1999	*Sagittaria montevidensis*	Brazil	ALS inhibitors (B/2)	bispyribac-sodium, pyrazosulfuron-ethyl, metsulfuron-methyl, ethoxysulfuron, cyclosulfamuron	Rice
	19	2001	*Raphanus sativus*	Brazil	ALS inhibitors (B/2)	imazethapyr, chlorimuron-ethyl, metsulfuron-methyl, nicosulfuron, cloransulam-methyl	Wheat
	20	2004	*Euphorbia heterophylla*	Brazil	ALS inhibitors (B/2), PPO inhibitors (E/14)	imazethapyr, metsulfuron-methyl, nicosulfuron, diclosulam, flumetsulam, cloransulam-methyl, fomesafen, lactofen, acifluorfen-sodium, flumiclorac-pentyl, saflufenacil	Corn (maize), Soybean
	21	2009	*Sagittaria montevidensis*	Brazil	ALS inhibitors (B/2), PSII inhibitors (Nitriles) (C3/6)	imazethapyr, bispyribac-sodium, pyrazosulfuron-ethyl, metsulfuron-methyl, ethoxysulfuron, bentazon, penoxsulam	Rice
	22	2013	*Raphanus raphanistrum*	Brazil	ALS inhibitors (B/2)	imazapyr, chlorimuron-ethyl, metsulfuron-methyl, sulfometuron-methyl, cloransulam-methyl, iodosulfuron-methyl-sodium, imazapic	Spring Barley, Wheat
	23	2015	*Echium plantagineum*	Brazil	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals, Wheat
	24	1988	*Stellaria media*	Canada (Alberta)	ALS inhibitors (B/2)	imazamethabenz-methyl, thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, ethametsulfuron-methyl, sulfometuron-methyl	Cereals, Wheat
	25	1989	*Kochia scoparia*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl	Spring Barley, Wheat
	26	1993	*Sinapis arvensis*	Canada (Alberta)	ALS inhibitors (B/2)	metsulfuron-methyl, ethametsulfuron-methyl	Spring Barley, Canola
	27	1996	*Sonchus asper*	Canada	ALS inhibitors	thifensulfuron-methyl,	Spring Bar-

				(Alberta)	(B/2)	chlorsulfuron, tribenuron-methyl, metsulfuron-methyl	ley, Pastures
	28	1996	*Galium spurium*	Canada (Alberta)	ALS inhibitors (B/2), Synthetic Auxins (O/4)	imazethapyr, thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl, triasulfuron, sulfometuron-methyl, quinclorac	Cereals, Wheat, Canola
	29	1998	*Neslia paniculata*	Canada (Alberta)	ALS inhibitors (B/2)	metsulfuron-methyl	Cropland, Wheat
	30	2001	*Thlaspi arvense*	Canada (Alberta)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, metsulfuron-methyl, ethametsulfuron-methyl	Spring Barley, Wheat, Canola, Peas
	31	2011	*Crepis tectorum*	Canada (Alberta)	ALS inhibitors (B/2)	metsulfuron-methyl	Grass seed
	32	2012	*Vaccaria hispanica*	Canada (Alberta)	ALS inhibitors (B/2)	thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl	Wheat
	33	1988	*Kochia scoparia*	Canada (Manitoba)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron	Spring Barley, Industrial sites, Wheat
	34	1992	*Sinapis arvensis*	Canada (Manitoba)	ALS inhibitors (B/2)	metsulfuron-methyl, ethametsulfuron-methyl	Spring Barley, Cropland, Wheat, Canola
	35	1995	*Galeopsis tetrahit*	Canada (Manitoba)	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals, Wheat
	36	2010	*Raphanus sativus*	Chile	ALS inhibitors (B/2)	imazapyr, metsulfuron-methyl, triasulfuron, imazamox, iodosulfuron-methyl-sodium, flucarbazone-sodium, pyroxsulam	Wheat
	37	2010	*Anthemis cotula*	Chile	ALS inhibitors (B/2)	metsulfuron-methyl, iodosulfuron-methyl-sodium, pyroxsulam	Wheat
	38	2012	*Silene gallica*	Chile	ALS inhibitors (B/2)	imazapyr, metsulfuron-methyl, imazamox, iodosulfuron-methyl-sodium, pyroxsulam	Wheat
	39	1996	*Kochia scoparia*	Czech Republic	ALS inhibitors (B/2), Photosystem II inhibitors (C1/5)	imazapyr, sulfosulfuron, thifensulfuron-methyl, chlorsulfuron, triflusulfuron-methyl, tribenuron-methyl, prosulfuron, metsulfuron-methyl, nicosulfuron, rimsulfuron, atrazine	Railways, Roadsides
	40	2006	*Avena sterilis*	France	ALS inhibitors (B/2)	metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl, pyroxsulam	Wheat
	41	2006	*Avena fatua*	France	ALS inhibitors (B/2)	metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl, pyroxsulam	Wheat
	42	2007	*Papaver rhoeas*	France	ALS inhibitors (B/2)	metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Wheat
	43	2009	*Senecio vulgaris*	France	ALS inhibitors (B/2)	tribenuron-methyl, prosulfuron, metsulfuron-methyl, flazasulfuron, imazamox, florasulam, iodosulfuron-methyl-sodium, mesosulfuron-methyl, thiencarbazone-methyl	Grapes, Wheat
	44	2010	*Tripleurospermum perforatum (=T. inodorum)*	France	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat

	45	2012	*Stellaria media*	France	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, florasulam, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Wheat
	46	2016	*Papaver rhoeas*	France	ALS inhibitors (B/2), Synthetic Auxins (O/4)	metsulfuron-methyl, MCPA, 2,4-D, iodosulfuron-methyl-sodium, mesosulfuron-methyl	Cereals
	47	2017	*Rumex obtusifolius*	France	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, florasulam	Wheat
	48	2009	*Sinapis arvensis*	Iran	ALS inhibitors (B/2)	sulfosulfuron, tribenuron-methyl, metsulfuron-methyl, iodosulfuron-methyl-sodium	Winter wheat
	49	1996	*Stellaria media*	Ireland	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
	50	2000	*Bacopa rotundifolia*	Malaysia	ALS inhibitors (B/2)	bensulfuron-methyl, pyrazosulfuron-ethyl, metsulfuron-methyl	Rice
	51	2010	*Clidemia hirta*	Malaysia	ALS inhibitors (B/2)	metsulfuron-methyl	Palm oil
	52	2002	*Stellaria media*	Norway	ALS inhibitors (B/2)	tribenuron-methyl, metsulfuron-methyl, iodosulfuron-methyl-sodium	Cereals
	53	2012	*Matricaria recutita (= M. chamomilla)*	Norway	ALS inhibitors (B/2)	tribenuron-methyl, metsulfuron-methyl	Wheat, Winter barley
	54	2011	*Avena fatua*	Poland	ACCase inhibitors (A/1), ALS inhibitors (B/2)	fenoxaprop-P-ethyl, metsulfuron-methyl, sulfometuron-methyl, iodosulfuron-methyl-sodium, pinoxaden, propoxycarbazone-sodium	Spring Barley, Spring wheat
	55	1997	*Raphanus raphanistrum*	South Africa	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron, iodosulfuron-methyl-sodium	Spring Barley, Wheat
	56	2002	*Stellaria media*	South Africa	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, metsulfuron-methyl, triasulfuron	Cereals
	57	2000	*Stellaria media*	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl, florasulam	Cereals
	58	2001	*Papaver rhoeas*	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
	59	2002	*Tripleurospermum perforatum (=T. inodorum)*	United Kingdom	ALS inhibitors (B/2)	metsulfuron-methyl	Cereals
	60	2016	*Sonchus asper*	United Kingdom	ALS inhibitors (B/2)	thifensulfuron-methyl, metsulfuron-methyl, imazamox	Wheat
	61	1989	*Kochia scoparia*	United States (Colorado)	ALS inhibitors (B/2)	metsulfuron-methyl, triasulfuron	Roadsides, Wheat
	62	2005	*Ambrosia artemisiifolia*	United States (Delaware)	ALS inhibitors (B/2), PPO inhibitors (E/14)	imazethapyr, imazapyr, imazaquin, pyrithiobac-sodium, chlorimuron-ethyl, metsulfuron-methyl, halosulfuron-methyl, primisulfuron-methyl, cloransulam-methyl, oxyfluorfen, fomesafen, lactofen, acifluorfen-sodium, flumioxazin, flumiclorac-pentyl, carfentrazone-ethyl, sulfentrazone, imazamox, pyraflufen-ethyl, iodosulfuron-methyl-sodium, trifloxysulfuron-sodium	Soybean
	63	2014	*Chamaesyce macu-*	United States	ALS inhibitors	metsulfuron-methyl	Turf

		lata	(Georgia)	(B/2)		
64	1987	*Lactuca serriola*	United States (Idaho)	ALS inhibitors (B/2)	imazethapyr, thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron	Cereals, Lentils, Wheat, Canola, Peas, Chickpea
65	1995	*Kochia scoparia*	United States (Illinois)	ALS inhibitors (B/2), Photosystem II inhibitors (C1/5)	metsulfuron-methyl, atrazine	Corn (maize), Cropland, Wheat
66	1995	*Kochia scoparia*	United States (Indiana)	ALS inhibitors (B/2), Photosystem II inhibitors (C1/5)	metsulfuron-methyl, atrazine, cyanazine	Railways
67	2005	*Erysimum repandum*	United States (Kansas)	ALS inhibitors (B/2)	sulfosulfuron, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron, imazamox, propoxycarbazone-sodium	Winter wheat
68	2006	*Descurainia sophia*	United States (Kansas)	ALS inhibitors (B/2)	sulfosulfuron, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, triasulfuron, imazamox, pyroxsulam	Winter wheat
69	2011	*Conyza canadensis*	United States (Kansas)	ALS inhibitors (B/2)	thifensulfuron-methyl, chlorsulfuron, tribenuron-methyl, metsulfuron-methyl, rimsulfuron, iodosulfuron-methyl-sodium, thiencarbazone-methyl	Corn (maize), Cotton, Soybean, Wheat
70	1989	*Kochia scoparia*	United States (Montana)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Cropland, Wheat
71	2013	*Kochia scoparia*	United States (Montana)	ALS inhibitors (B/2), EPSP synthase inhibitors (G/9)	thifensulfuron-methyl, tribenuron-methyl, metsulfuron-methyl, glyphosate	Wheat
72	1987	*Kochia scoparia*	United States (North Dakota)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Cropland, Wheat
73	1992	*Kochia scoparia*	United States (Oklahoma)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, sulfometuron-methyl	Roadsides, Wheat
74	2018	*Conyza canadensis*	United States (Oklahoma)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Cotton, Soybean, Wheat
75	1993	*Salsola tragus*	United States (Oregon)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, triasulfuron	Wheat
76	1993	*Lactuca serriola*	United States (Oregon)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, triasulfuron	Wheat
77	1993	*Kochia scoparia*	United States (Oregon)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl, triasulfuron	Wheat
78	1999	*Camelina microcarpa*	United States (Oregon)	ALS inhibitors (B/2)	chlorsulfuron, metsulfuron-methyl	Wheat
79	1998	*Kochia scoparia*	United States (Texas)	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat
80	1996	*Kochia scoparia*	United States (Wyoming)	ALS inhibitors (B/2)	metsulfuron-methyl	Wheat

Cross-resistance to multiple active substances from the group of ALS inhibitors is common in biotypes with resistance to ALS inhibitors. Different mutations on the binding site for the ALS enzyme result in different cross-resistance patterns. In the case of ALS resistant biotypes with metabolic resistance mechanisms, cross-resistance may also occur towards substances from other HRAC groups. For example the *Kochia scoparia* population in Czech Republic appears to be cross-resistant to photosystem II inhibitors (HRAC group C1). Evidence of resistance was observed in Europe for active substance under evaluation and also for the whole ALS group of herbicides, involving broadleaved weeds. Furthermore, the possibility of cross re-

	sistance has to be taken into account. **Conclusions on risk of the possible occurrence of the development of resistance or cross-resistance:** • The product has a high inherent and agronomical risk for resistance weed development. • A resistance risk management as proposed by the HRAC will avoid resistance of weeds to TOTO 75 SG / Tytan 75 SG / Herkules 75 SG. • Experts of the HRAC follow developments on potential resistance issues for sulfonylurea herbicides very closely. • Recommendations of the HRAC will be followed in labelling: ✓ *"When herbicides with the same mode of action are used repeatedly over several years in the same field, selection of resistant biotypes can take place. These can propagate and may become dominating. A weed species is considered resistant to a herbicide if it survives a correctly-applied treatment at the recommended dose.* ✓ *Development of resistance within a weed species can be avoided or delayed by sequencing or tank-mixing with suitable products having a different mode of action".* ✓ *"A strategy for preventing and managing resistance should be adopted.* **In order to minimize the risk of occurrence and development of herbicide weed resistance we should follow Good Agricultural Practice:** • follow strictly the directions provided in the plant protection product label, • plant protection product should been used at the recommended dose in the recommended time to ensure optimum weed control • use integrated weed control practices covering fields such as history crop rotation, herbicides used and various tillage (mechanical, cultural, biological and chemical) • use rotation of herbicides (active substances) with different mechanisms of action, • use a mixture of herbicides (active substances) with different mechanisms of action, • use herbicides acting on several life processes in rotation and / or a mixture • weeds (with different mechanisms of action). **Label for the plant protection product TOTO 75 SG / Tytan 75 SG / Herkules 75 SG:** • observe the field after applying the herbicide to ensure that weeds are being controlled, • use different methods of weed control, including crop rotations, etc., • use certified seed, • inform the authorization holder of unsatisfactory weed control, • for more information please contact your advisor, holder permit or a representative of the permit holder. **In the opinion of Evaluator each of cMS can change or adjust risk assessment considering the national requirements and may designate additional measures relating to resistance prevention on the national level.**

3.4 Adverse effects on treated crops (KCP 6.4)

Please research to core dossier.

Comments of zRMS:	Statement accepted. In accordance with the Article 43 of Regulation (EC) No 1107/2009, the already submitted data will not be re-evaluated because the conclusions of previous assessments are still considered valid in the case of no significant change of the GAP table.

3.5 Observations on other undesirable or unintended side-effects (KCP 6.5)

Please research to core dossier.

Comments of zRMS:	Statement accepted. In accordance with the Article 43 of Regulation (EC) No 1107/2009, the already submitted data will not be re-evaluated because the conclusions of previous assessments are still considered valid in the case of no significant change of the GAP table.

3.6 Other/special studies

Please research to core dossier.

Comments of zRMS:	Statement accepted. In accordance with the Article 43 of Regulation (EC) No 1107/2009, the already submitted data will not be re-evaluated because the conclusions of previous assessments are still considered valid in the case of no significant change of the GAP table.

3.7 List of test facilities including the corresponding certificates

Please research to core dossier.