FINAL REGISTRATION REPORT

Part B

Section 3

Efficacy Data and Information

Concise summary

Product code: CHR/H/TERIZ 650 WG

Product name(s): Untido 650 WG/ Jotamun 650/ Metodus 650 WG

Chemical active substance(s):

Terbuthylazine, 400 g/kg

Isoxaflutole, 100 g/kg

Mesotrione, 150 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(reneval of authorization)

Applicant: Innvigo Sp. z o.o.

Submission date: 03/2023

MS Finalisation date: 05/2023; 06/2023

Version history

When	What
May 2023	ZRMs evaluated submitted dRR by Applicant
June 2023	Final Registration Report

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

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:	Comments of zRMS are presented in commenting boxes at the end of each chapter. The text of dRR was generally not changed or rewritten (small changes in the document are marked by grey colour).

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

Abstract

The product Untido 650 WG/ Jotamun 650/ Metodus 650 WG (containing: terbuthylazine, 400 g/kg; isaxaflutole, 100 g/kg and mesotrione, 150 g/kg as an active compounds), is currently registered in Poland (Reg. No. R-119/2019) in maize. **In our opinion submitted documentation is sufficient for re-registered in line to Article 43 – Untido 650 WG/ Jotamun 650/ Metodus 650 WG.**

3.2 Intended uses (only NATIONAL GAP)

GAP rev. , date: 2023-03-23

PPP (product name/code):	Untido 650 WG/Jotamun 650 WG/ Metodus 650 WG - CHR/H/TERIZ	Formulation type:	WG [a, b]
Active substance 1:	terbuthylazine	Conc. of as 1:	400 g/kg [c]
Active substance 2:	mesotrione	Conc. of as 2:	150 g/kg [c]
Active substance 3:	isoxaflutole	Conc. of as 3:	100 g/kg [c]
Safener:	-	Conc. of safener:	- [c]
Synergist:	-	Conc. of synergist:	- [c]
Applicant:	Innvigo Sp. z o.o.	Professional use:	☒
Zone(s):	Centarl [d]	Non professional use:	☐
Verified by MS:	no		

Field of use: herbicide

1	2	3	4	5	6	7	8	9	10	11	12	13	14
Use-No. [e]	**Member state(s)**	**Crop and/ or situation** **(crop destination / purpose of crop)**	**F, Fn, Fpn G, Gn, Gpn or I**	**Pests or Group of pests controlled** (additionally: developmental stages of the pest or pest group)	**Application**				**Application rate**			**PHI** (days)	**Remarks:** e.g. g safener/synergist per ha [f]
					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		

Zonal uses (field or outdoor uses, certain types of protected crops)													
1	PL	Maize (ZEAMX)	F	Mono and dicotsweeds	Spray, medium sprayer	Spring BBCH 00, max. 3 days after sowing	a)1 b)1	n/a	a) 0.8 kg/ha b) 0.8 kg/ha	a) 0.52 kg a.s./ha (T 0.32 + I 0.08 + M 0.12) b) 0.52 kg a.s./ha (T 0.32 + I 0.08 + M 0.12)	200-250	n/a	Acceptable for re-registered.
Interzonal uses (use as seed treatment, in greenhouses (or other closed places of plant production), as post-harvest treatment or for treatment of empty storage rooms)													
2													
3													
Minor uses according to Article 51 (zonal uses)													
4													
5													
Minor uses according to Article 51 (interzonal uses)													
6													
7													

Remarks table heading:

(a) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(b) Catalogue of pesticide formulation types and international coding system CropLife International Technical Monograph n°2, 6th Edition Revised May 2008
(c) g/kg or g/l
(d) Select relevant
(e) Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
(f) No authorization possible for uses where the line is highlighted in grey, Use should be crossed out when the notifier no longer supports this use.

Remarks columns:

1 Numeration necessary to allow references
2 Use official codes/nomenclatures of EU Member States
3 For crops, the EU and Codex classifications (both) should be used; when relevant, the use situation should be described (e.g. fumigation of a structure)
4 F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
5 Scientific names and EPPO-Codes of target pests/diseases/ weeds or, when relevant, the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named.
6 Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
7 Growth stage at first and 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
8 The maximum number of application possible under practical conditions of use must be provided.
9 Minimum interval (in days) between applications of the same product
10 For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products.
11 The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
12 If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.
13 PHI - minimum pre-harvest interval
14 Remarks may include: Extent of use/economic importance/restrictions

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1.

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Column 15: zRMS conclusion.

A	Acceptable
R	Acceptable with further restriction
C	To be confirmed by cMS
N	Not acceptable / evaluation not possible
n.r.	Not relevant for section 3

3.3 Efficacy data (KCP 6)

Please research to core dossier.

Comments of zRMS:	This is an Article 43 application (of Reg. (EC) 1107/2009) and as such only specific new data in order to comply with changes in the assessment of the active substance (new endpoints, new guidance applied, conditions or restrictions in the renewal regulation) can be considered (SANCO/2010/13170 rev 13). Plant protection products based on terbuthylazine, isaxaflutole and mesotrione as active compounds are known and used for many years. In Poland 6 herbicides with isaxaflutole, 58 PPP with mesotrione and 17 PPP with terbuthylazine are registered and used to control weeds in crops. On the basis on the registry of plant protection products (dated 28.04.2023) – in Poland are registered 3 plant protection products containing isaxaflutole, mesotrione and terbuthylazine as active compound. These PPPs are now evaluated for re-registration: Untido 650 WG/ Jotamun 650/ Metodus 650 WG (containing: terbuthylazine, 400 g/kg; isaxaflutole, 100 g/kg and mesotrione, 150 g/kg as an active compounds). For now, these three active compounds (terbuthylazine, isaxaflutole and mesotrione) are on the list of approved active substances. All needed information's are presented by Applicant in core dossier. Untido 650 WG/ Jotamun 650/ Metodus 650 WG (product code: CHR/H/TERIZ 650 WG) was submitted and positively evaluated during the authorization process of this product (permit of the Ministry of Agriculture and Rural Development No. R-119/2019 dated 24.07.2019). This report has been discontinued to re-registration of this product. The GAP has not been changed compared to current registration. Therefore, in intended uses, there has been no GAP change that impacts the previous efficacy evaluation of CHR/H/TERIZ 650 WG, and the effectiveness does not have to be reassessed (according to the regulations). No new efficacy and selectivity data trials of this product have been submitted and no new uses will be considered in this application. Thus, the conclusions of previous assessments are still considered valid and the only aspect that will be considered is the resistance risk assessment, which requires updating at renewal. **The data presented in this dossier fully support the renewal under Article 43 of Untido 650 WG/ Jotamun 650/ Metodus 650 WG (product code: CHR/H/TERIZ 650 WG) in Poland.**

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

Resistance Risk Assessment (*accroding to EPPO PP 1/213 (4) Resistance risk analysis*)

Mode of action

CHR/H/TERIZ 650 WG is a herbicide containing active substance: terbuthylazine 400 g/kg (HRAC group 9: inhibition of enolpyruvyl shikimate phosphate synthase), isoxaflutole 100 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase) and mesotrione 150 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase). This groups of herbicides is quite well known and has been applied commercially for decades.

Terbuthylazine is an inhibitor of photosystem II (PS II) (HRAC mode of action group C1, WSSA group 5). By binding to the QB binding site of photosystem II it blocks the Hill reaction, which takes place in the chloroplast. Photosynthesis is prevented at the solar energy collected by the leaf is diverted into the formation of destructive compounds (free radicals) rather than into the normal photosynthesis products. These free radicals build up to the point where chlorophyll, carotenoids and cell membranes are destroyed. The rate of plant death is rapid and too fast to be accounted for by starvation (by stopping photosynthesis alone) and the destruction of cell walls and membranes are the major causes of the foliar chlorosis, necrosis and finally death of the plant. Selectivity of the crop is due to the ability of corn to rapidly metabolise terbuthylazine into non-toxic compounds.
Mesotrione belongs to the chemical group of the triketones (2-benzylcyclohexane-1,3-diones), which acts by blocking the function of the essential plant enzyme 4-hydroxy-phenyl-pyruvatedioxygenase (4-HPPD) in the cytosol of sensitive plants. Mesotrione is a systemic herbicide and controls most annual broadleaf and annual grass weed species in maize. It is taken up via roots and shoots and translocated rapidly in both the xylem and phloem into all plant parts. In sensitive plants symptoms of white chlorosis become visible within a few days after application in actively growing tissues being in the cell elongation phase. Complete death of sensitive plants may occur up to 2 weeks after application.
Isoxaflutole is a systemic herbicide belonging to HRAC group 27 – 4-HPPD inhibitors. Isoxaflutole was developed for agricultural use. The use evaluated for the first EU approval was for the control of broad leaved and annual grass weeds in maize (silage, grain, seed and sweet corn). In maize isoxaflutole is applied as a single application at the stage of growth of maize BBCH 00 – 13 i.e. pre-emergence of the maize up to the third true leaf. In sweet corn there is a single application at the stage of BBCH 00 – 09 i.e. pre-emergence only. Following uptake, isoxaflutole is very xylem mobile when taken up via the roots and phloem mobile when taken up via the shoots and it accumulates in the leaf margins and tips. Eventually lethal amounts of isoxaflutole accumulate in the foliage and meristem. Germinating seedlings that contact the product either do not emerge or emerge white and stop growing. Isoxaflutole may also be adsorbed by foliage and roots of already emerged weeds and will injure or control young weeds that are emerged at application.

Mechanism of resistance
CHR/H/TERIZ 650 WG is a herbicide containing active substance: terbuthylazine 400 g/kg (HRAC group 9: inhibition of enolpyruvyl shikimate phosphate synthase), isoxaflutole 100 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase) and mesotrione 150 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase). The mode of action involving a ‘multi-site’ action may indicate a lower risk to developing weeds resistance. This groups of herbicides is quite well known and has been applied commercially for decades.
Accroding to EPPO PP 1/213 (4) Resistance risk analysis weeds usually only produce one generation per year and development of resistance is usually a relatively slow process. It is difficult to class any weed species as inherently more or less likely to develop resistance to a particular herbicide.

Evidence of resistance
Terbuthylazine, belonging to the chemical group of Triazine, is classified with HRAC code C1 and with the biochemical mode of action “Inhibition of photo-synthesis at photosystem”.

According to Ian Heap's website (http://www.weedscience.org) there are five species which have been reported as resistant to: terbuthylazine (Table 1).

According to https://weedscience.org/ :
Table 1. Herbicide resistance cases

Year	Species	Country	Actives	Crops
1982	*Polygonum lapathifolium*	Czech Republic	atrazine, terbuthylazine, terbutryne, prometryne, cyanazine, lenacil	Railways
1985	*Amaranthus retroflexus*	Czech Republic	atrazine, terbuthylazine, terbutryne, prometryne, cyanazine, metamitron	Corn (maize), Railways, Roadsides, Sugar beets
1986	*Chenopodium album*	Czech Republic	atrazine, simazine, terbuthylazine, terbutryne, prometon, cyanazine, metamitron, lenacil	Corn (maize), Sugar beets
1988	*Senecio vulgaris*	Czech Republic	atrazine, simazine, terbuthylazine, terbutryne, prometryne, cyanazine, lenacil	Orchards, Railways
1999	*Amaranthus retroflexus*	Italy	chloridazon/pyrazon, terbuthylazine, metamitron	Corn (maize), Soybean, Sugar beets
1999	*Solanum nigrum*	New Zealand	atrazine, terbuthylazine, prometryne, cyanazine	Corn (maize)

Mesotrione belongs to HRAC group 27 (Legacy F2). According to Ian Heap's website (http://www.weedscience.org) there are only three species which have been reported as resistant to HRAC group 27 (Legacy F2). These are *Amaranthus palmeri*, *Amaranthus tuberculatus* (=*A. rudis*) and *Raphanus raphanistrum*. All cases reported have been in the United States and Australia with no evidence of resistance in Europe. Overall the risk of resistance development to HRAC group 27 (Legacy F2) is low.

According to https://weedscience.org/ :
Table 2. Herbicide resistance cases to 4-HPPD inhibitors

Year	Species	Country	Actives	Crops
2009	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, chlorimuron-ethyl, atrazine, mesotrione, tembotrione, topramezone	Seed corn
2009	*Amaranthus tuberculatus (=A. rudis)*	United States	thifensulfuron-methyl, rimsulfuron, atrazine, mesotrione, tembotrione, topramezone	Seed corn
2009	*Amaranthus palmeri*	United States	thifensulfuron-methyl, atrazine, mesotrione, pyrasulfotole, tembotrione, topramezone	Corn (maize), Sorghum
2011	*Amaranthus tuberculatus (=A. rudis)*	United States	imazamethabenz-methyl, thifensulfuron-methyl, chlorimuron-ethyl, atrazine, isoxaflutole, glyphosate, mesotrione	Corn (maize), Soybean
2011	*Amaranthus tuberculatus (=A. rudis)*	United States	mesotrione, tembotrione, topramezone	Corn (maize)
2011	*Amaranthus palmeri*	United States	mesotrione, tembotrione, topramezone	Corn (maize)
2014	*Amaranthus palmeri*	United States	atrazine, mesotrione, tembotrione, topramezone	Corn (maize)
2014	*Amaranthus palmeri*	United States	imazethapyr, thifensulfuron-methyl, tembotrione	Corn (maize)
2015	*Raphanus raphanistrum*	Australia	chlorsulfuron, atrazine, diflufenican, fluridone, isoxaflutole, 2,4-D, mesotrione, tembotrione	Wheat
2015	*Amaranthus palmeri*	United States	chlorsulfuron, atrazine, glyphosate, 2,4-D, mesotrione	Sorghum

2016	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, chlorimuron-ethyl, atrazine, fomesafen, lactofen, acifluorfen, 2,4-D, mesotrione, tembotrione, topramezone	Corn (maize), Soybean
2016	*Amaranthus palmeri*	United States	mesotrione	Corn (maize)
2020	*Raphanus raphanistrum*	Australia	metsulfuron-methyl, dicamba, 2,4-D, mesotrione, topramezone, pyroxasulfone	Wheat
2020	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, atrazine, fomesafen, glyphosate, mesotrione	Soybean

Isoxaflutole is grouped into the isoxazole chemical group. The mode of action is based on the inhibition of ~~of~~ Hydroxyphenyl Pyruvate Dioxygenase (HRAC group: 27, legacy F2). This group of herbicides is quite well known and has been applied commercially for decades.
According to Ian Heap's website (http://www.weedscience.org) there are only two species which have been reported as resistant to isoxaflutole: *Raphanus raphanistrum* and *Amaranthus tuberculatus (=A. rudis)* (Table 3). Both cases have been reported in the Australia and USA with no evidence of resistance in Europe. Taking into account the entire HRAC group 27, 14 cases of weed resistance to 4-HPPD inhibitors in three weed species were reported: *Raphanus raphanistrum, Amaranthus tuberculatus (=A. rudis)* and *Amaranthus palmeri* (Table 4). All cases reported have been in the Australia and USA with no evidence of resistance in Europe.

According to https://weedscience.org/ :
Table 3. Herbicide resistance cases to isoxaflutole

Year	Species	Country	Actives	Crops
2011	*Amaranthus tuberculatus (=A. rudis)*	United States	imazamethabenz-methyl, thifensulfuron-methyl, chlorimuron-ethyl, atrazine, isoxaflutole, glyphosate, mesotrione	Corn (maize), Soybean
2015	*Raphanus raphanistrum*	Australia	chlorsulfuron, atrazine, diflufenican, fluridone, isoxaflutole, 2,4-D, mesotrione, tembotrione	Wheat

According to https://weedscience.org/ :
Table 4. Herbicide resistance cases to 4-HPPD inhibitors

Year	Species	Country	Actives	Crops
2009	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, chlorimuron-ethyl, atrazine, mesotrione, tembotrione, topramezone	Seed corn
2009	*Amaranthus tuberculatus (=A. rudis)*	United States	thifensulfuron-methyl, rimsulfuron, atrazine, mesotrione, tembotrione, topramezone	Seed corn
2009	*Amaranthus palmeri*	United States	thifensulfuron-methyl, atrazine, mesotrione, pyrasulfotole, tembotrione, topramezone	Corn (maize), Sorghum
2011	*Amaranthus tuberculatus (=A. rudis)*	United States	imazamethabenz-methyl, thifensulfuron-methyl, chlorimuron-ethyl, atrazine, isoxaflutole, glyphosate, mesotrione	Corn (maize), Soybean
2011	*Amaranthus tuberculatus (=A. rudis)*	United States	mesotrione, tembotrione, topramezone	Corn (maize)
2011	*Amaranthus palmeri*	United States	mesotrione, tembotrione, topramezone	Corn (maize)
2014	*Amaranthus palmeri*	United States	atrazine, mesotrione, tembotrione, topramezone	Corn (maize)
2014	*Amaranthus palmeri*	United States	imazethapyr, thifensulfuron-methyl, tembotrione	Corn (maize)

2015	*Raphanus raphanistrum*	Australia	chlorsulfuron, atrazine, diflufenican, fluridone, isoxaflutole, 2,4-D, mesotrione, tembotrione	Wheat
2015	*Amaranthus palmeri*	United States	chlorsulfuron, atrazine, glyphosate, 2,4-D, mesotrione	Sorghum
2016	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, chlorimuron-ethyl, atrazine, fomesafen, lactofen, acifluorfen, 2,4-D, mesotrione, tembotrione, topramezone	Corn (maize), Soybean
2016	*Amaranthus palmeri*	United States	mesotrione	Corn (maize)
2020	*Raphanus raphanistrum*	Australia	metsulfuron-methyl, dicamba, 2,4-D, mesotrione, topramezone, pyroxasulfone	Wheat
2020	*Amaranthus tuberculatus (=A. rudis)*	United States	imazethapyr, atrazine, fomesafen, glyphosate, mesotrione	Soybean

Cross-resistance

According to https://hracglobal.com/files/Herbicide-Cross-Resistance-and-Multiple-Resistance-in-Plants.pdf

Cross resistance is defined as the expression of a genetically-endowed mechanism conferring the ability to withstand herbicides from different chemical classes. There are two broad cross resistance categories; target site cross resistance and non-target site cross resistance.

Target site cross resistance occurs when a change at the biochemical site of action of one herbicide also confers resistance to herbicides from a different chemical class that inhibit the same site of action in the plant. Target site cross resistance does not necessarily result in resistance to all herbicide classes with a similar mode of action or indeed all herbicides within a given herbicide class.

Non target site cross resistance is defined as cross resistance to dissimilar herbicide classes conferred by a mechanism(s) other than resistant enzyme target sites. Until recently documented for *L. rigidum* and *A. myosuroides*, non-target site cross resistance was largely unknown in herbicide-resistant weeds but is well known in the insecticide resistance literature (Brattsten et al., 1986; Georghiou, 1986).

Cross resistance occurs mainly in the group of ALS inhibitors, acetyl-CoA carboxylase (ACCase)-inhibitors and photosystem two (PS2)-inhibitors. There is no evidence to cross resistance to 4-HPPD inhibitors, including mesotrione and isoxaflutole.

Weeds resistance to triazine herbicides were first identified in the late 1960’s. This resistance is not due to differential penetration, translocation, or herbicide degradation between the resistant and susceptible biotypes. The difference has been identified to be the result of differential activity at the site of action (chloroplast membrane), impairing binding of the triazines to the protein at the Q_B binding site. This resistance increases in frequency in the population as the result of natural selection of resistant biotypes. Such resistant biotypes are present as small component of the natural population and are “selected for” when the susceptible biotypes are suppressed by the application of triazine herbicides.

Resistant weeds include [1]: *Abutilon theophrasti, Amaranthus spp., Ambrosia artemisiifolia, Artiplex patula, Bidens tripartite, Brassica campestris, Bromus tectorum, Capsella bursa-pastoris, Chenopodium spp., Chloris inflate, Datura stramonium, Digitaria sanguinalis, Echinochlora crus-galli, Fallopia convolvulus, Galinsoga ciliate, Kochia scoparia, Lolium rigidum, Panicum spp., Phalaris paradoxa, Poa annua, polygonum spp., Raphanus raphanistrum, Senecio vulgaris, Setaria spp., Sinapis arvensis, Solanum nigrum, Stellaria media.*

Multiple resistance

Cross resistance and multiple resistance is a very dynamic ongoing process, and the major prevention strategy is this - included in Good Agricultural Practice and Integrated Pest Management strategies with avoidance of sequential use of herbicides belonging to the same SOAs and cross resistant groups (B/2 and C2/7) – in a first place. There are 2 cases of multiple weeds resistance to photosystem II inhibitors (C1/5) herbicides. It is important to notify that there are no cases of multiple resistance relative to Photosystem II inhibitors C1/5 group found in Poland up to date.

Sensitivity data
Applicant didn't conduct separately trials for sensitivity data, this data was evaluated in efficacy trials. The 9 field trials pre – emergence use were established in order to determine the sensitivity of weeds in the maize. The CHR/H/TERIZ 650 WG was tested at doses: 0.6 kg/ha, 0.7 kg/ha, 0.8 kg/ha, 0.9 kg/ha, 1.0 kg/ha (390.0 g – 650.0 g of active substances) in maize for the control of mono and dicot weeds. None of the tested weeds showed high tolerance to the product CHR/H/TERIZ 650 WG. Detailed studies on the weeds sensitivity are submitted and summarised in 3.2 Efficacy data (KCP 6) core dossier.

Use pattern
Herbicide CHR/H/TERIZ 650 WG has demonstrated good crop tolerance to maize. Therefore concluded that CHR/H/TERIZ 650 WG is safe usage at proposed rate and this support the label claim for the use in maize.
Undesirable effects are not expected on succeeding crops, adjacent crop, part of plants used for propagating purposes and beneficial organisms.

Based on submitted data the following regulation on the label is proposed:
maize:
Recommended dose at:
CHR/H/TERIZ 650 WG 0.8 kg/ha

CHR/H/TERIZ 650 WG is to be applied in spring:
Pre-emergence application: BBCH 00, max. 3 days after sowing.
Recommended volume of water 200-250 L/ha.
Recommended medium droplet spraying.

The product CHR/H/TERIZ 650 WG should be use once per season at spring pre-emergence.
To avoid resistance, products contain active substance with the same group shouldn't be used year after year on the same field.

Use of CHR/H/TERIZ 650 WG according to the proposed GAP does not represent a hazard to rotational crops and does not justify a specific labelling. CHR/H/TERIZ 650 WG is not persistent in soil or is it taken up by succeeding crops.
Resistance risk assessment of unrestricted use pattern
Not applicable

Test methods
Not applicable

Acceptability of the resistance risk
CHR/H/TERIZ SC is a herbicide containing active substances: 400 g/kg terbuthylazine + 100 g/kg

isoxaflutole + 150 g/kg mesotrione.

Terbuthylazine is an inhibitor of photosystem II (PS II) (HRAC mode of action group C1, WSSA group 5). By binding to the QB binding site of photosystem II it blocks the Hill reaction, which takes place in the chloroplast. Photosynthesis is prevented at the solar energy collected by the leaf is diverted into the formation of destructive compounds (free radicals) rather than into the normal photosynthesis products. These free radicals build up to the point where chlorophyll, carotenoids and cell membranes are destroyed. The rate of plant death is rapid and too fast to be accounted for by starvation (by stopping photosynthesis alone) and the destruction of cell walls and membranes are the major causes of the foliar chlorosis, necrosis and finally death of the plant. Selectivity of the crop is due to the ability of corn to rapidly metabolise terbuthylazine into non-toxic compounds.

Terbuthylazine provides control of annual broad-leaved weeds, pre-emergence and early-post emergence. Terbuthylazine is mainly taken up via plant roots, although entering the leaves is possible. The site of application is located in the chloroplast of leaf meristems where interference with the electron transport of photosystem II (‘Hill reaction’) takes place leading to inhibition of photosynthesis.

Generally, evidences of resistance to HRAC Group C1/5 (Photosystem II inhibitors) and specifically to terbuthylazine are well documented by Weed Science organization and Herbicide Resistance Action Committee. 6 weeds species are reported worldwide being resistant to terbuthylazine, out of which 5 were reported in Europe, and none in Poland so far.

Mesotrione belongs to the chemical group of the triketones (2-benzylcyclohexane-1,3-diones), which acts by blocking the function of the essential plant enzyme 4-hydroxy-phenyl-pyruvatedioxygenase (4-HPPD) in the cytosol of sensitive plants. Mesotrione is a systemic herbicide and controls most annual broadleaf and annual grass weed species in maize. It is taken up via roots and shoots and translocated rapidly in both the xylem and phloem into all plant parts. In sensitive plants symptoms of white chlorosis become visible within a few days after application in actively growing tissues being in the cell elongation phase. Complete death of sensitive plants may occur up to 2 weeks after application. Maize has a natural tolerance against mesotrione as it can detoxify the herbicide into inactive compounds. This detoxification is mediated by cytochrome-P450-oxygenase and is so rapid in maize that mesotrione is not translocated away from the treated zone to the point of action. Sensitive weed species cannot detoxify mesotrione in this way. Mesotrione belongs to HRAC group 27 (Legacy F2). According to Ian Heap’s website (http://www.weedscience.org) there are only three species which have been reported as resistant to HRAC group 27 (Legacy F2). These are *Amaranthus palmeri*, *Amaranthus tuberculatus* (=*A. rudis*) and *Raphanus raphanistrum*. All cases reported have been in the United States and Australia with no evidence of resistance in Europe.

Isoxaflutole belong to HRAC group 27 – 4-HPPD inhibitors. According HRAC Mechanism of resistance studies are ongoing. The mode of action is based on the inhibition of of Hydroxyphenyl Pyruvate Dioxygenase (HRAC group: 27, legacy F2). This group of herbicides is quite well known and has been applied commercially for decades.

According to Ian Heap’s website (http://www.weedscience.org) there are only two species which have been reported as resistant to isoxaflutole: *Raphanus raphanistrum and Amaranthus tuberculatus (=A. rudis*) (Table 3). Both cases have been reported in the Australia and USA with no evidence of resistance in Europe. Taking into account the entire HRAC group 27, 14 cases of weed resistance to 4-HPPD inhibitors in three weed species were reported: *Raphanus raphanistrum, Amaranthus tuberculatus (=A. rudis*) and *Amaranthus palmeri* (Table 4). All cases reported have been in the Australia and USA with no evidence of resistance in Europe (the risk of developing resistance to 4-HPPD inhibitors, including isoxaflutone is very low).

According to submitted efficacy data none of the tested weeds showed high tolerance to the product

CHR/H/TERIZ 650 WG.
Accroding to EPPO PP 1/213 (4) Resistance risk analysis weeds usually only produce one generation per year and development of resistance is usually a relatively slow process.
In conclusion, in the applicant's opinion, this level of weeds resistance risk should be considered to be acceptable.

Management strategy
Accroding to *Herbicide Resistance Action Committee (HRAC) (https://hracglobal.com/prevention-management/best-management-practices)*
Integrated Weed Management (IWM) refers to using chemical, cultural, mechanical and biological methods, in an integrated fashion, to control weeds. It does not rely excessively on any one method. When used in a integrated approach, the following tools help reduce selection pressure and survival of resistant weeds.

- Chemical - Applying herbicides to a crop.
- Mechanical - Includes measures such as hand-weeding using cultivation or ploughing to control emerged plants and bury non-germinated seed. It also includes harvest weed seed destruction such as stubble burning and cutting for hay or silage to prevent the weeds from setting seed.
- Cultural - Includes altering the crop planting date, row spacing and harvest timing to disrupt the weed cycle. It also includes planting crops that can out-compete weeds, buying certified seed that's free of weeds and using a diverse crop rotation. Growers should also sanitize farm equipment when moving between fields.
- Biological - Includes introducing insects and pathogens that control target weed species and introducing post-harvest grazing of growing weeds.

Using a diversified crop rotation allows farmers to use these different weed techniques. Avoid successive crops that use herbicides with the same mechanism of action to control the same weed species in the same field.
Guidelines for the sustainable use of herbicide site of action groups:
• Use mixtures or sequential treatments of herbicides having different sites of action. Each herbicide in the mixture should target the same weed species.
• Consider all chemical control options before planting, in-crop and after harvest.
• Avoid continued use of the same herbicides, or herbicides with the same site of action in the same field, unless integrated with other weed control practices.
• Limit the number of applications of a single herbicide or herbicides with the same site of action in a single growing season.
• Herbicide mixtures and herbicide rotations alone are not enough to prevent resistance. They must be used in a diversified plan than also incorporates mechanical, cultural and biological practices.
Growers should also do the following:
• Follow label use instructions, such as application rates, timing and equipment recommendations.
• Know the weeds in their fields and nearby non-crop areas and tailor their weed control program to weed densities and economic thresholds.
• Monitor herbicide results and be aware of any trends or changes in weed populations.
• Maintain detailed field records to confirm cropping and herbicide history.

Implementation of the management strategy
The herbicide label provides all the necessary information for preventing weed resistance to herbicides.

Monitoring, reporting and reaction to changes in performance

Accroding to https://hracglobal.com/files/Monitoring-and-Mitigation-of-Herbicide-Resistance.pdf
Managing the risk of herbicide resistance (HR) is an area of strategic importance for leading herbicide technology providers and is the focus of the Global Herbicide Resistance Action Committee (HRAC), an organization comprised of 8 major companies working as a part of Crop Life International. Early detection of HR, understanding the scope of HR in a defined area, and potential mitigation of resistance through efforts to limit its spread are important aspects of managing the risk of HR. Monitoring for HR populations has been employed by public and private weed scientists for both early detection and defining the scope of resistance. The primary methods used to monitor for resistance include:
1) field surveys where seed from putative resistant plants are collected and tested in a controlled environment using bioassay procedures,
2) market research surveys of farmers and weed management experts, and
3) tracking farmer performance inquiries with appropriate follow up field evaluation and testing.
The most common monitoring method is the use of field surveys designed to either qualitatively (i.e., determine whether the level of resistance is high, medium, or low) or quantitatively (i.e., determine the area infested with HR populations) define existing HR. The primary method to detect resistance in new species and in new geographies is to track farmer performance inquiries. Once resistance is detected, steps may be taken to mitigate its impact. A critical aspect to mitigation is the implementation of best management practices (BMPs) which is facilitated by effective education and training programs. Education efforts can be enhanced with information obtained from monitoring studies and early detection of resistant populations using appropriate monitoring methods can improve the outcome of mitigation efforts.

Comments of zRMS:	To avoid resistance, it is important to have a reasonable crop rotation and respect the label recommended application rates and doses. Resistance occurs generally when naturally existing unsusceptible biotypes are selected by repeated applications of the same “selecting factor” – e.g. one herbicide. The further development and spread of the resistance particularly depend on the seed production of the weed species and on the fitness of the resistant biotypes. However, herbicides mostly effect a specific target site, which are controlled by one or a few genes, so that one mutation of few genes already can cause a resistance. Use of herbicides with the same mode of action in one population can produce a considerable selection pressure, which may result in fast reproduction of the resistant biotypes. These biotypes can generate increased population sizes and may infest more arable land without limitation, because the sensitive species and varieties are controlled by the herbicide or the same MOS group of herbicides. According to HRAC org. cross resistance is defined as the expression of a genetically endowed mechanism conferring the ability to withstand herbicides from different chemical classes. It relates to herbicides from different chemical groups but of the same mode of action. If there is a resistance to at least two or more a.s. from the same chemical group or even from different chemical groups but of the same mode of action – cross resistance is a case. The risk of resistance was analysed following the EPPO-Standard (2003), the classification of the Herbicide Resistance Action Committee (HRAC) and the international Survey of Herbicide Resistant Weeds (Heap, 2016). According to EPPO PP 1/213 (4) Resistance risk analysis weeds usually only produce one generation per year and development of resistance is usually a relatively slow process. It is difficult to class any weed species as inherently more or less likely to develop resistance to a particular herbicide. Corn (*Zea mays* L.) production is increasing worldwide, and this trend is evident

	throughout Central Europe. We can expect this trend to continue in the future. Weed management has had a major impact on the success of corn growth, as the competitive ability of corn is relatively low with regard to weed control, due to the sowing season in Europe. This crop is very often characterized by a complex weed flora, consisting of grasses and broadleaf weeds. This weed flora has traditionally been controlled with terbuthylazine-based pre-emergence applications due to its broad spectrum of controlled weeds, excellent residual activity, Due to its broad spectrum of controlled weeds, excellent plant tolerance, perceptible rate of efficacy and suitability as a partner for other active ingredients. However, short rotation cycles or corn monoculture with repeated applications of the same pre-emergence herbicides have resulted in a significant increase in the frequency of several "difficult to control" weed species, forcing farmers to use less streamlined weed control strategies. To optimize weed control efficiency and minimize application costs, the use of complex combinations of pre-emergence and post-emergence herbicides, as well as herbicide mixtures, has become the rule rather than the exception in many countries. This strategy is also an important tool to avoid herbicide resistance problems. CHR/H/TERIZ 650 WG is a herbicide containing active substance: terbuthylazine 400 g/kg (HRAC group 9: inhibition of enolpyruvyl shikimate phosphate synthase), isoxaflutole 100 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase) and mesotrione 150 g/kg (HRAC group 27: inhibition of hydroxyphenyl pyruvate dioxygenase). This groups of herbicides are quite well known and has been applied commercially for decades. **Terbuthylazine** belongs to the chemical group of Triazines. Terbuthylazine is rapidly translocated to the chloroplasts of the plant cell. Terbuthylazine is primarily interrupting the electron transport in photosystem II (Hill-reaction) and consequently an inhibitor of photosynthesis. The herbicidal activity of Terbuthylazine was first reported in 1966. It is applied world-wide in a wide range of crops like maize, sorghum, vines, orchards, forest and potatoes as a broad-spectrum herbicide against broad-leaved weeds. Resistance occurs generally when naturally existing unsusceptible biotypes are selected by repeated applications of the same “selecting factor” – e.g. one herbicide. The further development and spread of the resistance particularly depend on the seed production of the weed species and on the fitness of the resistant biotypes. However, herbicides mostly effect a specific target site, which are controlled by one or a few genes, so that one mutation of few genes already can cause a resistance. Use of herbicides with the same mode of action in one population can produce a considerable selection pressure, which may result in fast reproduction of the resistant biotypes. These biotypes can generate increased population sizes and may infest more arable land without limitation, because the sensitive species and varieties are controlled by the herbicide or the same MOS group of herbicides. Although the development of resistance or even reduced susceptibility is a long-term process as weeds usually produce only one generation per year and new, resistant individuals spread quite slowly within the population, it is evident that a repeated application of herbicides with the same mode of action over 20-30 years results in selection pressure and induces selection of resistant eco-types. Triazine herbicides have been persistently used for weed control in maize production in many parts of the world and this practice has led to widespread resistance in target weeds. The first report of herbicide resistance involved a triazine herbicide (Ryan, 1970), and since then triazine resistance has become the most prevalent and well characterized example of herbicide resistance world-wide. It is noteworthy that biotypes highly resistant to triazine herbicides as a result of a modified D1 protein are not resistant to the chemically distinct substituted urea

	herbicides, despite the fact that the substituted urea herbicides are also potent PS2 inhibitors (reviewed by Gronwald, 1994). The substituted urea and triazine herbicides bind to overlapping, but not identical, sites in PS2 (reviewed by Trebst, 1991). As a result, the mutation Ser 264 Gly providing resistance to triazine herbicides does not affect binding of substituted urea herbicides (Arntzen et al., 1982; Trebst, 1991). Plants containing triazine-resistant PS2 are resistant to other PS2-inhibiting herbicide chemistries including the triazinones, uracils, and pyridazinones (Fuerst et al., 1986; Ducruet and De Prado, 1982; Oettmeier et al., 1982; De Prado et al., 1989). Cross resistance and multiple resistance is a very dynamic ongoing process, and the major prevention strategy is this - included in Good Agricultural Practice and Integrated Pest Management strategies with avoidance of sequential use of herbicides belonging to the same SOAs and cross resistant groups (B/2 and C2/7) – in a first place. There are 2 cases of multiple weeds resistance to photosystem II inhibitors (C1/5) herbicides. It is important to notify that there are no cases of multiple resistance relative to Photosystem II inhibitors C1/5 group found in Poland up to date. The overview of the Herbicide Resistance Action Committee (HRAC) about the evidence of resistance can replace baseline sensitivity studies. The International Survey of Herbicide Resistant Weeds (http://www.weedscience.org/in.asp) cites cases of resistance to HRAC herbicide group C1/5 in the Central Zone: in Germany, Poland and Czech Republic. Sensitivity data should be generated and available in the future to measure sensitivity shift and resistance development. **Mesotrione**, with the chemical name 2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione (IUPAC), belongs to the chemical group of Triketones. Mesotrione is a selective herbicide for pre- and post emergence applications against weeds in mainly maize across all climatic zones of Europe. Mesotrione acts by the inhibition of 4-hydroxyphenyl-pyruvate-dioxygenase which in turn inhibits carotenoid biosynthesis. Due to its primary target site and its chemical family, in the HRAC mode of action classification, it is classified as group F2 herbicide (4-hydroxyphenyl-pyruvate-dioxygenase (4-HPPD) inhibition). In the WSSA resistance classification system, the callistemones are classified as group 27. Based on the HRAC resistance classification, cross resistance should be expected to be likely between mesotrione and other HRAC group 27 herbicides. Thus, the analysis of the risk for the development of weed resistance to mesotrione is made under the assumption that cross resistance exists between all herbicides classified as HRAC group 27. Currently, there are no reported cases of weed resistance to mesotrione reported from within the EU (Heap, 2019). **Isoxaflutole** is a systemic herbicide belonging to HRAC group 27 – 4-HPPD inhibitors. Isoxaflutole was developed for agricultural use. The use evaluated for the first EU approval was for the control of broad leaved and annual grass weeds in maize (silage, grain, seed and sweet corn). Isoxaflutole is very xylem mobile when taken up via the roots and phloem mobile when taken up via the shoots and it accumulates in the leaf margins and tips. Eventually lethal amounts of isoxaflutole accumulate in the foliage and meristem. Germinating seedlings that contact the product either do not emerge or emerge white and stop growing. Isoxaflutole may also be adsorbed by foliage and roots of already emerged weeds and will injure or control young weeds that are emerged at application. According to Ian Heap's website (http://www.weedscience.org) there are only two species which have been reported as resistant to isoxaflutole: *Raphanus raphan-*

	istrum and *Amaranthus tuberculatus* (=*A. rudis*). Both cases have been reported in the Australia and USA with no evidence of resistance in Europe. **Applicant submitted detailed information's about possibilities of development the resistance or cross-resistance. Evaluator accepted the strategy management about possible development of resistance or cross-resistance proposed by Applicant.** The mode of action involving a 'multi-site' action may indicate a lower risk to developing weeds resistance. This groups of herbicides is quite well known and has been applied commercially for decades. The probability of development of resistance or cross-resistance of weeds to Untido 650 WG/ Jotamun 650/ Metodus 650 WG (product code: CHR/H/TERIZ 650 WG) is considered as low. The evaluation of the agronomic risk concludes that CHR/H/TERIZ 650 WG bears a low risk of resistance. **In the opinion of the ZRMs, the included provisions on resistance management strategies, accepted during the initial registration of the product, should still apply.** To minimize the risk of occurrence and development of weed resistance to herbicides, User should in accordance with Good Agricultural Practice: ✓ *follow strictly the directions on the label of the plant protection product - apply the product at the recommended dose, at the recommended time to ensure optimal,* ✓ *weed control,* ✓ *adjust the selection of the herbicide and the decision to carry out the treatment to the prevailing (possibly potential) weed infestation, taking into account the dominant species and the pest thresholds,* ✓ *use a rotation of herbicides (active substances) with different mechanisms of action,* ✓ *use a mixture of herbicides (active substances) with different mechanisms of action,* ✓ *use in rotation and/or mixture herbicides acting on several life processes weeds (with different mechanism of action),* ✓ *use an herbicide with a given mechanism of action only once during the growing season crop,* ✓ *adjust tillage operations to the conditions in the field, especially to the type and* ✓ *intensity of weeds,* ✓ *use various methods of weed control, including crop rotation, etc,* ✓ *use certified seed,* ✓ *clean agricultural machinery to prevent the transfer of weed propagating material to other sites,* ✓ *inform the permit holder of unsatisfactory weed control,* ✓ *for more information, contact your advisor, the permit holder of the permit or the permit holder's representative.*

3.5 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.

3.6 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.

3.7 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.

3.8 List of test facilities including the corresponding certificates

Please research to core dossier.

Appendix 1 Lists of data considered in support of the evaluation

Not applicable.

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Not applicable.

List of data submitted by the applicant and not relied on

Not applicable.

List of data relied on not submitted by the applicant but necessary for evaluation

Not applicable.