REGISTRATION REPORT

# Part B

# Section 6

# Mammalian Toxicology

Detailed summary of the risk assessment

Product code: MEZI 100 SC

Product name(s): Rumezo Twist 100 SC,

Malton Twist 100 SC

Chemical active substance(s):

Mesotrione, 100 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Innvigo Sp. z o.o.

Submission date: December 2023, October 2024

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| When | What |
|---|---|
| 06/2024 | Applicant update |
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| October 2024 | Applicant update |
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# 6 Mammalian Toxicology (KCP 7)

Callisto 100 SC is the original product to which Innvigo Sp. z o.o. would like to refer. 10 years for registration data of Callisto 100 SC was expired in Poland. Thus, the data protection of studies provided in registration report of Callisto 100 SC has expired. Innvigo Sp. z o.o. refers to above mentioned studies within this document.

## 6.1 Summary

**Table 6.1-1: Information on MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC***

| | |
|---|---|
| Product name and code | MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC |
| Formulation type | Suspension concentrate [Code: SC] |
| Active substance(s) (incl. content) | Mesotrione; 100 g/L |
| Function | Herbicide |
| Product already evaluated as the 'representative formulation' during the approval of the active substance(s) | No |
| Product previously evaluated in another MS according to Uniform Principles | No |

* Information on the detailed composition of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC can be found in the confidential dRR Part C.

**Justified proposals for classification and labelling**

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

**Table 6.1-2: Justified proposals for classification and labelling for MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC according to Regulation (EC) No 1272/2008**

| | |
|---|---|
| Hazard class(es), categories: | Eye ~~i~~rrit~~ation~~, Category 2; Repr. ~~Cat.~~ 2; ~~STOT RE 2~~ |
| Hazard pictograms or Code(s) for hazard pictogram(s): |  GHS07 , GHS08  |
| Signal word: | Warning |
| Hazard statement(s): | H319 Causes serious eye irritation<br>H361d Suspected of damaging the unborn child<br>~~H373: May cause damage to organs through prolonged or repeated exposure (eyes, nervous system~~ |
| Precautionary statement(s): | ~~P102 Keep out of reach of children.~~<br>P202 Do not handle until all safety precautions have been read and understood.<br>~~P260 Do not breathe spray.~~<br>P280 ~~Wear eye protection/ face protection. Wear protective gloves/ protective clothing/ eye protection/face protection.~~ Wear protective gloves/protective clothing/eye protection/face protection.<br>P308+P313 IF exposed or concerned: Get medical advice/attention.<br>P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove<br>contact lenses, if present and easy to do. Continue rinsing.<br>P337 + P313 If eye irritation persists: Get medical advice/ attention.<br>P405 Store locked up. |
| Additional labelling phrases: | To avoid risks to man and the environment, comply with the instructions for use. [EUH401] |

**Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for Mesotrione in MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC**

| | Result | PPE / Risk mitigation measures |
|---|---|---|
| Operators | Acceptable | ~~None~~ Workwear, gloves and protective googles or face protection during mixing/loading and application due to the fact that the product is classified as Repr. 2 H361d and Eye Irrit. 1 H319. |
| Workers | Acceptable | Workwear |
| Bystanders | Acceptable | None |
| Residents | Acceptable | None |

No unacceptable risk for operators, workers, bystanders and residents was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in Table 6.1-3 are applied.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and bystanders/residents is presented in the following table.

**Table 6.1-4 Critical uses and overall conclusion of exposure assessment**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Use-No.*** | **Crops and situation (e.g. growth stage of crop)** | **F, Fn, Fpn G, Gn, Gpn or I ****** | **Application** | | **Application rate** | | **PHI (d)** | **Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, bystander or resident exposure based on [Exposure model]** | **Acceptability of exposure assessment** | | | |
| | | | **Method / Kind** **(incl. application technique *****)** | **Max. number (min. interval between applications)** **a) per use** **b) per crop/ season** | **Max. application rate kg as/ha** **a) a.s. 1** **b) a.s. 2** | **Water L/ha** **min / max** | | | **Operator** | **Worker** | **Bystander** | **Residents** |
| 1 | Maize (BBCH 14-15) | F | Spraying, LCTM | 1 ; 1 | a) 0.1 kg as/ha | 200-300 | | EFSA OPEX | A | R | A | A |

* 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
*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 "Acceptability of exposure assessment"

| | |
|---|---|
| A | Exposure acceptable without PPE / risk mitigation measures |
| R | Further refinement and/or risk mitigation measures required |
| N | Exposure not acceptable/ Evaluation not possible |

### Data gaps

Noticed data gaps are:

## 6.2 Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in Table 6.2-1.

**Table 6.2-1: Information on active substance(s)**

| **Mesotrione** | |
|---|---|
| Common Name | Mesotrione |
| CAS-No. | 104206-82-8 |
| **Classification and proposed labelling** | |
| With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended) | **Hazard classes (s),** categories:<br>~~Retain:~~ ~~Aquatic Acute 1 Aquatic Chronic 1~~<br>~~Add:~~ Repr. 2 STOT RE 2<br><br>Code(s) for hazard pictogram(s):<br>~~Retain:~~ GHS09<br>~~Add:~~ GHS08<br><br>Signal word:~~ Retain:~~ Warning<br>Hazard statement(s):<br>~~Retain: H400 H410~~ |

| Mesotrione | |
|---|---|
| | ~~Add:~~ H361d Suspected of damaging the unborn child H373 May cause damage to organs (eyes, nervous system)<br><br>Precautionary statement(s):<br>P201 Obtain special instructions before use.<br>P202 Do not handle until all safety precautions have been read and understood. (Optional where P201 is assigned)<br>P280 Wear protective gloves/protective clothing/eye protection/face protection. |
| Additional C&L proposal | None |
| **Agreed EU endpoints** | |
| AOEL systemic | 0.005 mg/kg bw/d (corrected for 50 % oral absorption) |
| Reference | EFSA Journal 2016;14(3):4419 |
| **Conditions to take into account/critical areas of concern with regard to toxicology** | |
| EFSA Conclusion for active substance | None EFSA Journal 2016;14(3):4419 |

~~*Adjustments has been done to reflect ECHA/RAC opinion adopted in 14 September 2018. ZRMS:PL is aware of some EU-countries which in cases when RAC opinion has been adopted, the evaluating authority consider this opinion as the latest reliable scientific evidence even if the procedure for formal inclusion of the substance into Annex VI to the CLP Regulation is still on-going.~~

## 6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC is given in the following tables.
Toxicological Evaluation for MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC based on toxicological evaluation for Callisto 100 SC and calculation method.
Acute toxicity studies on the product have been previously considered within an EU peer review process and full study summaries are not provided in this document.

| | |
|---|---|
| Comments of zRMS: | Plant Protection Product MEZI 100 SC (Product name(s): Rumezo Twist 100 SC, Malton Twist 100 SC) is chemically equivalent to CALLISTO 100 SC (product code A12739A) – reference Plant Protection Product.<br>*In vivo* acute toxicity studies including irritancy and skin sensitisation with A12739A have been evaluated as the representative formulation in the EU review of mesotrione. Since the studies have been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment.<br>10 years for registration data of CALLISTO 100 SC was expired in Poland. Thus, the data protection of studies provided in registration report of CALLISTO 100 SC has expired. The applicant refers to above mentioned studies within this document. In opinion of zRMS according to current requirements the studies are acceptable for toxicological evaluation of MEZI 100 SC.<br>In addition, for the acute toxicity including irritancy and skin sensitisation the assessments have been conducted by the applicant based on the alternative method according to the Regulation (EC) 1272/2008. An assessment of reprotoxicity and specific target organ toxicity have been conducted by the applicant based on the |

| | |
|---|---|
| | alternative method according to the Regulation (EC) 1272/2008. Proposed classification based on alternative method according to Regulation (EC) 1272/2008 is acceptable by the zRMS where study data is not available. |

**Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC.**

| Type of test, species, model system (Guideline) | Result | Acceptability | Classification (acc. to the criteria in Reg. 1272/2008) | Reference |
|---|---|---|---|---|
| $LD_{50}$ oral, rat (OECD 425; ~~calculation method – alternative method~~) | (>) 2000 mg/kg bw | Yes* | None | [redacted], 2005 [redacted] ~~2023~~ |
| $LD_{50}$ oral, rat (calculation method – alternative method) | (>) 2000 mg/kg bw | ~~Yes~~ / ~~No~~ / Supplementary | None | [redacted], 2023 |
| $LD_{50}$ dermal, rat (OECD 402) | (>) 2000 mg/kg bw | Yes* | None | [redacted] 2005 |
| $LD_{50}$ dermal (calculation method – alternative method) | No ingredients classified in this class | ~~Yes~~ / ~~No~~ / Supplementary | None | K. Czerwińska, 2023 |
| $LC_{50}$ inhalation, rat** (OECD 403) | Waiver submitted | Yes* | None | N/A |
| $LC_{50}$ inhalation (calculation method – alternative method) | No ingredients classified in this class | Yes ~~/ No / Supplementary~~ | None | K. Czerwińska, 2023 |
| Skin irritation, rabbit (OECD 404; ~~calculation method – alternative method)~~ | Non-irritant | Yes* | None | [redacted], 2005 [redacted], ~~2023~~ |
| Skin irritation (calculation method – alternative method) | Irritant (≥ 10% concentration limit) | ~~Yes~~ / No / ~~Supplementary~~ | Skin Irrit 2, H315 | K. Czerwińska, 2023 |
| Eye irritation, rabbit (OECD 405; ~~calculation method – alternative method)~~ | Irritant | Yes* | H319 | [redacted] 2005 [redacted], ~~2023~~ |
| Eye irritation (calculation method – alternative method) | Eye Dam. (≥3,0 % concentration limit) | ~~Yes~~ / No / ~~Supplementary~~ | Eye Dam. 1, H318 | K. Czerwińska, 2023 |
| Skin sensitisation, guinea pig (OECD 406, Buehler (9 applications) | Non-sensitising | Yes* | None | [redacted] 2005 |
| Skin sensitisation (calculation method – alternative method) | | ~~Yes~~ / ~~No~~ / Supplementary | None | K. Czerwińska, 2023 |
| Supplementary studies for | No data-not | - | | |

| | | | | |
|---|---|---|---|---|
| combinations of plant protection products | required | | | |
| ~~Reproductive toxicity (calculation method – alternative method)~~ | ~~Classified~~ | ~~Yes / No / Supplementary~~ | ~~H361d~~ | ~~K.Czerwińska, 2023~~ |

* Studies have been reviewed and accepted during EU review of active substance and previous registration process of Callisto 100 SC, zRMS:PL did not performed a new assessment.
** No acute inhalation study was conducted, waiver reviewed and accepted during EU review of active substance and previous registration process of Callisto 100 SC, zRMS:PL did not performed a new assessment.

**Table 6.3-2: Additional toxicological information relevant for classification/labelling of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC.**

| | **Substance (Concentration in product, % w/w)** | **Classification of the substance (acc. to the criteria in Reg. 1272/2008)** | **Reference** | **Classification of product (acc. to the criteria in Reg. 1272/2008)** |
|---|---|---|---|---|
| Toxicological properties of active substance(s) (relevant for classification of product) | Mesotrione (9.~~17~~ 09 % (w/w)) | ~~Hazard statement(s) n/a~~ Repr. 2; H361d (trigger~~ed~~ value, CLP criteria ≥ 3,0 %) STOT RE 2, H373 (trigger value, CLP criteria ≥ 10 %) | Reg. 1272/2008 | ~~Hazard statement(s)~~ Eye Irrit. 2; H319 Causes serious eye irritation. Repr. 2; H361d Suspected of damaging the unborn child~~, H373 May cause damage to organs (eyes, nervous system)~~ |
| Toxicological properties of non-active substance(s) (relevant for classification of product) | 2-(8-methylnonoxy)ethanol (CAS No. 61827-42-7, 15 - 25% (w/w))* | ~~Hazard statement(s)~~ Acute Tox.4; H302 Eye Dam.1; H318 (trigger value, CLP criteria ≥ 3,0 %)** | Reg. 1272/2008 | |
| | Octan-1-ol CAS No. 111-87-5, 5 - 10% (w/w))* | ~~Hazard statement(s)~~ Eye Irrit.2; H319 | | |
| | Other co-formulants 2.2% 1.5 % 2.7 % | (trigger value, CLP criteria ≥ 10 %)** Skin Corr 1, H31 Skin Irrit 2, H315 Skin Irrit 2, H315 | Reg. 1272/2008 | |
| Further toxicological information | No data-not required | | | |

* Please use concentration range or concentration limit (e.g. 1-10 % or > 1 %) as provided in MSDS.
** Study data are available for this endpoint

## 6.4 Toxicological Evaluation of Groundwater Metabolites

All metabolite concentrations are predicted to stay below 0.1 µg/L – no groundwater assessment is required.

## 6.5 Dermal Absorption (KCP 7.3)

~~A summary of the dermal absorption rates for the active substances in MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC are presented in the following tables.~~

~~**Table 6.5-1: Dermal absorption rates for active substance in MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC.**~~

| ~~Mesotrione~~ | | |
|---|---|---|
| | ~~Value~~ | ~~Reference~~ |
| ~~Concentrate~~ | ~~0.1 %~~ | ~~EFSA Journal 2016;14(3):4419~~ |
| ~~Dilution (1:200)~~ | ~~3%~~ | ~~EFSA Journal 2016;14(3):4419~~ |
| ~~Dilution (1:400)~~ | ~~5%~~ | ~~EFSA Journal 2016;14(3):4419~~ |

### ~~6.5.1 Justification for proposed values - Mesotrione~~

Proposed dermal absorption rates for Mesotrione are based on dermal absorption studies~~y~~ on a formulation ~~similar~~ identical to ~~A12739A/Callisto 100SC~~ MEZI 100 SC. The study results are summarized in the following table. Full summaries~~y~~ of studies~~y~~ on the dermal absorption of A12739A/Callisto 100SC that have previously been evaluated within an EU peer review process are~~is~~ not described in detail ~~in Appendix 2~~ .The presented dermal absorption is agreed in the line with EFSA 2017.

**Table 6.5-2: Summary of the results of submitted dermal absorption studies for Mesotrione**

| Test | Concentrate | Spray dilution (1:200) | Spray dilution (1:400) | Formulation in study | Acceptability of study | Justification provided on representativity of study formulation for current product | Acceptability of justification | Reference* |
|---|---|---|---|---|---|---|---|---|
| In vitro (human) | 0.1 % | 3 % | 5% | Callisto 100SC/A12739A | Yes** | Not required | | xxx.2013 |

* indicates that a study was reviewed at EU level
** Study has been reviewed and accepted during EU review of active substance and previous registration process of Callisto 100 SC, zRMS:PL did not performed a new assessment.

## 6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

**Table 6.6-1: Product information and toxicological reference values used for exposure assessment**

| | |
|---|---|
| Product name and code | **MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC** |
| Formulation type | Suspension concentrate [Code:SC] |
| Category | Herbicide |
| Active substance(s) (incl. content) | **Mesotrione**<br>100 g/L |

| | |
|---|---|
| AOEL systemic | 0.005 mg/kg bw/d (corrected for 50 % oral absorption) |
| Inhalation absorption | 100 % |
| Oral absorption | 100 % |
| | Concentrate: 0.1 %<br>Dilution: 3% (Dilution rate: 1:200)<br>Dilution: 5% (Dilution rate: 1:400)<br>(Based on product (formulation)) |

### 6.6.1 Selection of critical use(s) and justification

The critical GAP(s) used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the central zone is given in Part B, Section 0.

### 6.6.2 Operator exposure (KCP 7.2.1)

#### 6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC according to the critical use(s) is presented in Table 6.6-2. Outcome of the estimation is presented in Table 6.6-3. Detailed calculations are in Appendix 3.

**Table 6.6-2: Exposure models for intended uses**

| | |
|---|---|
| Critical use(s) | Maize (max. 1 L product/ha) ~~Re-entry activity: Inspection, irrigation~~ Vehicle mounted |
| Model(s) | OPEX v.1.0.1, Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 |

**Table 6.6-3: Estimated operator exposure**

| | | **Mesotrione** | |
|---|---|---|---|
| **Model data** | **Level of PPE** | **Total absorbed dose (mg/kg/day)** | **% of systemic AOEL** |
| Vehicle mounted<br>Application rate:1x 0.1 kg a.s./ha<br>Buffer strip:2-3m<br>Drift reduction:0% | | | |
| **OPEX v.1.0.1**<br>Dermal absorption<br>0.1% for concentrate:<br>5% for dillution<br>(1:400)*** | no PPE* | 0.002 | 34 |
| | + type of PPE (workwear)** | 0.001 | 23.3 |

* no PPE: Operator wearing T-shirt and shorts

** ~~no~~ PPE: Operator wearing long sleeved shirt, long trousers (“permeable”) but no gloves

*** Dermal absorption 5% for dilution 1:400 is worse case than dermal absorption 3% for dilution 1:200

### 6.6.3 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

| | |
|---|---|
| Comments of zRMS<br>study comment 6.6.2 | The applicant presented calculations for the application of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC on maize: max dose 1x1 L/ha (Field).<br>The exposure calculations were conducted using the EFSA online calculator v. 1.0.1 (OPEX).<br>The calculations provided by the applicant were done correctly. |
| agreed endpoints 6.6.2 | According to EFSA OPEX calculations, it can be concluded that the risk of operator exposure during mixing & loading and application using the tractor-mounted on field on maize is acceptable in the absence of PPP.<br>Due to the fact that the product is classified as Repr. 2 H361d and Eye Irrit. 1 H319, the operator should wear workwear, gloves and protective googles or face protection during mixing/loading and application operations.<br>Thus, the operator using MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC will be safe as long as he wears workwear, gloves and protective googles or face protection. |

### 6.6.4 Worker exposure (KCP 7.2.2)

#### 6.6.4.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5. Detailed calculations are in Appendix 3.

**Table 6.6-5: Exposure models for intended uses**

| | |
|---|---|
| Critical use(s) | Maize (max. 1 x 1 L product/ha) Re-entry activity: Inspection, irrigation |
| Model | OPEX v.1.0.1, Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 |

**Table 6.6-7: Estimated worker exposure**

| | | Mesotrione | |
|---|---|---|---|
| **Model data** | **Level of PPE** | **Total absorbed dose (mg/kg/day)** | **% of systemic AOEL** |
| ~~Vehicle mounted, downward spraying~~ Re-entry activity: Inspection, irrigation<br>Number of applications and application rate: 1 x 0.1 kg a.s./ha | | | |

| | | | |
|---|---|---|---|
| Buffer strip: 2-3m<br>Drift reduction: 0% | | | |
| **OPEX model**<br>2 hours/day (1),<br>TC (potential): 12500 cm²/person/h (2)<br>TC (workwear (arms, body and legs covered)): 1400 cm²/h<br>TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h<br>TC (gloves): NA cm²/h<br>Body weight: 60 kg<br>Dermal absorption<br>0.1% for concentrate:<br>5% for dillution (1:400)* | no PPE (3) | 0.006 | 125 |
| | with PPE (workwear)(4)(3) | 0.0007 | 14 |

(1) e.g. 8 h/day for professional applications for harvesting, pruning, tying, thinning or weeding activities etc. or 2 h/day for professional applications for maintenance, inspection or irrigation activities etc.
(2) e.g. EUROPOEM II, 2002, Post-Application Exposure of Workers to Pesticides in Agriculture or US-EPA policy paper [EPA, Science Advisory Council for Exposure; Agricultural Transfer Coefficients, Policy # 3.]. TC: Transfer coefficient
(3) ~~no~~ PPE: Worker wearing long sleeved shirt, long trousers ("permeable") but no gloves
~~(4) with PPE: *type of PPE* / see 'Instructions for use'~~
* Dermal absorption 5% for dilution 1:400 is worse case than dermal absorption 3% for dilution 1:200

### 6.6.4.2 Refinement of generic DFR value (KCP 7.2)

Not required.

### 6.6.4.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

| | |
|---|---|
| Comments of zRMS<br>study comment 6.6.4 | The applicant presented calculations for worker exposure after entry into a previously treated area with MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC on maize: max dose 1x1 L/ha (Field).<br>The exposure calculations were conducted using the EFSA online calculator v. 1.0.1 (OPEX).<br>The calculations provided by the applicant were done correctly. |
| agreed endpoints 6.6.4 | According to EFSA OPEX calculations, it can be concluded that the risk of worker exposure during re-entry activities on area treated with MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC is acceptable under conditions of intended use when the workwear (long sleeved shirt, long trousers) is worn.<br>As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried. |

## 6.6.5 Bystander and resident exposure (KCP 7.2.3)

### 6.6.5.1 Estimation of bystander and resident exposure

Risk assessment for bystander is the same like risk assessment for resident, because there is no AAOEL value.
Table 6.6-6 shows the exposure model(s) used for estimation of bystander and resident exposure to Mesotrione. Outcome of the estimation is presented in Table 6.6-7. Detailed calculations are in Appendix 3.

**Table 6.6-8: Exposure models for intended uses**

| | |
|---|---|
| Critical use(s) | Maize (max. 1 x 1 L product/ha) |
| Model | OPEX v 1.0.1, , Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 |

**Table 6.6-9: Estimated bystander and resident exposure**

| | **Mesotrione** | |
|---|---|---|
| **Model data** | **Total absorbed dose (mg/kg bw/day)** | **% of systemic AOEL** |
| Vehicle mounted, downward spraying<br>Number of application and application rate: 1 x 0.1 kg a.s./ha<br>Buffer strip: 2-3m<br>Drift reduction: 0% | | |
| **OPEX v.1.0.1**<br>Residents (adult)<br>Body weight: 60 kg<br>Dermal absorption<br>0.1% for concentrate:<br>5% for dillution (1:400)* | Spray drift 0.0002<br>Vapour: 0.0003<br>Surface deposit 3E-5<br>Entry into treated crops 0.0005<br>All pathways (mean):0.0007 | 3.2<br>5.4<br>0.7<br>9.4<br>14.9 |
| **OPEX v.1.0.1**<br>Residents (children)<br>Body weight: 10 kg<br>Dermal absorption<br>0.1% for concentrate:<br>5% for dillution (1:400)* | Spray drift 0.0007<br>Vapour: 0.0008<br>Surface deposit: 0.0002<br>Entry into treated crops 0.0008<br>All pathways (mean):0.002 | 13.7<br>16<br>2.3<br>16.9<br>39.2 |

* Dermal absorption 5% for dilution 1:400 is worse case than dermal absorption 3% for dilution 1:200

### 6.6.5.2 Measurement of bystander and resident exposure

Since the bystander and/or resident exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for Mesotrione will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of bystander/resident exposure was not necessary and was therefore not performed.

| | |
|---|---|
| Comments of zRMS | The evaluator agrees with the estimation of resident exposure after application of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC provided by the applicant. |

| | |
|---|---|
| study comment 6.6.5 | The exposure estimation of resident (adult and child) to mesotrione, applied on a field of maize at dose of 1x1 L product/ha using tractor-mounted, calculated with the EFSA online calculator v 1.0.1. (OPEX) demonstrates that such an exposure for adult and child resident is 14.9 % to 39.2 % of respective AOEL, thus risk is acceptable. The calculations provided by the applicant were done correctly. |
| agreed endpoints 6.6.5 | The exposure assessment for residents also covers bystander exposure. According to calculations, it can be concluded that there is no unacceptable risk to any resident (child and adult) and bystander after application of MEZI 100 SC/ Rumezo Twist 100 SC, Malton Twist 100 SC on maize. |

### 6.6.6 Combined exposure

Not relevant. The product contains only one active substance.

# Appendix 1 Lists of data considered in support of the evaluation

**List of data submitted by the applicant and relied on**

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study Y/N | Owner |
|---|---|---|---|---|---|
| KCP 7.1.1<br>KCP 7.1.2<br>KCP 7.1.3<br>KCP 7.1.4<br>KCP 7.1.5<br>KCP 7.1.6<br>KCP 7.1.7 | K. Czerwińska | 2024 | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances;<br>Chemirol<br>Non GLP<br>Unpublished | N | Chemirol |
| KCP 7.2.1<br>KCP 7.2.2<br>KCP 7.2.3 | Stanio A. | 2023 | Exposure assessment for operator, worker, resident and bystander<br>Product: Rumezo Twist 100 SC, Malton Twist 100 SC.<br>OPEX version: 1.0.1<br>15 December 2023<br>Chemirol<br>Not GLP<br>Unpublished | N | Chemirol |

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

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study Y/N | Owner |
|---|---|---|---|---|---|
| KCP 7 | | 2005 | Mesotrione 100 g/l SC Formulation (A12739A): Acute Oral Toxicity Study In The Rat (Up And Down Procedure)<br>GLP<br>not published<br>[redacted] | Y | Syngenta |
| KCP 7 | [redacted] | 2005a | Mesotrione 100g/l SC Formulation (A12739A): Acute Dermal Toxicity Study In Rats<br>[redacted]<br>GLP<br>not published<br>[redacted] | Y | Syngenta |
| KCP 7 | [redacted] | 2005b | MESOTRIONE 100 G/L SC FORMULATION (A12739A): Primary Skin Irritation Study in Rabbits (4-Hour Semi-Occlusive Application)<br>[redacted]<br>GLP<br>not published<br>[redacted] | Y | Syngenta |
| KCP 7 | [redacted] | 2005c | Mesotrione 100g/l SC Formulation(A12739A): Primary Eye Irritation Study in Rabbits<br>[redacted]<br>GLP<br>not published<br>[redacted] | Y | Syngenta |
| KCP 7 | [redacted] | 2005 | Dermal Sensitization Study in Guinea Pigs (Buehler Method) with Mesotrione SC (100) (A12739A)<br>[redacted]<br>GLP<br>not published<br>[redacted] | Y | Syngenta |
| KCP 7.3 | xxxxxxxxxxx | 2013 | Mesotrione 100 SC (A12739A) - In Vitro Absorption through Human Dermatomed Skin using [14C-Radio-labelled]-Mesotrione | N | Syngenta |

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study Y/N | Owner |
|---|---|---|---|---|---|
| | | | xxxxxxxxxxxxxx<br>GLP<br>not published<br>Syngenta File No A12739A_10438 | | |

The following tables are to be completed by MS

**List of data submitted by the applicant and not relied on**

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study Y/N | Owner |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |

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

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study Y/N | Owner |
|---|---|---|---|---|---|
| | | | | | |

| Data point | Author(s) | Year | Title<br>Company Report No.<br>Source (where different from company)<br>GLP or GEP status<br>Published or not | Vertebrate study<br>Y/N | Owner |
|---|---|---|---|---|---|
| | | | | | |

# Appendix 2 Detailed evaluation of the studies relied upon

## A 2.1 Statement on bridging possibilities

Not required.

## A 2.2 Acute oral toxicity (KCP 7.1.1)

| | |
|---|---|
| Comments of zRMS: | The acute oral toxicity study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study no classification for acute oral toxicity is required according to Regulation (EC) No 1272/2008. In opinion of zRMS, according to current requirements, the study is acceptable for evaluation of acute oral toxicity of MEZI 100 SC. In addition, for acute oral toxicity the assessment has been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008.<br>According to calculation method, ATEmix is higher than 2000 mg/kg bw. Therefore according to Regulation (EC) No 1272/2008 classification is not required. Calculation method provided by the applicant is considered as supplementary information. |

~~Not required~~

| | |
|---|---|
| Reference: | KCP 7.1.1 |
| Report | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

According to point 7.1.1 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" A test for acute oral toxicity shall be carried out, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute oral toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture."

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation MEZI 100 SC are known, the acute oral toxicity test is not necessary.

**Materials and methods**

We use the summation method using the formula:

$$ATE_{mix} = \frac{100}{\sum_{i=1}^{n} \frac{C_i}{ATE_i}}$$

Where:

- Ci - concentration of ingredient i ( % w/w or % v/v)
- i – the individual ingredient from 1 to n
- n – the number of ingredients
- $ATE_i$ - Acute Toxicity Estimate of ingredient i.

We use the table:

**Table 3.1.2 Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for classification for the respective routes of exposure.**

| Exposure routes | Classification Category or experimentally obtained acute toxicity range estimate | Converted acute toxicity point estimate (see Note 1) |
|---|---|---|
| Oral (mg/kg bodyweight) | 0 < Category 1 ≤ 5<br>5 < Category 2 ≤ 50<br>50 < Category 3 ≤ 300<br>300 < Category 4 ≤ 2 000 | 0,5<br>5<br>100<br>500 |
| Dermal (mg/kg body-weight) | 0 < Category 1 ≤ 50<br>50 < Category 2 ≤ 200<br>200 < Category 3 ≤ 1 000<br>1 000 < Category 4 ≤ 2 000 | 5<br>50<br>300<br>1 100 |
| Gases (ppmV) | 0 < Category 1 ≤ 100<br>100 < Category 2 ≤ 500<br>500 < Category 3 ≤ 2 500<br>2 500 < Category 4 ≤ 20 000 | 10<br>100<br>700<br>4 500 |
| Vapours (mg/l) | 0 < Category 1 ≤ 0,5<br>0,5 < Category 2 ≤ 2,0<br>2,0 < Category 3 ≤ 10,0<br>10,0 < Category 4 ≤ 20,0 | 0,05<br>0,5<br>3<br>11 |
| Dust/mist (mg/l) | 0< Category 1 ≤ 0,05<br>0,05 < Category 2 ≤ 0,5<br>0,5 < Category 3 ≤ 1,0<br>1,0 < Category 4 ≤ 5,0 | 0,005<br>0,05<br>0,5<br>1,5 |

Note 1 These values are designed to be used in the calculation of the ATE for classification of a mixture based on its components and do not represent test results.

One ingredient is relevant.

- 20.1% (Acute Tox. 4, H302)
  For this ingredient estimated values ATEi are used.

$$ATE_{mix} = \frac{100}{\sum_{i=1}^{n} \frac{C_i}{ATE_i}} = \frac{100}{\frac{20.1}{500}} = 2487.6 \gg 2000$$

According to the table 3.1.2, the result ( 2487.6 mg/l bw > > 2 000 mg/l bw) is significantly higher than generic concentration level. Therefore the formulation is not classified as Acute Tox. 4, H302.

**Conclusion**

According to calculation method, the result 2487.6 mg/l bw is higher than result triggering classification. Therefore the formulation is not classified as Acute Tox. 4, H302.

## A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

| | |
|---|---|
| Comments of zRMS: | The acute dermal toxicity study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study no classification for acute dermal toxicity is required according to Regulation (EC) No 1272/2008. In opinion of zRMS, according to current requirements, the study is acceptable for evaluation of acute dermal toxicity of MEZI 100 SC.<br>In addition, for acute dermal toxicity the assessment has been conducted by the applicant based on the alternative method according to the Regulation (EC) 1272/2008.<br>No relevant ingredient is classified in this class of hazard. Therefore according to Regulation (EC) No 1272/2008 classification is not required. Alternative method provided by the applicant is considered as supplementary information. |

~~Not required.~~

| | |
|---|---|
| Reference: | KCP 7.1.2 |
| Report | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

According to point 7.1.2 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
”A test for dermal toxicity shall be carried out on a case by case basis, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute dermal toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.
Findings of severe skin irritation or corrosion in the dermal study may be used instead of performing a specific irritation study.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation MEZI 100 SC are known, the acute dermal toxicity test is not necessary.

**Conclusion**

No relevant ingredients classified in this class of hazard.

## A 2.4 Acute inhalation toxicity (KCP 7.1.3)

| | |
|---|---|
| Comments of zRMS: | A waiver for acute inhalation toxicity study has been evaluated in the EU review of active substance. It was concluded that an inhalation study is not required for A12739A. Since the waiver has been reviewed and accepted during EU review of mesotrione and within |

| | |
|---|---|
| | registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. In opinion of zRMS, according to current requirements, the same approach is acceptable to justify data waiving for inhalation toxicity study for MEZI 100 SC.<br>In addition, for acute inhalation toxicity the assessment has been conducted by the applicant taking into account Regulation (EU) No 284/2013.<br>It is concluded that an inhalation study is not required for MEZI 100 SC.<br>No relevant ingredient is classified in this class of hazard. Therefore according to Regulation (EC) No 1272/2008 classification is not required. Alternative method provided by the applicant is considered as acceptable. |

~~Not required.~~

| | |
|---|---|
| Reference: | KCP 7.1.3 |
| Report | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

Inhalation study on MEZI 100 SC is not required. According to point 7.1.3 of Part A of Annex to the ~~Commission~~ Regulation (EU) No 284/2013 as regards the data requirements for plant protection products the inhalation test must be carried out ~~since~~ where the preparation is:

- a gas or liquefied gas,
- a smoke generating formulation or fumigant,
- used with fogging equipment,
- a vapor releasing preparation,
- an aerosol,
- a powder containing a significant proportion of particles of diameter <50 µm (> 1% on a weight basis),
- to be applied from aircraft in cases where inhalation exposure is relevant,
- contains an active substance with a vapor pressure > 1x10-2 Pa and is to be used in enclosed spaces such as warehouses or glasshouses,
- ~~to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (> 1% on a weight basis).,~~
- to be applied by spraying.

The active substances and the other co-formulants are not classified as acute inhalation toxic, it can be assumed that entire formulation is not classified in this class. According to point 7.1.3 of part A of Annex Regulation No 284/2014, it is possible to waive from acute inhalation toxicity test.

The complete composition of the formulation with the classification of individual ingredients is available in part C.

**Conclusion**

No relevant ingredients classified in this class of hazard.

## A 2.5 Skin irritation (KCP 7.1.4)

| | |
|---|---|
| Comments of zRMS: | Skin irritation study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study no classification for skin irritation is required according to Regulation (EC) No 1272/2008. In opinion of zRMS, according to current requirements, the study is acceptable for evaluation of skin irritating properties of MEZI 100 SC.<br>In addition, for skin irritation the assessment has been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Calculated concentration is higher than a concentration 10% triggering classification therefore, according to calculation method the product should be classified as Skin Irrit. 2, H315, However, results of in vivo study indicates that no classification is required for skin irritating properties of A12739A. Since studies take precedence over calculation method, zRMS do not accept calculation method for evaluation of skin irritating properties of MEZI 100 SC. |

~~Not required.~~

Reference: KCP 7.1.4

Report: Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023

Guideline(s): Regulation (EC) No. 1272/2008

Deviations: -

GLP: No

Acceptability:

**Materials and methods**

According to point 7.1.4 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" The skin irritancy of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture."
The complete composition of the formulation with the classification of individual ingredients is available in part C.

Table 3.2.3
Generic concentration limits of ingredients classified for skin corrosive/irritant hazard (Category 1 or 2) that trigger classification of the mixture as corrosive/irritant to skin.

| Sum of ingredients classified as: | Concentration triggering classification of a mixture as: | |
|---|---|---|
| | Skin Corrosive | Skin Irritant |
| | Category 1 (see note below) | Category 2 |
| Skin Corrosive Categories 1A, 1B, 1C | ≥ 5 % | ≥ 1 % but < 5 % |
| Skin irritant Category 2 | | ≥ 10 % |

| | | |
|---|---|---|
| 10 × Skin Corrosive Category 1A, 1B, 1C) + Skin irritant Category 2 | | ≥ 10 % |

Note
The sum of all ingredients of a mixture classified as Skin Corrosive Category 1A, 1B or 1C respectively, shall each be ≥ 5 % respectively in order to classify the mixture as either Skin Corrosive Category 1A, 1B or 1C. If the sum of the Skin Corrosive Category 1A ingredients is < 5 % but the sum of Category 1A+1B ingredients is ≥ 5 %, the mixture shall be classified as Skin Corrosive Category 1B. Similarly, if the sum of Skin Corrosive Category 1A+1B ingredients is < 5 % but the sum of Category 1A+1B+1C ingredients is ≥ 5 % the mixture shall be classified as Skin Corrosive Category 1C.

Three ingredients are relevant.

- 2.2% ( Skin Corr 1, H314),
- 1.5 % ( Skin Irrit 2, H315),
- 2.7 %( Skin Irrit 2, H315).

We use the summation method, consisting in adding up the percentages of all ingredients classified in the each class.

$$\sum C_{SkinIrrit} = 10\ x\ 2.2 + 1.5 + 2.7 = 25.2 > 10\%$$

According to the table 3.2.3, the result does classify the whole formulation in this class of hazard- Skin Irrit 2, H315. However, original Applicant performed *in vitro* or *in vivo* studies to prove that product should not be classified as Skin Irrit 2, H315.

**Conclusion**

According to calculation method, the result 25.2 % is significantly higher than a concentration triggering classification (10%). However, original Applicant performed *in vitro* or *in vivo* studies to prove that product should not be classified as Skin Irrit 2, H315.

## A 2.6 Eye irritation (KCP 7.1.5)

| | |
|---|---|
| Comments of zRMS: | Eye irritation study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study classification as Eye Irrit. 2, H319 is required for A12739A according to Regulation (EC) No 1272/2008. In opinion of zRMS, according to current requirements, the study is acceptable for evaluation of eye irritating properties of MEZI 100 SC.<br>In addition, for eye irritation the assessment has been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Calculated concentration is higher than a concentration 3% triggering classification. Therefore, according to calculation method the product should be classified as Eye Dam. 1, H318. However, results of in vivo study indicates that classification as Eye Irrit. 2, H319 is required for A12739A. Since studies take precedence over calculation method, zRMS do not accept calculation method for evaluation of eye irritating properties of MEZI 100 SC. |

~~Not required.~~

| | |
|---|---|
| Reference: | KCP 7.1.5 |
| Report | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

According to point 7.1.5 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" Eye irritation tests shall be provided, unless it is likely that severe effects on the eyes may be produced or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, eye irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture."
The complete composition of the formulation with the classification of individual ingredients is available in part C.

For consideration of corrosive and irritant properties the following table applies:

Table 3.3.3
Generic concentration limits of ingredients of a mixture classified as Skin corrosive Category 1 and/ or eye Category 1 or 2 for effects on the eye that trigger classification of the mixture for effects on the eye (Category 1 or 2).

| Sum of ingredients classified as: | Concentration triggering classification of a mixture as: | |
|---|---|---|
| | Irreversible Eye Effects | Reversible Eye Effects |
| | Category 1 | Category 2 |
| Eye Effects Category 1 or Skin Corrosive Category 1A, 1B, 1C | ≥ 3 % | ≥ 1 % but < 3 % |
| Eye Effects Category 2 | | ≥ 10 % |
| (10 × Eye Effects Category 1) + Eye effects Category 2 | | ≥ 10 % |
| Skin Corrosive Category 1A, 1B, 1C + Eye effects Category 1 | ≥ 3 % | ≥ 1 % but < 3 % |
| 10 × (Skin Corrosive Category 1A, 1B, 1C + Eye Effects Category 1) + Eye Effects Category 2 | | ≥ 10 % |

One ingredient is relevant.

- 20.1 % (Eye Dam. 1. H318)

The concentration of component (Eye Dam. 1, H318) is 20.1 %.

Based on classification method product should be classified as Eye Dam. 1, H318. However, original Applicant performed *in vitro* or *in vivo* studies to prove that product should be classified as Eye Irrit 2, H319.

**Conclusion**

According to calculation method, the result 20.1% is significantly higher than a concentration triggering classification (3%). However, original Applicant performed *in vitro* or *in vivo* studies to prove that product should be classified as Eye Irrit 2, H319.

## A 2.7 Skin sensitisation (KCP 7.1.6)

| | |
|---|---|
| Comments of zRMS: | Skin sensitisation study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study no classification for skin sensitisation is required according to Regulation (EC) No 1272/2008. In opinion of zRMS, according to current requirements, the study is acceptable for evaluation of skin sensitisating properties of MEZI 100 SC.<br>In addition, for skin sensitisation the assessment have been conducted by the applicant based on the alternative method according to the Regulation (EC) 1272/2008.<br>No relevant ingredient is classified in this class of hazard. Therefore according to Regulation (EC) No 1272/2008 classification is not required. Alternative method provided by the applicant is considered as supplementary information. |

~~Not required.~~

| | |
|---|---|
| Reference: | KCP 7.1.6 |
| Report | Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

According to point 7.1.6 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”The skin sensitisation test shall be carried out unless the active substances or co-formulants are known to have sensitising properties or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin sensitisation properties of all components shall be provided or reliably predicted with a validated method.
Consideration shall be given to the possible effects of components on the sensitising potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

**Conclusion**

No relevant ingredients classified in this class of hazard.

## A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

Not applicable.

## A 2.9 Data on co-formulants (KCP 7.4)

### A 2.9.1 Material safety data sheet for each co- formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

### A 2.9.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

## A 2.10 Studies on dermal absorption (KCP 7.3)

| | |
|---|---|
| Comments of zRMS: | Dermal absorption study with A12739A has been evaluated as the representative formulation in the EU review of active substance. Since the study has been reviewed and accepted during EU review of mesotrione and within registration and renewal of registration process of Callisto 100 SC in Poland, zRMS:PL did not performed a new assessment. Taking into account results of the study dermal absorption is 0.1 %, 3% and 5% for concentrate Dilution rate: 1:200 and Dilution rate: 1:400 accordingly. In opinion of zRMS, according to current requirements (Guidance on Dermal Absorption, EFSA 2017), the study is acceptable for evaluation of dermal absorption of MEZI 100 SC. |

~~Not required~~

## A 2.11 Other/Special Studies

### A 2.11.1 Specific target organ toxicity

| | |
|---|---|
| Comments of zRMS: | For specific target organ toxicity the assessment has been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Concentration of ingredient that is classified in this hazard class (STOT RE 2, H373) is below concentration 10% triggering classification. Thus, according to Regulation (EC) No 1272/2008 classification is not required. Calculation method provided by the applicant is acceptable. |

~~Not required.~~

Reference: KCP 7.1.7

Report Toxicological classification of product MEZI 100 SC based on calculation

| | |
|---|---|
| | method taking into consideration health hazards of constituent substances; K. Czerwińska; 2023 |
| Guideline(s): | Regulation (EC) No. 1272/2008 |
| Deviations: | - |
| GLP: | No |
| Acceptability: | |

According to point 3.8.3 of Regulation (EC) No 1272/2008 as regards the data requirements for plant protection products:
" Mixtures are classified using the same criteria as for substances, or alternatively as described below. As with substances, mixtures shall be classified for specific target organ toxicity following ~~single~~ repeated exposure.
Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following ~~single~~ repeated exposure, when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate generic concentration limit as mentioned in Table 3.~~8.3~~9.4 for Category 1 and 2 respectively".

**Materials and Methods**

For consideration of specific target organ toxicity, the following table applies:

Table 3.~~8.3~~9.4 Generic concentration limits of ingredients of a mixture classified as a specific target organ toxicant that trigger classification of the mixture as Category 1 or 2.

| Ingredient classified as: | Generic concentration limits triggering classification of the mixture as: | |
|---|---|---|
| | Category 1 | Category 2 |
| Category 1 Specific Target Organ Toxicant | Concentration ≥ 10 % | 1,0 % ≤ concentration < 10 % |
| Category 2 Specific Target Organ Toxicant | | Concentration ≥ 10 % [(Note 1)] |

Note 1 If a Category 2 specific target organ toxicant is present in the mixture as an ingredient at a concentration ≥ 1,0 % a SDS shall be available for the mixture upon request.
~~We also took into account the point 3.8.3.4.5.: "Care shall be exercised when extrapolating toxicity of a mixture that contains Category 3 ingredient(s). A generic concentration limit of 20 % is appropriate; however, it shall be recognised that this concentration limit may be higher or lower depending on the Category 3 ingredient(s) and that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such as narcotic effects may occur below this 20 % value. Expert judgement shall be exercised."~~

Only one ingredient is classified in this hazard class.

- 9.09 % (STOT RE 2, H373)

The content of ingredient (9.09 %) doesn't classified in this hazard class not exceeds the concentration triggering classification - 10%. According to point 3.8.3.4.5. CLP Regulation, the formulation is not classified as STOT RE 2, H373

**Conclusions**

The concentration of one of the ingredients (9.09 %) is lower than concentration triggering STOT RE 2, H373 classification of whole formulation (10 %). Therefore the whole product will not be classified as STOT RE 2, H373.

### A 2.11.2 Reproductive toxicity

| | |
|---|---|
| Comments of zRMS: | For specific reproductive toxicity the assessment has been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Concentration of ingredient that is classified in this hazard class (Repr. 2, H361d) is above concentration 3% triggering classification. Thus, according to Regulation (EC) No 1272/2008 the product should be classified as Repr. 2, H361d. Calculation method provided by the applicant is acceptable. |

Reference: KCP 7.1.7

Report: Toxicological classification of product MEZI 100 SC based on calculation method taking into consideration health hazards of constituent substances; K. Czerwińska, 2023

Guideline(s): Regulation (EC) No. 1272/2008

Deviations: -

GLP: No

Acceptability:

We use table:

Table 3.7.2
Generic concentration limits of ingredients of a mixture classified as reproduction toxicants or for effects on or via lactation that trigger classification of the mixture

| Ingredient classified as: | Generic concentration limits triggering classification of a mixture as: | | | |
|---|---|---|---|---|
| | Category 1 reproductive toxicant | | Category 2 reproductive toxicant | Additional category for effects on or via lactation |
| | Category 1A | Category 1B | | |
| Category 1A reproductive toxicant | ≥ 0,3 % [Note 1] | - | - | - |
| Category 1B reproductive toxicant | - | ≥ 0,3 % [Note 1] | - | - |
| Category 2 reproductive toxicant | - | - | ≥ 3,0 % [Note 1] | - |
| Additional category for effects on or via lactation | - | - | - | ≥ 0,3 % [Note 1] |

Note
The concentration limits in the table above apply to solids and liquids (w/w units) as well as gases (v/v units).
Note 1
If a Category 1 or Category 2 reproductive toxicant or a substance classified for effects on or via lactation is present in the mixture as an ingredient at a concentration ≥ 0,1 % a SDS shall be available for the mixture upon request.

One ingredient are relevant in this class of hazard:

- 9.09 % (Repr. 2, H361d)

One ingredient is classified as Repr. 2, H361d at the concentration of 9.09 %. This concentration is higher than generic concentration level (3.0%). According to the table 3.7.2, CLP Regulation, the formulation should be classified as Repr. 2, H361d.

**Conclusion**

The concentration of ingredient (9.09 %) exceeds the generic concentration level for this class of hazard (3.0%). Therefore whole formulation is classified as **Repr. 2, H361d.**

# Appendix 3 Exposure calculations

## A 3.1 Operator exposure calculations (KCP 7.2.1.1)

### A 3.1.1 Calculations for Mesotrione

**Table A 10: Input parameters considered for the estimation of operator exposure**

*Mesotrione , Input Data*

| | | | |
|---|---|---|---|
| **Formulation type** | Soluble concentrates, emulsifiable concentrate, etc. | **Name of active substance** | Mesotrione |
| **Concentration of active substance [g a.s./l or kg]** | 100 | **Crops** | Field crops |
| **Area treated [ha/day]** | 50 | **Application method** | Downward spraying |
| **Dermal absorption [%] (concentrate)** | 0.1 | **Application technique** | Vehicle-mounted |
| **Dermal absorption [%] (dilution)** | 5 | **Indoor/outdoor** | Outdoor |
| **Oral absorption [%]** | 100 | **Drift reduction [%]** | 0 |
| **Inhalation absorption [%]** | 100 | **Type of cultivation** | Normal |
| **Body weight (kg)** | 60 | | |
| **AOEL [mg/kg bw/day]** | 0.005 | | |
| **AAOEL [mg/kg bw]** | | | |

**Table A 11: Estimation of operator exposure towards Mesotrione using the OPEX model**

**Summary data - Short term exposure**

| **Model data** | | **Level of PPE** | **Total absorbed dose [mg/kg bw per day]** | **% of systemic AOEL** |
|---|---|---|---|---|
| Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile<br>Crop density: Normal | | | | |
| Mesotrione | Number of applications and application rate: 1 x 0.1 kg a.s./ha<br>Dermal absorption (concentrate): 0.1 %<br>Dermal absorption (in-use dilution): 5 % | | | |
| | | M/L: Workwear<br>App: Workwear | 0.001 | 23.3 |

**Summary data - Acute exposure**

| **Model data** | **Level of PPE** | **Total absorbed dose [mg/kg bw]** | **% of systemic AAOEL** |
|---|---|---|---|

| Model data | Level of PPE | Total absorbed dose [mg/kg bw] | % of systemic AA-OEL |
|---|---|---|---|
| Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/95th percentile<br>Crop density: Normal | | | |
| Mesotrione | Number of applications and application rate: 1 x 0.1 kg a.s./ha<br>Dermal absorption (concentrate): 0.1 %<br>Dermal absorption (in-use dilution): 5 % | | |
| | M/L: Workwear + Protected hands + FP2, P2 and similar | | No results! |
| | App: Workwear + Protected hands + FP2, P2 and similar | | |

## A 3.2 Worker exposure calculations (KCP 7.2.3.1)

### A 3.2.1 Calculations for Mesotrione

**Table A 12: Input parameters considered for the estimation of worker exposure**

| | | | |
|---|---|---|---|
| **Indoor/outdoor** | Outdoor | **AOEL [mg/kg bw/day]** | 0.005 |
| **Re-entry activity** | Inspection, irrigation | **Dermal transfer coefficient - Total potential exposure [cm²/h]** | 12500 |
| **Crops** | Field crops | **Dermal transfer coefficient - Arm, body and legs covered [cm²/h]** | 1400 |
| **Application method** | Downward spraying | **Dermal transfer coefficient - Hands, arm, body and legs covered [cm²/h]** | 1250 |
| **Application technique** | Vehicle-mounted | **Dermal transfer coefficient - Hands covered, no workwear [cm²/h]** | |
| **Max. application rate of the product [l or kg/ha]** | 1 | **DFR refined worker [µg/cm² foliage per kg a.s./ha]** | 3 |
| **Max. no. of applications** | 1 | **DT50 foliar worker [days]** | 30 |
| **Interval between multiple applications [days]** | NA | | |
| **Multiple application factor** | 1 | | |
| **Body weight (kg)** | 60 | | |
| **Name of active substance** | Mesotrione | | |
| **Dermal absorption [%] (dilution)** | 5 | | |
| **Inhalation absorption [%]** | 100 | | |
| **Time [hours per day]** | 2 | | |

**Table A 13: Estimation of worker exposure towards Mesotrione using the OPEX model**

| | Level of PPE | Total absorbed dose [mg/kg bw per day] | % of systemic AOEL | Re-entry restriction [days] |
|---|---|---|---|---|
| | | | | Inspection, irrigation / Outdoor<br>Work rate: 2 hours/day<br>Interval: NA<br>Body weight: 60 kg<br>TC (potential): 12500 cm²/h<br>TC (workwear (arms, body and legs covered)): 1400 cm²/h<br>TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h<br>TC (gloves): NA cm²/h |
| | **Mesotrione** | | | Number of applications & application rate: 1 x 0.1 kg a.s./ha<br>Dermal absorption: 5 %<br>DFR: 3 µg/cm² foliage per kg a.s./ha<br>DT50: 30 days |
| | Potential | 0.006 | 125 | 10 |
| | Workwear | 0.0007 | 14 | 0 |
| | Workwear and gloves | 0.0006 | 12.5 | 0 |
| | Hands covered, no workwear | | | |

## A 3.3 Bystander and resident exposure calculations (KCP 7.2.2.1)

### A 3.3.1 Calculations for Mesotrione

**Table A 14: Estimation of resident exposure towards Mesotrione using the OPEX model**

| Model data | Level of PPE | Total absorbed dose [mg/kg bw per day] | % of systemic AOEL |
|---|---|---|---|
| | | | Season: Not relevant<br>Buffer zone: 2-3 m<br>Drift reduction technology: 0 %<br>Interval between treatments: NA<br>Minimum volume of water: 200 l |
| **Mesotrione** | | | Number of applications and application rate: 1 x 0.1 kg a.s./ha<br>Dermal absorption: 5 %<br>DFR: 3 µg/cm² foliage per kg a.s./ha<br>DT50: 30 days |
| Resident child<br>Body weight: 10 kg | Drift (75th perc.) | 0.0007 | 13.7 |
| | Vapour (75th perc.) | 0.0008 | 16 |
| | Deposits (75th perc.) | 0.0001 | 2.3 |
| | Re-entry (75th perc.) | 0.0008 | 16.9 |
| | Sum (mean) | 0.002 | 38.6 |
| Resident adult<br>Body weight: 60 kg | Drift (75th perc.) | 0.0002 | 3.2 |
| | Vapour (75th perc.) | 0.0003 | 5.4 |
| | Deposits (75th perc.) | 3e-05 | 0.7 |

| Model data | Level of PPE | Total absorbed dose [mg/kg bw per day] | % of systemic AOEL |
|---|---|---|---|
| | Re-entry (75th perc.) | 0.0005 | 9.4 |
| | Sum (mean) | 0.0007 | 14.9 |

### A 3.4 Combined exposure calculations for Mesotrione

This product has got only one substance.

## Appendix 4 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)

Not required.