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| --- |
| FINAL REGISTRATION REPORT  **Part B**  Section 6  Mammalian Toxicology  Detailed summary of the risk assessment |
| Product code: SHA 2600 E  Product name(s): PENTAGON  Chemical active substance:  pendimethalin 445 g/L |
| Central Zone  Zonal Rapporteur Member State: Poland |
| CORE ASSESSMENT |
| Applicant: SHARDA Cropchem Limited  Submission date: December 2023  Finalisation date: July 2024; November 2024 |

Version history

|  |  |
| --- | --- |
| When | What |
| July 2024 | RMS assessment |
| November 2024 | ZRMs made changes in dossier according to reviewed comments |
|  |  |
|  |  |

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# Mammalian Toxicology (KCP 7)

## Summary

Table 6.1‑1: Information on Pendimethalin 45.5% CS \*

|  |  |
| --- | --- |
| Product name and code | Pendimethalin 45.5% CS |
| Formulation type | Capsule suspension (CS) |
| Active substance(s) (incl. content) | pendimethalin 445 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 Pendimethalin 45.5% CS 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** **Pendimethalin 45.5% CS according to Regulation (EC) No 1272/2008**

|  |  |
| --- | --- |
| Hazard class(es), categories | Repr. 2  Skin Sens.1  Resp. Sens.1  Carc. 2 |
| Hazard pictograms or Code(s) for hazard pictogram(s) | GHS08  GHS07 |
| Signal word | ~~Warning~~  Danger |
| Hazard statement(s) | H361d Suspected of damaging the unborn child  H317 May cause an allergic skin reaction  H334 May cause allergy or asthma symptoms or breathing difficulties ifinhaled  H351 Suspected of causing cancer. |
| Precautionary statement(s) | **Warning section of the label (first page):**  P201: Obtain special instructions before use  P280+P284: Wear protective gloves, protective clothing.and respiratory protection.  P302+P352: IF ON SKIN: Wash with plenty of water.  P304+P340: IF INHALED: Remove person to fresh air and keep comfortable for breathing.  P308 + P313: IF exposed or concerned: Get medical advice/attention.  .  Other section of the label:  P202: Do not handle until all safety precautions have been read and understood.  P270: Do not eat, drink or smoke when using this product.  P271: Use only outdoors or in a well-ventilated area.  P272: Contaminated work clothing should not be allowed out of the workplace.  P362+P364: Take off contaminated clothing and wash it before reuse.  P405: Store locked up.  P501: Dispose of contents/container to …  And P280 as follows:  Operator:  „*Stosować rękawice ochronne, odzież ochronną oraz ochronę dróg oddechowych w trakcie przygotowywania cieczy użytkowej oraz odzież roboczą w trakcie wykonywania zabiegu*.”  “Wear protective gloves and work wear (coverall) during mixing and loading and work wear application.”  Worker:  „*Stosować rękawice ochronne oraz odzież roboczą podczas wchodzenia na teren poddany opryskowi* .”  “Wear protective gloves and work wear when entering treated area.”  Section First aid:  P308 + P313: IF exposed or concerned: Get medical advice/attention.  P304+P340: IF INHALED: Remove person to fresh air and keep comfortable for breathing.  P342+311: If experiencing respiratory symptoms: Call a POISON CENTER/doctor.  P302+P352: IF ON SKIN: Wash with plenty of water.  P333+P313: If skin irritation or rash occurs: Get medical advice/attention. |
| Additional labelling phrases | To avoid risks to ~~man~~ human health and the environment, comply with the instructions for use.  [EUH401] |

Table 6.1‑3: Summary of risk assessment for operators, workers, residents and bystanders for Pendimethalin 45.5% CS

|  | Result | PPE / Risk mitigation measures |
| --- | --- | --- |
| Operators | Acceptable | Based on exposure: work wear (arms, body and legs covered) during M/L and A  Based on classification: protective gloves, protective clothing and respiratory protection during M/L. |
| Workers | Acceptable | Work wear (arms, body and legs covered) – cereals & potatoes  Work wear (arms, body and legs covered) and protective gloves – low vegetables |
| Residents& Bystanders | Acceptable | None |

No unacceptable risk for operator, workers and resident was identified when the product is used as intended and provided that the PPE stated in Table 6.1‑3 are applied.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and residents/bystanders 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, resident or bystander 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 | Residents | Bystander |
| 1 | Pre emergence  Potato, ware potato  BBCH 00-09 | F | Foliar spraying  LCTM | a) 1  b) 1 | a) 1.137  b) 1.137 | 200-400 | - |  |  |  |  |  |
| 2 | Pre emergence  Winter cereals (rye, oats, triticale) (BBCH 00-09) | F | Foliar spraying  LCTM | a) 1  b) 1 | a) 1.137  b) 1.137 | 200-400 | - |  |  |  |  |  |
| 3 | Post emergence  Winter cereals (rye, oats, triticale), Winter oilseed rape (BBCH 10-16) | F | Foliar spraying  LCTM | a) 1  b) 1 | a) 1.137  b) 1.137 | 200-400 | - |  |  |  |  |
| 4 | Pre emergence  Onion, Shallots (BBCH 00-09) | F | Foliar spraying  LCTM | a) 1  b) 1 | a) 1.3  b) 1.3 | 200-400 | - |  |  |  |  |
| 5 | Post-emergence  Onion, Shallots (BBCH 10-13) | F | Foliar spraying  LCTM  LCHH | a) 2(7)  b) 2(7) | a) 1.0  b) 1.3 | 200-400 | - |  |  |  |  |
| 6 | Pre-emergence  Flower bulb and flower tuber crops (BBCH 00-09) | F | Foliar spraying  LCTM | a) 1  b) 1 | a) 1.6  b) 1.6 | 200-400 | - |  |  |  |  |

\* 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 |

## Toxicological Information on Active Substance

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)

|  | Pendimethalin |
| --- | --- |
| Common Name | Pendimethalin |
| CAS-No. | 40487-42-1 |
| Classification and proposed labelling | |
| With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended) | **Hazard classes, categories**: Repr. Cat. 2  **Code(s) for hazard pictogram:** GHS08  **Signal word:** Warning  **Hazard statements:** H361d |
| Additional C&L proposal | - |
| Agreed EU endpoints | |
| AOEL systemic | 0.17 mg/kg bw/d (corrected for 57% oral absorption) |
| Reference | SANTE/11656/2016, 18 May 2017 rev.2 |
| Conditions to take into account/critical areas of concern with regard to toxicology | |
| According to EFSA Conclusion | The operators have to use proper PPE |

## Toxicological Evaluation of Plant Protection Product

The assessment of all acute toxicological properties of Pendimethalin 45.5% CS are derived from the classi-fication of the active compound and co-formulants. When considering the properties of all co-formulants and toxicity study Pendimethalin 45.5% CS is classified as “H361d: Suspected of damaging fertility or the unborn child.” . Details in Appendix 2

Table 6.3‑1: Additional toxicological information relevant for classification/labelling of Pendimethalin 45.5% CS

|  | 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) | Pendimethalin (45.5% (w/w)) | H361d | Reg. 1272/2008 | H361d |
| Toxicological properties of non-active substance(s) (relevant for classification of product) | mixture  1.32% | Acute Tox. 4; H332  Skin Irrit. 2 H315  Eye Irrit. 2; H319  STOT SE 3; H335  Skin. Sens. 1; H317  Resp. Sens. 1; H334  Carc. 2; H351  STOT RE 2; H373 | - | Skin. Sens. 1; H317  Resp. Sens. 1; H334  Carc. 2; H351 |
| Further toxicological information | No data – not required |  |  |  |

\*Please use concentration range or concentration limit (e.g. 1-10% or > 1%) as provided in MSDS.

\*\*Material safety data sheet by the applicant

## Toxicological Evaluation of Groundwater Metabolites

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

## Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in Pendimethalin 45.5% CS are presented in the following table.

Table 6.5‑1: Dermal absorption rates for active substances in Pendimethalin 45.5% CS

|  | Pendimethalin | |
| --- | --- | --- |
|  | Value | Reference |
| Concentrate | 2.2% | New study reported in Appendix 2 – Nabanita Sam, 2021 |
| Dilution | 22% | New study reported in Appendix 2 – Nabanita Sam, 2021 |

### Justification for proposed values - Pendimethalin

Proposed dermal absorption rates for Pendimethalin are based on dermal absorption studies on formulation Pendimethalin 45.5% CS. The study results are summarised in the following table. Full summaries of studies on the dermal absorption of Pendimethalin 45.5% CS that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

Table 6.5‑2: Summary of in vitro human dermal absorption

| **Test** | **Concentrate** | **Spray dilution**  **(dilution concentration)** | **Formulation in study** | **Acceptability of study** | **Justification provided on representativity of study formulation for current product** | **Acceptability of justification** | **Reference\*** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| In vitro (human) | 2.2 % | 22 % | SHA 2600 E/ PET | Yes | Yes (see Appendix A 2.10) | Justification accepted. Endpoint can be used for current product | Nabanita Sam, 2021 |

## 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 | Pendimethalin 45.5% CS |
| Formulation type | CS |
| Category | Herbicide |
| Active substance(s) (incl. content) | **Pendimethalin**  445 g/L |
| AOEL systemic | 0.17 mg/kg bw/d |
| Inhalation absorption | 100% |
| Oral absorption | 57% |
| Dermal absorption | Concentrate: 2.2 %  Dilution: 22 % |

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

The critical GAP 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 zone is given in Part B, Section 0.

Justification

Intended uses of the GAP given in Part B, Section 0, were separated here in two critical GAPs between uses with pre-emergence applications and uses with post-emergence applications.

### Operator exposure (KCP 7.2.1)

|  |  |
| --- | --- |
| Comments of zRMS: | The results of the estimation of operator exposure to pendimethalin contained in the product SHA 2600 E (PENTAGON), presented by the applicant are accepted.  According to the estimation based on Calculator OPEX version (v.2022), the use of SHA 2600 E (PENTAGON) containing pendimethalin (445 g/L) causes acceptable health risk for:   * an **unprotected operator** during mixing/loading and application in the case of vehicle-mounted application technique in field crops; * an **operator equipped with work wear** (arms, body and legs covered) during mixing/loading and application in the case of manual (hand held and knapsack) application.   **Conclusions:**  Taking into account the results of exposure estimations and classification of the product (Repr.2, H361d, Skin Sens 1, H317, Resp. Sens.1, H334, Carc. 2, H351), the use of SHA 2600 E (PENTAGON) causes **acceptable exposure risk for an operator equipped with protective gloves, protective clothing and respiratory protection during mixing & loading and work wear during application**.  Following sentence regarding the use of PPE is recommended by the evaluator to be placed in the **section of precautions for the operators:**  „*Stosować rękawice ochronne, odzież ochronną oraz ochronę dróg oddechowych w trakcie przygotowywania cieczy użytkowej oraz odzież roboczą w trakcie wykonywania zabiegu*.”  “Wear protective gloves and work wear (coverall) during mixing and loading and work wear application.” |

#### Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of Pendimethalin 45.5% CS according to the critical use(s) is presented in Table 6.6‑2. The outcome of the estimation is presented in Table 6.6‑3 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6‑2: Exposure models for intended uses

|  |  |
| --- | --- |
| Critical use(s) | Pre-emergence (Winter cereals) (max. 2.5 L product/ha)  Pre-emergence (Potato, ware potato ) (max. 2.5 L product/ha)  Pre-emergence (Onion, Shallot ) (max. 2.85 L product/ha)  Post-emergence (Winter cereals, Winter oilseed rape) (max 2.5 L product/ha)  Post-emergence (Onion, Shallot) (max. 2.85 L product/ha)  Pre-emergence (Ornamentals) (max 3.5 L product/ha) |
| Model | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874  calculator version: 2022 |

Table 6.6‑3: Estimated operator exposure (longer term exposure) – OPEX version 2022

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Pendimethalin | |
| Model data | Level of PPE | Total absorbed dose  (mg/kg/day) | % of systemic AOEL |
| Normal & Vehicle-mounted **Pre-emergence (Winter cereals, Potato, ware potato) and Post-emergence (Winter cereals, Winter oilseed rape)** | | | |
| Application rate | | 1 x 1.137 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 0.1 | 68.7 |
| Work wear (arms, body and legs covered) at M/L and A | 0.07 | 43.3 |
| Normal & Vehicle-mounted **Pre-emergence** (**Onion, Shallot)** | | | |
| Application rate | | 1 x 1.3 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 0.1 | 76.5 |
| Work wear (arms, body and legs covered) at M/L and A | 0.08 | 48.1 |
| Normal & Vehicle-mounted **Post-emergence** (**Onion, Shallot)** | | | |
| Application rate | | 1 x 1.3 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 0.1 | 76.5 |
| Work wear (arms, body and legs covered) at M/L and A | 0.08 | 48.1 |
| Normal & Manual-Hand held **(Onion, Shallot)** | | | |
| Application rate | | 1 x 1.3 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 1.2 | 686 |
| Work wear (arms, body and legs covered) at M/L and A | 0.1 | 84.1 |
| Normal & Manual-Knapsack **(Onion, Shallot)** | | | |
| Application rate | | 1 x 1.3 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 0.3 | 198 |
| Work wear (arms, body and legs covered) at M/L and A | 0.04 | 25.2 |
| Normal & Vehicle-mounted **Pre-emergence** **(Ornamentals)** | | | |
| Application rate | | 1 x 1.6 kg a.s./ha | |
| **Short term (75th percentile)** | Without RPE/PPE | 0.2 | 90.6 |
| Work wear (arms, body and legs covered) at M/L and A | 0.1 | 56.8 |

**Conclusion**

According to the OPEX (version 2022) calculations, it can be concluded that the risk for operator is acceptable without the use of gloves during mixing/loading and application.

**Implication for labelling:** None

#### 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 consideration of the above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

### Worker exposure (KCP 7.2.3)

|  |  |
| --- | --- |
| Comments of zRMS: | The estimations of worker exposure to pendimethalin contained in SHA 2600 E (PENTAGON) performed by the Applicant are accepted.  According to the estimation results, the use of SHA 2600 E (PENTAGON) **causes acceptable health risk for worker equipped with:**   * **work wear** assuming 2 hour working day (inspection, irrigation – relevant for cereals and potatoes); * **work wear and protective gloves** assuming 8 hour working day (reaching, picking – relevant for low vegetables).   Following sentence is recommended by the evaluator to be placed in the **section of precautions for the workers**:  „*Stosować rękawice ochronne oraz odzież roboczą podczas wchodzenia na teren poddany opryskowi* .”  “Wear protective gloves and work wear when entering treated area.” |

#### 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 Pendimethalin 45.5 % CS according to the critical use(s). Outcome of the estimation is presented in Table 6.6‑5 (longer term exposure). Detailed calculations are in Appendix 3.

**Table 6.6‑4: Exposure models for intended uses**

|  |  |
| --- | --- |
| Critical use(s) | Post-emergence (Winter cereals, Winter oilseed rape) (max 2.5 L product/ha)  Post-emergence (Onion, Shallot) (max. 2.85 L product/ha) |
| Models | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874  calculator version: OPEX 2022 |

**Table 6.6‑5: Estimated worker exposure (longer term exposure) – OPEX version 2022**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Pendimethalin | | |
| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL  At day 0 | Safe re-entry interval (days) |
| **Post-emergence (**Winter cereals, Winter oilseed rape)  Inspection, irrigation / Outdoor  Work rate: 2 hours/day,  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 365 days | | | | |
| Number of applications and application rate | | 1 x 1.137 kg a.s./ha | | |
| Body weight: 60 kg | Potential  TC: 12500 cm2/person/h | 0.3 | 184 | 27 |
| Work wear (arms, body and legs covered)  TC: 1400 cm2/person/h | 0.04 | 20.6 | 0 |
| Work wear (arms, body and legs covered) and gloves TC : 1250 cm2/person/h | 0.03 | 18.4 | 0 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Post-emergence (**Onion, Shallot)  Reaching, picking / Outdoor  Work rate: 8 hours/day,  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 7 days | | | | |
| Number of applications and application rate | | 2 x 1.3 kg a.s./ha | | |
| Body weight: 60 kg | Potential  TC: 5800 cm2/person/h | ~~1.2~~  1 | ~~720~~  568 | ~~86~~  76 |
| Work wear (arms, body and legs covered)  TC: 2500 cm2/person/h | ~~0.5~~  0.4 | ~~310~~  245 | ~~50~~  39 |
| Work wear (arms, body and legs covered) and gloves TC : 580 cm2/person/h | 0.1 | ~~72~~  57 | 0 |

**Conclusion**

For an application on low crops (Winter cereals, Winter oilseed rape) it is concluded that there is no unac-ceptable risk anticipated for the worker wearing adequate work clothing and with personal protective equipment for maintenance treated with PENTAGON.

For an application on low crops (Onion, Shallot) it is no unacceptable risk anticipated for the worker wearing adequate work clothing and with personal protective equipment (gloves) for maintenance ac-tivities when for re-entering cotton treated with PENTAGON.

**Implication for labelling:** P280: Wear protective gloves.

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

If no DFR data for the specific compound are available, a conservative default value for the DFR may be taken as 3 μg/cm2 per kg s.a/ha.

#### Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for Pendimethalin 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.

### Resident and bystander exposure (KCP 7.2.2)

|  |  |
| --- | --- |
| Comments of zRMS: | The AAOEL value for pendimethalin is not allocated. Consequently, it is assumed that the estimation of bystander exposure is covered by the calculation of resident exposure towards the active substance.  The results of exposure estimations demonstrate that the use of SHA 2600 E (PENTAGON) according to the list of intended uses presented in the GAP Table and anticipating the introduction of buffer zone presented (2-3m), **cause acceptable health risk for bystander/resident (adult and child).** |

#### Estimation of resident and bystander exposure

The acute exposure assessment for bystanders covers the exposure that a resident could reasonably be expected to incur in a single day. Therefore, there is no need for a separate acute risk assessment for residents.

No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure.

Table 6.6‑6 shows the exposure model(s) used for estimation of resident exposure to Pendimethalin. The outcome of the estimation is presented in

Table 6.6‑7 (longer term resident exposure). Detailed calculations are in Appendix 3.

Table 6.6‑6: Exposure models for intended uses

|  |  |
| --- | --- |
| Critical use(s) | Pre-emergence (Winter cereals) (max. 2.5 L product/ha)  Pre-emergence (Potato, ware potato ) (max. 2.5 L product/ha)  Pre-emergence (Onion, Shallot ) (max. 2.85 L product/ha)  Post-emergence (Winter cereals, Winter oilseed rape) (max 2.5 L product/ha)  Post-emergence (Onion, Shallot) (max. 2.2 L product/ha)  Pre-emergence (Ornamentals) (max 3.5 L product/ha) |
| Model(s) | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874  calculator version: OPEX 2022 |

Table 6.6‑7: Estimated resident exposure (OPEX version 2022)

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Pendimethalin | |
| Model data |  | Total absorbed dose  (mg/kg bw/day) | % of systemic AOEL |
| Tractor mounted boom spray application outdoors to **Pre-emergence (Winter cereals, Potato, ware potato) and Post-emergence (Winter cereals, Winter oilseed rape)**  Buffer zone: 2-3 (m)  Drift reduction technology: no  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 365 days | | | |
| Application rate | | 1 × 1.137 kg a.s./ha | |
| Resident child  Body weight: 10 kg | Drift (75th perc.) | 0.03 | 20 |
| Vapour (75th perc.) | 0.0008 | 0.5 |
| Deposits (75th perc.) | 0.004 | 2.5 |
| Re-entry (75th perc.) | 0.04 | 24.8 |
| **Sum (mean)** | 0.06 | 33 |
| Resident adult  Body weight: 60 kg | Drift (75th perc.) | 0.008 | 4.7 |
| Vapour (75th perc.) | 0.0003 | 0.2 |
| Deposits (75th perc.) | 0.002 | 1 |
| Re-entry (75th perc.) | 0.02 | 13.8 |
| **Sum (mean**) | 0.02 | 14.1 |
| Tractor mounted boom spray application outdoors to **Pre-emergence (Onion, Shallot)**  Buffer zone: 2-3 (m)  Drift reduction technology: no  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 365 days | | | |
| Application rate | | 1 × 1.3 kg a.s./ha | |
| Resident child  Body weight: 10 kg | Drift (75th perc.) | 0.04 | 22.8 |
| Vapour (75th perc.) | 0.00008 | 0.5 |
| Deposits (75th perc.) | 0.005 | 2.8 |
| Re-entry (75th perc.) | 0.05 | 28.3 |
| **Sum (mean)** | 0.06 | 37.5 |
| Resident adult  Body weight: 60 kg | Drift (75th perc.) | 0.009 | 5.4 |
| Vapour (75th perc.) | 0.0003 | 0.2 |
| Deposits (75th perc.) | 0.002 | 1.1 |
| Re-entry (75th perc.) | 0.03 | 15.7 |
| **Sum (mean**) | 0.03 | 16.1 |
| Tractor mounted boom spray application outdoors to **Post-emergence (Onion, Shallot)**  Buffer zone: 2-3 (m)  Drift reduction technology: no  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 7 days | | | |
| Application rate | | 2 × 1.3 kg a.s./ha | |
| Resident child  Body weight: 10 kg | Drift (75th perc.) | 0.04 | 22.8 |
| Vapour (75th perc.) | 0.00008 | 0.5 |
| Deposits (75th perc.) | 0.009 | 5.2 |
| Re-entry (75th perc.) | 0.09 | 52.4 |
| **Sum (mean)** | 0.1 | 58.4 |
| Resident adult  Body weight: 60 kg | Drift (75th perc.) | 0.009 | 5.4 |
| Vapour (75th perc.) | 0.0003 | 0.2 |
| Deposits (75th perc.) | 0.004 | 2.1 |
| Re-entry (75th perc.) | 0.05 | 29.1 |
| **Sum (mean**) | 0.05 | 27.4 |
| Tractor mounted boom spray application outdoors to **Pre-emergence (Ornamentals)**  Buffer zone: 2-3 (m)  Drift reduction technology: no  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: 365 days | | | |
| Application rate | | 1 × 1.6 kg a.s./ha | |
| Resident child  Body weight: 10 kg | Drift (75th perc.) | 0.05 | 28 |
| Vapour (75th perc.) | 0.00008 | 0.5 |
| Deposits (75th perc.) | 0.006 | 3.4 |
| Re-entry (75th perc.) | 0.08 | 34.8 |
| **Sum (mean)** | 0.01 | 46 |
| Resident adult  Body weight: 60 kg | Drift (75th perc.) | 0.0003 | 6.6 |
| Vapour (75th perc.) | 0.002 | 0.2 |
| Deposits (75th perc.) | 0.03 | 1.4 |
| Re-entry (75th perc.) | 0.03 | 19.3 |
| **Sum (mean**) | 0.03 | 19.7 |

### Combined exposure

Not relevant. The product contains only one active substance.

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 Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
| KCP 7.6.2 | Nabanita S. | 2021. | In vitro percutaneous dermal absorption study of Pendimethalin 455 g/L CS, through human skin, Study No.: G18511 |  |  |
|  |  |  |  |  |  |

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

No additional study submitted

1. Detailed evaluation of the studies relied upon

|  |  |
| --- | --- |
| Comments of zRMS: | Data and calculations presented by the Applicant in the dRR part C and B6 are incoherent.  Toxicological information about components has been verified (details see dRR partC). |

* 1. Statement on bridging possibilities
  2. Acute oral toxicity (KCP 7.1.1)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation SHA 2600 E (PENTAGON) **does not require classification in regards to oral acute toxicity.** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the acute oral toxicity of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The acute oral toxicity of Pendimethalin 45.5 % CS was calculated as follow:

Conclusion

The acute oral toxicity of Pendimethalin 45.5% CS was estimated to be > 2000 mg/kg. Therefore, according to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is **not classified**. No signal word or hazard statement is required for this hazard.

* 1. Acute percutaneous (dermal) toxicity (KCP 7.1.2)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation SHA 2600 E (PENTAGON) **does not require classification in regards to dermal acute toxicity.** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the acute ~~oral~~ dermal toxicity of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The acute dermal toxicity of Pendimethalin 45.5 % CS was calculated as follow:

Conclusion

The acute dermal toxicity of Pendimethalin 45.5% CS was estimated to be > 2000 mg/kg. Therefore, according to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is **not classified**. No signal word or hazard statement is required for this hazard.

* 1. Acute inhalation toxicity (KCP 7.1.3)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation SHA 2600 E (PENTAGON**) does not require classification in regards to inhalation acute toxicity.** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the acute ~~oral~~ inhalation toxicity of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The acute inhalation toxicity of Pendimethalin 45.5 % CS was calculated as follow:

Conclusion

The acute inhalation toxicity of Pendimethalin 45.5% CS was estimated to be > 5 mg/l.

Therefore, according to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is **not classified**. No signal word or hazard statement is required for this hazard.

* 1. Skin irritation (KCP 7.1.4)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product, the formulation SHA 2600 E (PENTAGON) **does not require classification in regards to skin irritation.** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the ~~acute oral toxicity~~ skin irritation of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The product contains < 1% of co-formulants considered as skin corrosive (classified as: Skin Corr. 1; H314) and < 10% of co-formulants considered as skin irritant (classified as: Skin Irrit. 2; H315). Under the GHS classification system this component is below the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.

According to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is **not classified**. No signal word or hazard statement is required for this hazard.

* 1. Eye irritation (KCP 7.1.5)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product, the formulation SHA 2600 E (PENTAGON) **does not require classification in regards to eye irritation.** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the ~~acute oral toxicity~~ eye irritation of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The product contains < 1% of co-formulants considered as eye damage (classified as: Eye Dam. 1; H318) and < 10% of co-formulants considered as eye irritant (classified as: Eye Irrit. 2; H319). Under the GHS classification system this component is below the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.

According to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is **not classified**. No signal word or hazard statement is required for this hazard.

* 1. Skin and respiratory sensitisation (KCP 7.1.6)

|  |  |
| --- | --- |
| Comments of zRMS: | Taking into account the composition of the product, the formulation SHA 2600 E (PENTAGON) **requires classification in regards to respiratory sensitization (Resp Sens.1, H334) and skin sensitization (Skin Sens, H317).** |

Acute toxicity studies for Pendimethalin 45.5 % CS were **not** evaluated as part of the EU review of a pendimethalin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the ~~acute oral toxicity~~ skin and respiratory sensitization of Pendimethalin 45.5 % CS can be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).

The product contains ingredient classified in regards skin and respiratory sensitisation in the concentration (> 1%) triggering classification of the mixture. ~~of co-formulants considered as skin sensitiser (classified as:~~ Skin Sens. 1; H317, Resp. Sens.1, H334). ~~Under the GHS classification system this component gets the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.~~

~~According to the Regulation EC No. 1272/2008, Pendimethalin 45.5% CS is not classified. No signal word or hazard statement is required for this hazard.~~

|  |  |
| --- | --- |
| Comments of zRMS: | Product SHA 2600 E (PENTAGON) contains ingredients which must be taken into account for the purpose of product classification in regards to reproductive toxicity and specific target organ toxicity – single and repeated exposure.  Conclusions:  Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation SHA 2600 E (PENTAGON) **requires classification in regards to reproductive toxicity (Repr. Cat. 2, H361d)** but it does not require classification regarding specific target organ toxicity . |

|  |  |
| --- | --- |
| Comments of zRMS: | **Carcinogenic effect:**  Product SHA 2600 E (PENTAGON) contains ingridients which were taken into account for the purpose of product classification in regards to carcinogenicity.  Conclusion:  Taking into account the composition of the product as well as the provisions of the EC Regulation 1272/2008, the formulation SHA 2600 E (PENTAGON) **requires classification in regards to carcinogenicity (Carc. 2, H351).** |

* 1. Supplementary studies for combinations of plant protection products (KCP 7.1.7)

No supplementary studies are necessary.

* 1. Data on co-formulants (KCP 7.4)
     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).

* + 1. 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).

* 1. Studies on dermal absorption (KCP 7.3)

|  |  |
| --- | --- |
| Comments of zRMS: | Study provided by the Applicant (Nabanita Sam., 2021. Study No.: G18511) is accepted. The endpoints can be used for the exposure assessment to active substance: 2.2% (concentrated product) and 22% (spray dilution). |

* + 1. **Study 1 – Pendimethalin in** **Pendimethalin 45.5% CS**
    2. **Comparative dermal absorption, in vitro human skin**

|  |  |
| --- | --- |
| Reference | KCP 7.6.2 |
| Report | In vitro percutaneous dermal absorption study of Pendimethalin 455 g/L CS, through human skin, Nabanita Sam., 2021. Study No.: G18511 |
| Guideline(s) | OECD Guideline 428 “Skin Absortion: in vitro Method” April 2004 |
| Deviations | No |
| GLP | Yes |
| Acceptability | Yes |
| Duplication  (if vertebrate study) | No |

**Materials and methods**

|  |  |  |
| --- | --- | --- |
| **Test material** | Name (Lot/Batch No.) | 14C- Pendimethalin (TJBIOS-NB67-170-30) |
|  | Test preparation | radioformulation |
| Specific activity | 28.6 mCi/mmol |
| Radiochemical purity | 98.9 % |
| Product | Name (Lot/Batch No.) | Pendimethalin 455 g/L CS (SCL-80067) |
| Company code | Pendimethalin |
| Concentration a.s. | 455 g/L |
| Formulation type | Pendimethalin 455 g/L CS |
| Blank product | Name (Lot/Batch No.) | Pendimethalin 455 g/L CS blank formulation (SCL-45623) |
| Concentration a.s. | 0 g/L |

|  |  |  |
| --- | --- | --- |
| **Test system** |  |  |
| Diffusion cell | Cell type | Dynamic |
| (if dynamic) Flow rate | 1.8 mL/hr |
| Exposed skin area | 0.64 cm2 |
| Membrane | Skin type | isolated epidermis |
| Skin thickness range | 0.2-0.4 mm |
| Skin donors age | 51, 53, 47, 45 years |
| Skin donors sex | Female |
| Location | abdomen |
| Source | post-mortem |
| Integrity test | Yes |
| Receptor | Receptor medium | Ethanol: Wather (50:50 v/v) supplemented with 6% PEG |
| Solubility in receptor medium | Yes |
| Sample Time | Exposure time | 8 h |
| Observation time | 16 h |
| Sampling | Sample intervals | At 0-1 h, 1-2 h, followed by 2-h intervals until 24 hours after application |
| Washing |  | At 8 h using water and a mild soap solution (3% Dove) |
| Final Procedure | Tape stripping | y |
| TS1-2 analysed separately | Y |

|  |  |  |
| --- | --- | --- |
| **Tested doses** | Concentrate | Spray dilution |
| Target concentration | 456.67 g·L-1 | 1.516 g·L-1 |
| Area dose | 4566.72 µg/cm-2 | 15.16 µg/cm-2 |
| Specific activity | 3.7122 MBq.mL-1 | 5.7554 MBq.mL-1 |
| No. of donors | 4 | 4 |
| No of cells used/valid cells\* | 8/8 | 8/8 |

**Results and discussions - Pendimethalin**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Dose group** | | High dose | | Low dose | | |
| (Formulation  concentrate) | | (Spray dilution 1:300) | | |
| Target concentration |  | 455 g·L-1 | | 1.52 g·L-1 | | |
| Mean actual applied dose |  | 4566.72 ± 9.40. µg/cm-2 | | 15.16 ± 0.07µg/cm-2 | | |
| Number of replicates (n) | | 8 | | 8 | | |
|  | | Mean | S.D. | Mean | | S.D. |
| **Dislodgeable dose** | |  |  |  | |  |
| Skin wash | | 94.64 | 1.25 | 68.69 | | 2.81 |
| Donor chamber wash | | 1.16 | 0.25 | 4.80 | | 1.81 |
| **Dose associated to skin** | |  |  |  | |  |
| Tape strips: 1st sample, strips 1 + 2 | | 1.26 | 0.18 | 5.40 | | 0.86 |
| Tape strips: 2nd sample; strips 3 - n | | 1.08 | 0.12 | 13.94 | | 0.73 |
| Skin preparation | | 0.19 | 0.05 | 6.22 | | 0.54 |
| **Absorbed dose** | |  |  |  | |  |
| Receptor fluid | | 0.77 | 0.11 | 1.48 | | 0.24 |
| Receptor chamber wash | | 0.02 | 0.01 | 0.22 | 0.06 | |
| **Total recovery1** | | 99.12 | 1.32 | 100.74 | | 1.55 |
| Absorption essentially complete at end of study (>75% absorption within half the study duration) [%Absorption at t0.5] | | No  [60.12 ± 2.54] | | No  [63.63± 2.42] | | |
| If no:  Absorption estimates  = absorbed dose + skin preparation + tape strips sample 2)2 | | 2.05 | 0.12 | 21.85 | | 0.63 |
| If yes:  Absorption estimates  = absorbed dose + skin preparation | | N/A | N/A | N/A | | N/A |
| Absorption estimate considering variability3  (Absorption (mean value) + ks) | | 2.05± 0.84 × 0.12 | | 21.85 ± 0.84 × 0.63 | | |
| Relevant absorption estimate | | 2.1508 | | 22.3792 | | |
| **Absorption estimates 4** | | **2.2** | | **22** | | |

1 Values may not calculate exactly due to rounding of figures

2 In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873) the radioactivity in the second tape-strip pool (3rd to nth tape strip) is considered potentially absorbable if less than 75% of the absorption occurred in the first half of the study (see Table 7.6.2‑1) Finally, the skin preparation is also considered potentially absorbable.

3 In accordance with the EFSA Guidance on Dermal Absorption (2017), dermal absorption should be calculated as follows: Absorption (mean value) + ks, where s is the sample standard deviation. The multiplication factor required depends on the number of replicates and is given in Table 1 of EFSA Guidance.

4 Relevant absorption estimate was rounded to the required number of significant figures.

N/A: not applicable

**Conclusion/endpoint**: 2.2 % of dose for undiluted Pendimethalin formulation (concentrate: 455g/al) Pendimethalin)

22 % of dose for actual spray strength used in the field dilution (1.52 g/ Pendimethalin)

* 1. Other/Special Studies

No data submitted.

1. Exposure calculations

Please refer to KCP reports

 

1. 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)

None.