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| FINAL REGISTRATION REPORT  **Part B**  Section 6  Mammalian Toxicology  Detailed summary of the risk assessment |
| Product code: NIC-HER 060 OD  Product name(s): -  Chemical active substance:  nicosulfuron, 60 g/L |
| Central Zone  Zonal Rapporteur Member State: Poland |
| CORE ASSESSMENT  (authorization) |
| Applicant: Pestila Sp. z o.o.  Submission date: 07/2022  MS Finalisation date: 09/2023; 12/2023 |

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Table of Contents

[6 Mammalian Toxicology (KCP 7) 5](#_Toc108601082)

[6.1 Summary 5](#_Toc108601083)

[6.2 Toxicological Information on Active Substance(s) 6](#_Toc108601084)

[6.3 Toxicological Evaluation of Plant Protection Product 7](#_Toc108601085)

[6.4 Toxicological Evaluation of Groundwater Metabolites 8](#_Toc108601086)

[6.5 Dermal Absorption (KCP 7.3) 8](#_Toc108601087)

[6.5.1 Justification for proposed values - nicosulfuron 8](#_Toc108601088)

[6.6 Exposure Assessment of Plant Protection Product (KCP 7.2) 10](#_Toc108601089)

[6.6.1 Selection of critical use(s) and justification 10](#_Toc108601090)

[6.6.2 Operator exposure (KCP 7.2.1) 10](#_Toc108601091)

[6.6.2.1 Estimation of operator exposure 10](#_Toc108601092)

[6.6.2.2 Measurement of operator exposure 11](#_Toc108601093)

[6.6.3 Worker exposure (KCP 7.2.3) 11](#_Toc108601094)

[6.6.3.1 Estimation of worker exposure 11](#_Toc108601095)

[6.6.3.2 Refinement of generic DFR value (KCP 7.2) 13](#_Toc108601096)

[6.6.3.3 Measurement of worker exposure 13](#_Toc108601097)

[6.6.4 Resident and bystander exposure (KCP 7.2.2) 13](#_Toc108601098)

[6.6.4.1 Estimation of resident and bystander exposure 13](#_Toc108601099)

[6.6.4.2 Measurement of resident and/or bystander exposure 14](#_Toc108601100)

[6.6.5 Combined exposure 14](#_Toc108601101)

[Appendix 1 Lists of data considered in support of the evaluation 15](#_Toc108601102)

[Appendix 2 Detailed evaluation of the studies relied upon 17](#_Toc108601103)

[A 2.1 Statement on bridging possibilities 17](#_Toc108601104)

[A 2.2 Acute oral toxicity (KCP 7.1.1) 17](#_Toc108601105)

[A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2) 17](#_Toc108601106)

[A 2.4 Acute inhalation toxicity (KCP 7.1.3) 17](#_Toc108601107)

[A 2.5 Skin irritation (KCP 7.1.4) 18](#_Toc108601108)

[A 2.6 Eye irritation (KCP 7.1.5) 18](#_Toc108601109)

[A 2.7 Skin sensitisation (KCP 7.1.6) 18](#_Toc108601110)

[A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7) 19](#_Toc108601111)

[A 2.9 Data on co-formulants (KCP 7.4) 19](#_Toc108601112)

[A 2.9.1 Material safety data sheet for each co-formulant 19](#_Toc108601113)

[A 2.9.2 Available toxicological data for each co-formulant 19](#_Toc108601114)

[A 2.10 Studies on dermal absorption (KCP 7.3) 19](#_Toc108601115)

[A 2.11 Other/Special Studies 19](#_Toc108601116)

[Appendix 3 Exposure calculations 20](#_Toc108601117)

[A 3.1 Operator exposure calculations (KCP 7.2.1.1) 20](#_Toc108601118)

[A 3.1.1 Calculations for nicosulfuron 20](#_Toc108601119)

[A 3.2 Worker exposure calculations (KCP 7.2.3.1) 25](#_Toc108601120)

[A 3.2.1 Calculations for nicosulfuron 25](#_Toc108601121)

[A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1) 27](#_Toc108601122)

[A 3.3.1 Calculations for nicosulfuron 27](#_Toc108601123)

[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) 30](#_Toc108601124)

# Mammalian Toxicology (KCP 7)

## Summary

Table 6.1‑1: Information on NIC-HER 060 OD \*

|  |  |
| --- | --- |
| Product name and code | NIC-HER 060 OD |
| Formulation type | oil dispersion [Code: OD] |
| Active substance (incl. content) | nicosulfuron; 60 g/L |
| Function | herbicide |
| Product already evaluated as the ‘representative formulation’ during the approval of the active substance | No |
| Product previously evaluated in another MS according to Uniform Principles | No |

\* Information on the detailed composition of NIC-HER 060 OD 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 NIC-HER 060 OD according to Regulation (EC) No 1272/2008

|  |  |
| --- | --- |
| Hazard class(es), categories | NR |
| Hazard pictograms or Code(s) for hazard pictogram(s) | NR |
| Signal word | NR |
| Hazard statement(s) | NR |
| Precautionary statement(s) | P280 - Wear protective gloves/protective clothing.  P391 - Collect spillage |
| 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, residents and bystanders for NIC-HER 060 OD

|  | Result | PPE / Risk mitigation measures |
| --- | --- | --- |
| Operators | Acceptable | None  Recommended: Workwear and gloves during mixing/loading and during application |
| Workers | Acceptable | None  Recommended: Workwear and gloves when inspecting the treated crops |
| Residents | Acceptable | None |
| Bystanders | Acceptable | None |

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended. No specific PPE is necessary.

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) max. rate per appl. b) max. total rate per crop/season | Water L/ha  min / max | Operator | Worker | Residents | Bystander |
| 1 | Maize (BBCH 12-17) | F | Spraying, LCTM | a) 1 b) 1 | a) 0.042 b) 0.042 | 200 -300 | NR | Operators (EFSA model AOEM], workers [EFSA model AOEM, EUROPOEM II re-entry model], residents and bystanders [EFSA model AOEM] |  |  |  |  |

\* 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

N/A).

## 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)

|  | nicosulfuron |
| --- | --- |
| Common Name | nicosulfuron |
| CAS-No. | 111991-09-4 |
| Classification and proposed labelling | |
| With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended) | Hazard classes (s), categories: none  Code(s) for hazard pictogram(s): none  Signal word: none  Hazard statement(s): none  Precautionary statement(s): none |
| Additional C&L proposal | NR |
| Agreed EU endpoints | |
| AOEL systemic | 0.8 mg/kg bw/d (correction for oral absorption/bioavailibility: 40 %) |
| Reference | EFSA Scientific Report (2007) 120, 1-91 |
| Conditions to take into account/critical areas of concern with regard to toxicology | |
| EFSA Conclusion for active substance | None |

## Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for NIC-HER 060 OD is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

Table 6.3‑1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for NIC-HER 060 OD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type of test, species, model system (Guideline) | Result | Acceptability | Classification  (acc. to the criteria in Reg. 1272/2008) | Reference |
| LD50 oral, rat  (OECD xxx) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| LD50 dermal, rat  (OECD xxx) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| LC50 inhalation, rat  (OECD xxx) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| Skin irritation, model system  (OECD xxx) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| Eye irritation, model system  (OECD xxx) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| Skin sensitisation, guinea pig/mouse  (OECD xxx, Buehler (xx applications)/M&K/LLNA) | Estimation based on composition of the product (additivity formula) | Yes | None | - |
| Supplementary studies for combinations of plant protection products | - | - | - | - |

Table 6.3‑2: Additional toxicological information relevant for classification/labelling of NIC-HER 060 OD

|  | 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) | NR | None | - | - |
| Toxicological properties of non-active substance(s) (relevant for classification of product) | NR | None | - | - |
| Further toxicological information | No data – not required | - | - | - |

## Toxicological Evaluation of Groundwater Metabolites

The nicosulfuron metabolites HMUD, ASDM, AUSN, MU-466 and UCSN are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Part B10 point 10). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.10 is therefore required and was performed in dRR Section 10. No toxicological studies for metabolites were performed and submitted with this application.

**HMUD**

The relevance of the groundwater metabolite HMUD has already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PECgw values obtained for NIC-HER 060 OD differ from PECgw values evaluated at EU level.

HMUD does not meet the criteria for products of no concern as defined in Step 1 of the guidance and therefore needs further assessment. A further assessment in Step 2 is required.

PECgw calculations after leaching from soil for HMUD were performed (see Part B10 ). In case of most scenarios PECgw values were above the trigger of 0.1 µg/L. A further assessment in Step 3 is required.

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, HMUD was screened for genotoxic activity by the data package of *in vitro* and *in vivo* genotoxicity studies. HMUD is considered not relevant and is further evaluated in Stage 3.

The parent nicosulfuron is not classified as toxicologically dangerous in accordance with regulation CLP 1272/2008. The structure of HMUD is very similar to that of nicosulfuron and in soil HMUD is formed by O-demethylation of a methoxy group on the pyrimidine ring of nicosulfuron. From a toxicological perspective it is likely that a toxicology profile of HMUD is comparable to that of the active substance. HMUD is considered not relevant and is further evaluated in Step 4.

HMUD was not considered relevant in the hazard assessment of Step 3. The potential exposure to HMUD is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

STEP 5:

HMUD has a PECgw between 0.75 µg/L and 10 µg/L. A refined assessment of the potential toxicological significance including the selected ADI is presented here.

ADI value for HMUD equals 2 mg/kg bw/day (ADI for nicosulfuron).

Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 l/day).

Refined risk assessment is point 10.3.5 in dRR part B10

In accordance with the performed risk assessment, it was concluded that HMUD is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. No further action is required.

**ASDM**

The relevance of the groundwater metabolite ASDM has already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PECgw values obtained for NIC-HER 060 OD differ from PECgw values evaluated at EU level.

ASDM is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10.

ASDM does not meet the criteria for products of no concern as defined in Step 1 of the guidance and therefore needs further assessment. A further assessment in Step 2 is required.

PECgw calculations after leaching from soil for ASDM were performed (see Part B10 point10). In case of all scenarios PECgw values were above the trigger of 0.1 µg/L. A further assessment in Step 3 is required.

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, biological activity of ASDM was evaluated and it was concluded that it does not have comparable target activity as the parent active compound. ASDM is considered not relevant and is further evaluated in Stage 2.

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, ASDM was screened for genotoxic activity by the data package of *in vitro* genotoxicity studies. ASDM is considered not relevant and is further evaluated in Stage 3.

The parent nicosulfuron is not classified as toxicologically dangerous in accordance with regulation CLP 1272/2008. ASDM is a rat metabolite as well as an impurity in technical nicosulfuron. Therefore, ASDM was present during the development of the toxicology database for nicosulfuron and did not impact the favourable toxicology profile for this active substance. ASDM is considered not relevant and is further evaluated in Step 4.

ASDM was not considered relevant in the hazard assessment of Step 3.

The potential exposure to ASDM is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

ASDM has a PECgw between 0.75 µg/L and 10 µg/L. A refined assessment of the potential toxicological significance including the selected ADI is presented here.

ADI value for ASDM equals 2 mg/kg bw/day (ADI for nicosulfuron).

Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 l/day).

In accordance with the performed risk assessment, it was concluded that ASDM is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. No further action is required

**AUSN**

The relevance of the groundwater metabolite AUSN has already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PECgw values obtained for NIC-HER 060 OD differ from PECgw values evaluated at EU level.

AUSN is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10.

AUSN does not meet the criteria for products of no concern as defined in Step 1 of the guidance and therefore needs further assessment. A further assessment in Step 2 is required.

PECgw calculations after leaching from soil for AUSN were performed (see Part B10 point10). In case of most scenarios PECgw values were above the trigger of 0.1 µg/L. A further assessment in Step 3 is required.

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, biological activity of AUSN was evaluated and it was concluded that it does not have comparable target activity as the parent active compound. AUSN is considered not relevant and is further evaluated in Stage 2.

AUSN was screened for genotoxic activity by the data package of *in vitro* genotoxicity studies. AUSN is considered not relevant and is further evaluated in Stage 3.

The parent nicosulfuron is not classified as toxicologically dangerous in accordance with regulation CLP 1272/2008. Low toxicity profiles were demonstrated for AUSN. AUSN is considered not relevant and is further evaluated in Step 4.

AUSN was not considered relevant in the hazard assessment of Step 3.

The potential exposure to AUSN is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required

AUSN has a PECgw between 0.75 µg/L and 10 µg/L. A refined assessment of the potential toxicological significance including the selected ADI is presented here.

ADI value for AUSN equals 2 mg/kg bw/day (ADI for nicosulfuron).

Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 l/day).

In accordance with the performed risk assessment, it was concluded that AUSN is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. No further action is required.

**MU-466**

The relevance of the groundwater metabolite MU-466 has already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PECgw values obtained for NIC-HER 060 OD differ from PECgw values evaluated at EU level.

MU-466 is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10.

MU-466 does not meet the criteria for products of no concern as defined in Step 1 of the guidance and therefore needs further assessment. A further assessment in Step 2 is required.

PECgw calculations after leaching from soil for MU-466 were performed (see Part B10 point 10). In case of most scenarios PECgw values were above the trigger of 0.1 µg/L. A further assessment in Step 3 is required.

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, biological activity of MU-466 was evaluated and it was concluded that it does not have comparable target activity as the parent active compound. MU-466 is considered not relevant and is further evaluated in Stage 2.

MU-466 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies. MU-466 is considered not relevant and is further evaluated in Stage 3.

The parent nicosulfuron is not classified as toxicologically dangerous in accordance with regulation CLP 1272/2008. MU-466 is a rat metabolite and in view of this minor difference in structure from ASDM, the toxicological profile of MU-466 is predicted to be low. MU-466 is considered not relevant and is further evaluated in Step 4.

MU-466 was not considered relevant in the hazard assessment of Step 3.

The PECgw for MU-466 was < 0.75 µg/L. There is no consumer exposure via other routes. MU-466 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.10.

**UCSN**

The relevance of the groundwater metabolite UCSN has already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PECgw values obtained for NIC-HER 060 OD differ from PECgw values evaluated at EU level.

UCSN is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10.

UCSN does not meet the criteria for products of no concern as defined in Step 1 of the guidance and therefore needs further assessment. A further assessment in Step 2 is required.

PECgw calculations after leaching from soil for UCSN were performed (see Part B10 point 10). In case of all scenarios PECgw values were above the trigger of 0.1 µg/L. A further assessment in Step 3 is required

In accordance with information included in EFSA Scientific Report (2007) 120, 1-91 for nicosulfuron, biological activity of UCSN was evaluated and it was concluded that it does not have comparable target activity as the parent active compound. UCSN is considered not relevant and is further evaluated in Stage 2.

UCSN was screened for genotoxic activity by the data package of *in vitro* genotoxicity studies. UCSN is considered not relevant and is further evaluated in Stage 3.

The parent nicosulfuron is not classified as toxicologically dangerous in accordance with regulation CLP 1272/2008. UCSN structure is similar to AUSN, the toxicological profile of UCSN is predicted to be low as well. UCSN is considered not relevant and is further evaluated in Step 4.

UCSN was not considered relevant in the hazard assessment of Step 3.

The potential exposure to UCSN is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

In accordance with the performed risk assessment, it was concluded that UCSN is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. No further action is required.

## Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in NIC-HER 060 OD are presented in the following table.

Table 6.5‑1: Dermal absorption rates for active substances in NIC-HER 060 OD

| nicosulfuron | | |
| --- | --- | --- |
|  | Value | Reference |
| Concentrate | 25 % | EFSA Journal 2017;15(6):4873 |
| Dilution | 70 % | EFSA Journal 2017;15(6):4873 |

### Justification for proposed values - nicosulfuron

No data on dermal absorption for nicosulfuron in NIC-HER 060 OD is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873) are presented in the following table.

Table 6.5‑2: Default dermal absorption rates for nicosulfuron

|  | Value | Justification for value | Acceptability of justification |
| --- | --- | --- | --- |
| Concentrate | 25 % | According to EFSA Journal 2017;15(6):4873 a default dermal absorption value of 25% may be applied for concentrated products that are organic solvent-formulated(a) or in other(b) types of formulations. | Acceptable |
| Dilution | 70 % | According to EFSA Journal 2017;15(6):4873 a default dermal absorption value of 70% may be applied for (in use) dilutions of organic solventformulated(a) or in other(b) types of formulations. | Acceptable |

(a): Formulation types: emulsifiable concentrate (EC), emulsion, oil in water (EW), suspo-emulsion (SE), dispersible concentrate (DC), oil miscible liquids (OL/OF), oil-based suspension concentrates (OD), emulsion for seed treatment (ES), microemulsion (ME).

(b): Formulation types: bait concentrate (CB), capsule suspension (CS), gel for direct application (GEL/GD), bait, ready for use (RB), mixture of capsule suspension and suspension concentrate (ZC), seed coated with a pesticide (PS), experimental solution of active substances in solvent (AI).

## 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 | NIC-HER 060 OD |
| Formulation type | OD |
| Category | Herbicide |
| Container size(s), short description | 1 L, made of HDPE, opening 50mmTE |
| Active substance (incl. content) | **nicosulfuron**  60 g/L |
| AOEL systemic | 0.8 mg/kg bw/d (correction for oral absorption/bioavailibility: 40 %) |
| Inhalation absorption | 100 % |
| Oral absorption | 40 % |
| Dermal absorption | Concentrate: 25 %  Dilution: 70 %  (Default) |

### 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.

### Operator exposure (KCP 7.2.1)

#### Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of NIC-HER 060 OD according to the critical use 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 | Maize (max. 0.7 L product/ha) |
| Model | **EFSA model AOEM** (Agricultural Operator Exposure 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: 30/03/2015] |

Table 6.6‑3: Estimated operator exposure (longer term exposure)

|  |  |  |  |
| --- | --- | --- | --- |
| Nicosulfuron | | | |
| Model data | Level of PPE | Total absorbed dose  (mg/kg/day) | % of systemic AOEL |
| Cereals  Outdoor  Downward spraying  Vehicle-mounted | | | |
| Application rate | | 0.042 kg a.s./ha | |
| **Spray application** (AOEM**;** 75th percentile)  Body weight: 60 kg | Potential exposure | 0.0671831 | 8.40 |
| Work wear (arms, body and legs covered) M/L and A | 0.0403592 | 5.04 |
| Work wear (arms, body and legs covered) M/L and A + gloves | 0.0018711 | 0.23 |

**Conclusion**

**According to the model calculations, it can be concluded that the risk for the operator using NIC-HER 060 OD on intended uses presented in GAP table is acceptable even if operator is not equipped with work wear (arms, body and legs covered) and no protective gloves during mixing/loading and during application. However, it is recommended to wear workwear and protective gloves during mixing/loading and during application.**

#### 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)

#### Estimation of worker exposure

Table 6.6‑4 shows the exposure models used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with NIC-HER 060 OD according to the critical use. 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 | Maize (max. 1 x 0.7 L product/ha) |
| Models | **EFSA model AOEM** (Agricultural Operator Exposure 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: 30/03/2015]  **EUROPOEM II re-entry model** [Hemmen et al (2002) Post-application exposure of workers to pesticides in agriculture. Report of the re-entry working group. EUROPOEM II project. FAIR3 CT96-1406] |

Table 6.6‑5: Estimated worker exposure (long term exposure)

|  |  |  |  |
| --- | --- | --- | --- |
| Nicosulfuron | | | |
| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL |
| Cereals (maize)  Outdoor  Downward spraying  Vehicle-mounted  Inspection, irrigation  Work rate: 2 hours/day  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: NA | | | |
| **EFSA model AOEM** | | | |
| Number of applications and application rate | | 1 x 0.042 kg a.s./ha | |
| Body weight: 60 kg | Potential  TC: 12500 cm2/person/h | 0.0367500 | 4.59 |
| Work wear (arms, body and legs covered)  TC: 1400 cm2/person/h | 0.0041160 | 0.51 |
| Work wear (arms, body and legs covered) and gloves  TC: not available | - | - |
| **EUROPOEM II re-entry model** | | | |
| **Model data** | **Level of PPE** | **Total absorbed dose**  **(mg a.s./day)** | **% of systemic AOEL** |
| Body weight: 60 kg  TC: 0.15 m2/h | Without PPE | 0.247 | 1 |
| With PPE (gloves) | 0.049 | 0 |

**Conclusion**

**The results of the exposure estimations show that the use of NIC-HER 060 OD according to the list of intended uses presented in GAP Table, causes no health risk for the worker even if the workwear (arms, body and legs covered) and gloves are not used. The calculated exposure level to nicosulfuron is lower than the value of AOEL for this active substance.**

**Taking into account hygienic rules, it is recommended that a worker inspecting treated area was dressed properly (long trousers, long-sleeve shirt) and equipped with protective gloves. 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.**

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

Not required

#### 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.

### Resident and bystander exposure (KCP 7.2.2)

#### Estimation of resident and bystander exposure

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 used for estimation of resident and bystander exposure to nicosulfuron. 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 | Maize (max. 1 x 0.7 L product/ha) |
| Model | **EFSA model AOEM** (Agricultural Operator Exposure 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: 30/03/2015] |

Table 6.6‑7: Estimated resident exposure (longer term exposure)

|  |  |  |  |
| --- | --- | --- | --- |
| Nicosulfuron | | | |
| Model data | | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL |
| Cereals  Outdoor  Downward spraying  Vehicle-mounted  Buffer zone: 2-3 (m)  Drift reduction technology: no  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha  Interval between treatments: NA | | | |
| Number of applications and application rate | | 1 x 0.042 kg a.s./ha | |
| Resident child  Body weight: 10 kg | Drift (75th perc.) | 0.0039463 | 0.49 |
| Vapour (75th perc.) | 0.0010700 | 0.13 |
| Deposits (75th perc.) | 0.0004417 | 0.06 |
| Re-entry (75th perc.) | 0.0049613 | 0.62 |
| **Sum (mean)** | 0.0075225 | 0.94 |
| Resident adult  Body weight: 60 kg | Drift (75th perc.) | 0.0009446 | 0.12 |
| Vapour (75th perc.) | 0.0002300 | 0.03 |
| Deposits (75th perc.) | 0.0002003 | 0.03 |
| Re-entry (75th perc.) | 0.0027563 | 0.34 |
| **Sum (mean**) | 0.0030230 | 0.38 |

**Conclusion**

**The reference value acutely toxic active substance (RVAAS) for nicosulfuron is not allocated. Consequently, it is assumed that the estimation of bystander exposure is covered by the calculation of resident exposure towards this active substance.**

**All estimated values are below the systemic AOEL for nicosulfuron. It can be concluded that the incidental short-time exposure of bystander and resident (children and adult) to nicosulfuron contained in the formulation NIC-HER 060 OD causes no risk to human health if the product is used in accordance with the intended uses listed in the GAP Table.**

#### Measurement of resident and/or bystander exposure

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

### Combined exposure

Not relevant. The product contains only one active substance.

1. Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

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 |
| --- | --- | --- | --- | --- | --- |
| - | - | - | - | - | - |

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 Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
| - | - | - | - | - | - |

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 Company Report No.  Source (where different from company) GLP or GEP status 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 Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

1. Detailed evaluation of the studies relied upon
   1. Statement on bridging possibilities

Not relevant.

* 1. Acute oral toxicity (KCP 7.1.1)

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as Acute tox 4 (oral)** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

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

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as Acute tox 4 (dermal** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

* 1. Acute inhalation toxicity (KCP 7.1.3)

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as Acute tox 4 (inhalation)** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

* 1. Skin irritation (KCP 7.1.4)

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as skin irritation** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

* 1. Eye irritation (KCP 7.1.5)

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as eye irritation** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

* 1. Skin sensitisation (KCP 7.1.6)

|  |  |
| --- | --- |
| Comments of zRMS: | **These substances contained in the formulation are not classified as dangerous according to Regulation (EC) No. 1272/2008. Therefore NICORN GRANDE (NIC-HER 060 OD) is unclassified as skin sensitisation** |

No studies submitted with this application. Classification based on composition of the product.

According to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 *on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* classification of NIC-HER 060 OD for toxicological part was based on ingredients of the mixture (Additivity formula) and concentration limits. The CLP calculation method is an alternative method based on the concentration addition of all adverse substances in a mixture. The additivity approach is often accepted as a worst-case estimation of chemical interaction.

For more details, please refer to Part C.

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

Not relevant. No new/additional supplementary studies were submitted.

* 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)

No studies submitted with this application.

* 1. Other/Special Studies

No studies submitted with this application

1. Exposure calculations
   1. Operator exposure calculations (KCP 7.2.1.1)
      1. Calculations for nicosulfuron

Table A 1: Input parameters considered for the estimation of operator exposure

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Formulation type | OD | | Crop type | Cereals (maize) |
| Application rate (AR) | 0.042 | kg a.s./ha | Application method | Downward spraying |
| Area treated per day (A) | 50 | ha | Application equipment | Vehicle-mounted |
| Dermal absorption (DA) | 25 | % (concentr.) | Indoor/outdoor | Outdoor |
| 70 | % (dilution) | Closed cabin | No |
| Inhalation absorption (IA) | 100 | % | Drift reduction | No |
| Body weight (BW) | 60 | kg/person | Cultivation | Normal |
| AOEL | 0.8 | mg/kg bw/d | Water soluble bag | No |
| AAOEL | - | mg/kg bw/d | - | - |

Table A 2: Estimation of longer term operator exposure towards nicosulfuron according to EFSA guidance (AOEM EFSA model)

Without gloves





With gloves





* 1. Worker exposure calculations (KCP 7.2.3.1)
     1. Calculations for nicosulfuron

Table A 3: Input parameters considered for the estimation of worker exposure

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Intended use | maize, inspection/irrigation, outdoor | | Dislodgeable foliar residue (DFR) | 3 | µg/cm2/kg a.s./ha |
| Application rate (AR) | 0.042 | kg a.s./ha | Dermal absorption (DA) | 70 | % (worst case) |
| Number of applications (NA) | 1 |  | Inhalation absorption (IA) | 100 | % |
| Interval between applications | NR | days | Work rate per day (WR) | 2 | h/d |
| Half-life of active substance | 30 | days | TC dermal (potential) | 12500 | cm2/h |
| Multiple application factor (MAF) | NR |  | TC dermal (work wear) | 1400 | cm2/h |
| Body weight (BW) | 60 | kg/person | TC dermal (work wear, gloves) | NR | cm2/h |
| AOEL | 0.8 | mg/kg bw/d | Task specific factor inhalation | NR | ha/h x 10-3 |
| AAOEL | - | mg/kg bw/d | - | - | - |

Table A 4: Estimation of acute worker exposure towards active substance according to EFSA guidance (AOEL EFSA model)



Table A 5: Estimation of acute worker exposure towards active substance according to EFSA guidance (EUROPOEM II re-entry model)



* 1. Resident and bystander exposure calculations (KCP 7.2.2.1)
     1. Calculations for nicosulfuron

Table A 6: Input parameters considered for the estimation of longer term resident exposure



Table A 7: Estimation of longer term resident exposure towards nicosulfuron according to EFSA guidance (AOEM EFSA model)





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)

Not relevant.