|  |
| --- |
| REGISTRATION REPORT  Part B  Section 7  Metabolism and Residues  Detailed summary of the risk assessment |
| Product code: ADM.09250.H.1.A  Product name(s): **2,4-D 95 SP**  Chemical active substance:  2,4-dichlorophenoxy acetic acid 80.4% or 804 g/kg |
| Central zone  Zonal Rapporteur Member State: Poland |
| CORE ASSESSMENT  (authorization) |
| Applicant: XXXX  Sponsor: XXXX  Submission date: March 2023  Evaluation date: December 2023  MS Finalisation date: March 2024 |

Version history

|  |  |
| --- | --- |
| When | What |
| March 2023 | 1st applicant version |
| October 2023 | Initial RR |
|  |  |
|  |  |

Table of Contents

[7 Metabolism and residue data (KCA section 6) 5](#_Toc152593736)

[7.1 Summary and zRMS Conclusion 5](#_Toc152593737)

[7.1.1 Critical GAP(s) and overall conclusion 5](#_Toc152593738)

[7.1.2 Summary of the evaluation 8](#_Toc152593739)

[7.1.2.1 Summary for 2,4-D 8](#_Toc152593740)

[7.1.2.2 Summary for ADM.09250.H.1.A 9](#_Toc152593741)

[7.2 2,4-D (2,4-dichlorophenoxy acetic acid) 10](#_Toc152593742)

[7.2.1 Stability of Residues (KCA 6.1) 11](#_Toc152593743)

[7.2.1.1 Stability of residues during storage of samples 11](#_Toc152593744)

[7.2.1.2 Stability of residues in sample extracts (KCA 6.1) 12](#_Toc152593745)

[7.2.2 Nature of residues in plants, livestock and processed commodities 13](#_Toc152593746)

[7.2.2.1 Nature of residue in primary crops (KCA 6.2.1) 13](#_Toc152593747)

[7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1) 14](#_Toc152593748)

[7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1) 14](#_Toc152593749)

[7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1) 15](#_Toc152593750)

[7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5) 15](#_Toc152593751)

[7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1) 17](#_Toc152593752)

[7.2.3 Magnitude of residues in plants (KCA 6.3) 18](#_Toc152593753)

[7.2.3.1 Summary of European data and new data supporting the intended uses 18](#_Toc152593754)

[7.2.3.2 Conclusion on the magnitude of residues in plants 20](#_Toc152593755)

[7.2.4 Magnitude of residues in livestock 20](#_Toc152593756)

[7.2.4.1 Dietary burden calculation 20](#_Toc152593757)

[7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3) 21](#_Toc152593758)

[7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3) 24](#_Toc152593759)

[7.2.6 Magnitude of residues in representative succeeding crops 24](#_Toc152593760)

[7.2.7 Other / special studies (KCA 6.10, 6.10.1) 24](#_Toc152593761)

[7.2.8 Estimation of exposure through diet and other means (KCA 6.9) 25](#_Toc152593762)

[7.2.8.1 Input values for the consumer risk assessment 25](#_Toc152593763)

[7.2.8.2 Conclusion on consumer risk assessment 27](#_Toc152593764)

[7.3 Active substance 2 27](#_Toc152593765)

[7.4 Combined exposure and risk assessment 27](#_Toc152593766)

[7.5 References 28](#_Toc152593767)

[Appendix 1 Lists of data considered in support of the evaluation. 29](#_Toc152593768)

[Appendix 2 Detailed evaluation of the additional studies relied upon 33](#_Toc152593769)

[A 2.1 2,4-D 33](#_Toc152593770)

[A 2.1.1 Stability of residues 33](#_Toc152593771)

[A 2.1.2 Nature of residues in plants, livestock and processed commodities 33](#_Toc152593772)

[A 2.1.3 Magnitude of residues in plants 33](#_Toc152593773)

[A 2.1.4 Magnitude of residues in livestock 36](#_Toc152593774)

[A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) 36](#_Toc152593775)

[A 2.1.6 Magnitude of residues in representative succeeding crops 36](#_Toc152593776)

[A 2.1.7 Other/Special Studies 36](#_Toc152593777)

[Appendix 3 Pesticide Residue Intake Model (PRIMo) 37](#_Toc152593778)

[A 3.1 TMDI calculations 37](#_Toc152593779)

[A 3.2 IEDI calculations 38](#_Toc152593780)

[A 3.3 IESTI calculations - Raw commodities 39](#_Toc152593781)

[A 3.4 IESTI calculations - Processed commodities 40](#_Toc152593782)

Metabolism and residue data (KCA section 6)

## Summary and zRMS Conclusion

The applicant's dRR text was not rewritten by the zRMS. In the resulting RR all comments /corrections/add-ons were placed on the grey background

### Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation ADM.09250. H.1.A are presented in Table 7.1‑1. They have been selected from the individual GAPs in the Central EU for wheat (spring). A list of all intended uses within the Central EU is given in Part B, Section 0.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRL of 2 mg/kg for 2,4-D as laid down in Reg. (EU) 2022/1363 is not expected.

The chronic and the short-term intakes of 2,4-D residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, PL agrees with the authorization of the intended use.

According to available data, no specific mitigation measures should apply.

Data gaps

Noticed data gaps are: none

Table 7.1‑1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **1** | **2** | **3** | **4** | **5** | **6** | **7** | | **8** | | | | **9** | | | **10** | **11** |
| GAP number (see part B.0)\* | Crop and/  or situation \*\* | Zone | Product code | F, Fn, Fpn G, Gn, Gpn or I\*\*\* | Pests or  Group of pests  controlled | Formulation | | Application | | | | Application rate per treatment | | | PHI  (days) | Conclusion |
| Type | Conc.  of as | method  kind | growth  stage & season | number  min max | interval between applications (min) | g as/hL  min max | water L/ha  min max | g as/ha  min max |
| 1 | Spring wheat | CEU | ADM.09250.H.1.A | F | Broadleaf weeds, CENCY, VERPE, BRSNW, THLAR, CAPBP | SP | 804 g/kg | Broadcast foliar spray | BBCH  15-25 | 1 | (-) | 187.5 - 750 | 200 - 300 | 750 | N/A |  |

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

\*\* Use also code numbers according to Annex I of Regulation (EU) No 396/2005

\*\*\* 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

Explanation for Column 11 “Conclusion”

|  |  |
| --- | --- |
| A | Exposure acceptable without risk mitigation measures, safe use |
| R | Further refinement and/or risk mitigation measures required |
| N | Exposure not acceptable, no safe use |

**Revised Renewal report for the active substance 2,4-D**

**SANCO/11961/2014 Rev 5**

**6 October 2017**

**APPENDIX II**

**List of uses supported by available data**

**2,4-D**



### Summary of the evaluation

The preparation ADM.09250.H.1.A is composed of 2,4-D (2,4-dichlorophenoxy acetic acid).

Table 7.1‑2: Toxicological reference values for the dietary risk assessment of 2,4-D

| Reference value | Source | Year | Value | Study relied upon | Safety factor |
| --- | --- | --- | --- | --- | --- |
| 2,4-D - Parent compound | | | | | |
| ADI | EFSA | 2017 | 0.02 mg/kg bw/day | 2,4-DB 1-year study in dog, supported by the rat, 2-year and two-generation reproduction toxicity studies | 100 |
| ARfD | EFSA | 2017 | 0.3 mg/kg bw | 2,4-DB developmental toxicity in rats | 100 |
| In 2016, the toxicological profile of 2,4-DB was re-assessed and adopted. It was agreed that these lower toxicological reference values apply also to 2,4-D as the toxicological profile of 2,4-DB and 2,4-D is qualitatively similar. | | | | | |

#### Summary for 2,4-D

Table 7.1‑3: Summary for 2,4-D

| Use-No.\* | Crop | Plant metabolism covered? | Sufficient residue trials? | PHI sufficiently supported? | Sample sto­rage covered by stability data? | MRL compliance | Chronic risk for consumers identified? | Acute risk for consumers identified? |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1, 2 | Wheat (spring) | Yes | Yes (13) | Yes | Yes | Yes | No | No |

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

**EFSA Journal 2014;12(9):3812:**

Metabolism in plants was investigated in cereals (wheat) and root/tuber crops (potato) using foliar applications and in fruit crops (apple) following soil applications. The studies on apple and wheat were conducted with a total application rate of 4260 and 1680 g a.s./ha, respectively, but limited to a maximum of 560 g a.s./ha on potato, due to phototoxic effects. Studies by stem injection (maize, soya bean) or cell cultures (soya bean) provided additional information on the metabolism of 2,4-D in plants. It was concluded that the metabolic pathway is expected to be similar in all crop categories and the residue definition for monitoring and risk assessment was proposed as "*sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D”.*

The residue trials data are supported by storage stability studies, where 2,4-D residues were shown to be stable at least 18 months in high water-, high starch- and dry matrices, when stored at -18 °C, and at least 12 months in high oil matrices when stored at -23 °C to -27 °C. Considering the mean DT90 estimated to be less than 15 days, rotational crop studies were not provided and are not required. As residues in cereal grains were all below the LOQ, processing studies were not required.

Animal metabolism studies conducted on lactating goat and laying hens with exaggerated dose rates. The parent 2,4-D, free and conjugated, was identified as the major compound in milk (47 % TRR), eggs (23 % TRR), chicken liver, fat and kidney (18, 25 and 76 % TRR). Considering that 2,4-D conjugates were identified in animal matrices, the same residue definitions as for plant commodities were proposed for products of animal origin. MRLs for ruminant products were derived from a livestock feeding study conducted on lactating cow at four feeding levels, in the range of 53 to 312 mg/kg bw per day. Based on the low expected intakes estimated on the representative uses voluntarily limited to 750 g a.s./ha and excluding the uses on pasture, 2,4-DCP is not expected to be present in significant levels in ruminant matrices. No MRLs were proposed for poultry and pig products.

Based on the available information, the residue definition for monitoring and risk assessment was proposed as "sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D" for plant and animal products. MRLs were proposed for some cereal commodities and for ruminant products. Based on the available data, no chronic or acute concerns were identified for the consumers.

#### Summary for ADM.09250.H.1.A

Table 7.1‑4: Information on ADM.09250.H.1.A (KCA 6.8)

| Crop | PHI for ADM.09250.H.1.A  proposed by applicant | PHI/ Withholding period\* sufficiently supported for | PHI for ADM.09250.H.1.A proposed by zRMS | zRMS Comments  (if different PHI proposed) |
| --- | --- | --- | --- | --- |
| 2,4-D |
| Wheat (spring) | N/A | N/A | N /A | N/A |

NR: not relevant

\* Purpose of withholding period to be specified

\*\* F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

Assessment

## 2,4-D (2,4-dichlorophenoxy acetic acid)

General data on ~~2,4-dichlorophenoxy acetic acid~~ 2,4-D (2,4-dichlorophenoxy acetic acid) are summarized in the table below (last updated 2022/10/05)

Table 7.2‑1: General information on 2,4-D

|  |  |
| --- | --- |
| Active substance (ISO Common Name) | 2,4-D |
| IUPAC | (2,4-dichlorophenoxy)acetic acid |
| Chemical structure |  |
| Molecular formula | C8H6Cl2O3 |
| Molar mass | 221 g/mol |
| Chemical group | Phenoxy herbicide |
| Mode of action (if available) | Selective, systemic, absorbed through roots and increases biosynthesis and production of ethylene causing uncontrolled cell division and so damages vascular tissue. Synthetic auxin |
| Systemic | Yes |
| Company (ies) | XXXX\* |
| Rapporteur Member State (RMS) | Greece/Poland |
| Approval status | Approved (01/01/2016)  Commission Implementing Regulation (EU) 2015/2033  [EUR-Lex - 32015R2033 - EN - EUR-Lex (europa.eu)](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32015R2033) |
| Restriction | the restriction to uses as a herbicide |
| Review Report | SANCO/11961/2014 Rev 5 (6 October 2017) |
| Current MRL regulation | Reg. (EU) 2022/1363 (03 August 2022) |
| Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed | Yes |
| EFSA Journal : Conclusion on the peer review | Yes (EFSA, 2014 – see list of references) |
| EFSA Journal: Conclusion on article 12 | Yes (EFSA, 2011 – see list of references) |
| Current MRL applications on intended uses | None for intended uses |

\* Notifier in the EU process to whom the a.s. belong(s)

### Stability of Residues (KCA 6.1)

#### Stability of residues during storage of samples

**Available data**

No new data submitted in the framework of this application.

Table 7.2‑2: Summary of stability data achieved at ≤ ‑ 18°C (unless stated otherwise)

| Matrix | Characteristics of the matrix | Acceptable Maximum Storage duration | Reference |
| --- | --- | --- | --- |
| Data relied on in EU | | | |
| Plant products | | | |
| Sugarcane | High water content | 12 months | DAR (Greece, 1996) and further addenda |
| Grass | High water content |
| Wheat forage | High water content |
| Maize forage | High water content |
| Sorghum grain | High starch content |
| Wheat grain | High starch content |
| Rice | High starch content |
| Maize grain | High starch content |
| Soybean seed | High oil content |
| Cereal straw and hay | Dry matrices |
| Cereal greens | High water content | 18 months | RAR (Greece, 2013) |
| Cereal grain | High starch content |
| Cereal straw | Dry matrices |
| Animal Products | | | |
| Beef | Muscle | 4 months | DAR (Greece, 1996) and further addenda |
| Beef | Fat |
| Beef | Kidney |
| Beef | Liver |
| Beef | Milk |

**Conclusion on stability of residues during storage**

2,4-D residues were shown to be stable at least 18 months on cereal green plant, grain and straw, and 12 months in the following: corn (grain, forage and fodder), sorghum grain, wheat (grain, forage and straw), sugarcane, rice grain, rangeland grass (grass and hay), soybean seed and in the following processed fractions: corn (starch, flour and crude corn oil), wheat flour, sugarcane (sugar molasses and bagasse) and rice (bran and hulls), when stored at target -18 °C.

2,4-D residues were shown to be stable in beef muscle, fat, kidney, liver and milk when stored frozen for at least 4 months.

Sufficient stability has been demonstrated to support the residue data presented in the submission.

#### Stability of residues in sample extracts (KCA 6.1)

**Available data**

The stability of residues in sample extracts was shown as part of two magnitude of residue studies conducted in wheat (Report No. S10-02109) and maize (Report No. S10-02224) which were reviewed during the renewal of approval procedure.

The stability of 2,4-D acid in the specimen extracts of spring wheat (stored at 4°C for a period of 1 up to 12 days) was proved by the corresponding procedural recovery specimens which were stored under the same conditions together with the treated samples. Residues of 2,4-D in wheat extracts were found to be stable when stored at 4°C for up to 12 days.

The stability of 2,4-D in the field and processed specimen extracts of maize (stored at 4°C for a period of 1 up to 9 days) was proved by the corresponding procedural recovery specimens which were stored under the same conditions together with the treated samples. Residues of 2,4-D in maize extracts were found to be stable when stored at 4°C for up to 9 days.

In addition to these studies, acceptable batch concurrent recoveries, which were carried out in parallel with analysis of field samples, demonstrate stability of residues in sample extracts for the relevant periods of storage.

**Conclusion on stability of residues in sample extracts**

Sufficient stability has been demonstrated to support the residue data presented in the submission.

### Nature of residues in plants, livestock and processed commodities

#### Nature of residue in primary crops (KCA 6.2.1)

**Available data**

No new data submitted in the framework of this application. The metabolism of 2,4-D was investigated for foliar applications on cereals (wheat) and root and tuber vegetables (potato) and for soil treatment in fruits and fruiting vegetables (apple). Metabolism of 2,4-D was also investigated for local treatments by injection in plants or cell cultures of pulses and oilseeds (soybean), and cereals (maize).

Table 7.2‑3: Summary of plant metabolism studies

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Crop Group | Crop | Label position | Application and sampling details | | | | | Reference |
| Method,  F or G (a) | Rate  (kg a.s./ha) | No | Sampling (DAT) | Remarks |
| EU data | | | | | | | | |
| Fruits and fruiting vegetable | Apple | U-14C-phenyl labelled | Application around the trunk | 2.13 | 2 | 56 | - | DAR (Greece, 1996) and further addenda |
| Root and tuber vegetables | Potato | U-14C-phenyl labelled | Foliar | 0.07 | 2 | 82 | - |
| Potato | U-14C-phenyl labelled | Foliar | 0.14  0.28 | 2 | 29 | - |
| Pulses and oilseeds | Soybean | 1-14C-2,4-D | Injection, G | 21 µg/plant or callus | 1 | Plants: 14  Callus: 7 | - |
| Cereals | Wheat | U-14C-phenyl labelled | Foliar | 1.68 | 1 | 0, 10, 28, 49 | - |
| Wheat | Unlabelled | Foliar, F | 0.50 | 1 | 1, 2, 3, 5, 9, 19, 35 | - |
| Maize | 1-14C-2,4-D | Injection, G | 21 µg/plant or callus | 1 | Plants: 14 | - |

**Summary of plant metabolism studies reported in the EU**

Due to the low residue level at harvest (0.009 mg/kg), no identification of residues was attempted in apple.

In wheat forage and straw, most of the radioactive residues were extractable and identified as the parent 2,4-D (72 to 77% TRR), mostly as conjugated. In contrast, in grain, 2,4-D accounted for 6% TRR only and the majority of the residues (ca. 50% TRR) were associated with natural products (protein, starch and cellulose fractions). Other components were less than 9% TRR and identified as 2,4-DCP or as hydroxylated metabolites (4-OH-2,5-D; 4-OH-2,3-D; 5-OH-2,4-D).

2,4-D was also identified as the major component in potato tuber, up to 0.15 mg/kg, while 2,4-DCP amounted for less than 0.01 mg/kg. Stem injection and cell cultures conducted on maize and soybean confirmed that 2,4-D and hydroxylated metabolites, mainly as amino acid conjugates, are the major components of the residues in plants.

**Conclusion on metabolism in primary crops**

Based on these studies, it was concluded that the metabolic pathway is expected to be similar in all crop categories and the residue definition for monitoring and risk assessment was proposed as “*sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D*”.

#### Nature of residue in rotational crops (KCA 6.6.1)

**Available data**

No new data submitted in the framework of this application.

Spring wheat may be grown in rotation but, according to the soil degradation studies evaluated in the framework of the peer review, the DT90 value calculated of 2,4-D, was 24.8 days which is below the trigger value of 100 days (RAR, Vol. 3, Revised Annex B.7, 2014, Greece). Relevant soil metabolites were also not identified. Further investigation of residues in rotational crops is not required and relevant residues in this crop are not expected.

#### Nature of residues in processed commodities (KCA 6.5.1)

**Available data**

No new data submitted in the framework of this application. As residues in cereal grains were all expected to be below 0.01 mg/kg, processing studies to investigate the nature of the residues were not required. No further studies have been performed.

#### Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2‑6: Summary of the nature of residues in commodities of plant origin

|  |  |
| --- | --- |
| **Endpoints** | |
| Plant groups covered | Fruits and fruity vegetable  Root and tuber vegetables  Pulses and oilseeds  Cereals |
| Rotational crops covered | No |
| Metabolism in rotational crops similar to metabolism in primary crops? | It is assumed that they are similar |
| Processed commodities | Not required (residues of 2,4-D < 0.01 mg/kg) |
| Residue pattern in processed commodities similar to pattern in raw commodities? | It is assumed that they are similar |
| Plant residue definition for monitoring | sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D  Reg. (EU) 2022/1363 (03 August 2022) |
| Plant residue definition for risk assessment | sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D (EFSA, 2014) |
| Conversion factor from enforcement to RA | None |

#### Nature of residues in livestock (KCA 6.2.2-6.2.5)

**Available data**

No new data submitted in the framework of this application. The nature of 2,4-D residues in commodities of animal origin was investigated in the framework of Directive 91/414/EEC. Reported metabolism studies include one study in lactating goats and one in laying hens using 14C-phenyl ring labelled 2,4-D.

Table 7.2‑7: Summary of animal metabolism studies

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Group | Species | Label position | No of animal | Application details | | Sample details | | Reference |
| Rate  (mg/kg bw/d) | Duration  (days) | Commodity | Time of samp­ling |
| EU data | | | | | | | | |
| Lactating ruminants | Goat | U-14C-phenyl labelled | 1 | 24a | 3 | Milk | Daily | DAR (Greece, 1996) and further addenda |
| Urine and faeces | Daily |
| Tissues | After sacrifice |
| Laying poultry | Hen | U-14C-phenyl labelled | 15 | 1.4 b | 7 | Eggs | Daily | DAR (Greece, 1996) and further addenda |
| Excreta | Daily |
| Tissues | After sacrifice |

(a) Equivalent to 483 mg/kg in feed, (b) Equivalent to 18 mg/kg in feed

**Summary of animal metabolism studies reported in the EU**

In both goat and poultry, 2,4-D was extensively excreted in urine and faeces and less than 0.1% of the administered radioactivity was recovered in milk, eggs and tissues, resulting in TRRs below 0.2 mg/kg in all animal matrices, except in kidney (0.7 and 1.4 mg/kg, for poultry and goat, respectively). The parent 2,4-D, free and conjugated, was identified as the major compound in milk (47% TRR), eggs (23% TRR), chicken liver, fat and kidney (18, 25 and 76% TRR, respectively). In addition, 4-chlorophenoxyacetic acid was observed in milk (6.9% TRR) and 2,4-DCP in milk, eggs and chicken liver, up to 7.3% TRR.

The metabolic patterns identified for goats were consistent with rat metabolism and therefore considered applicable to pigs as well. Therefore, results from the metabolism study conducted with goats / ruminants can also be considered as applicable to pigs without the need to conduct a separate metabolism study in pigs.

**Conclusion on metabolism in livestock**

Considering that 2,4-D conjugates were identified in animal matrices, the same residue definitions for monitoring and risk assessment as for plant commodities were proposed for products of animal origin: “sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D”.

#### Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2‑8: Summary on the nature of residues in commodities of animal origin

|  |  |
| --- | --- |
|  | Endpoints |
| Animals covered | Lactating goats |
| Laying hens |
| Time needed to reach a plateau concentration | Within 28 days in milk |
| Within 28 days in eggs |
| Animal residue definition for monitoring | sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D  Reg. (EU) 2022/1363 (03 August 2022) |
| Animal residue definition for risk assessment | sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D (EFSA, 2014) |
| Conversion factor | None |
| Metabolism in rat and ruminant similar | Yes |
| Fat soluble residue | No (Log Pow: -0.9) |

### Magnitude of residues in plants (KCA 6.3)

#### Summary of European data and new data supporting the intended uses

~~No new data~~ 2 trials are submitted in the framework of this application. Below on grey are data from EFSA: EJ 2014;12(9):3812:



Table 7.2‑9: Summary of EU reported and new data supporting the intended uses of ADM.09250.H.1.A and conformity to existing MRL

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Commodity | Source | Residue zone (N-EU, S-EU, EU, outside EU) | Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition | STMR (mg/kg) | HR (mg/kg) | Unrounded OECD calculator MRL (mg/kg) | Current EU MRL  (mg/kg)  \* | MRL compliance |
| Wheat  (grain) | RAR (Greece, 2013) | N-EU | Cereals (wheat, barley and oats)  Trials GAPs: 1 x 720-1303 g/ha, BBCH 28-32, outdoor  Barley grain: <0.01, <0.02, 6x <0.05  Oat grain: <0.05  Wheat grain: <0.01, 5x <0.02, <0.04, 2x < 0.05, 2x < 0.05 (overdosed) | N/A | | | | |
| New – see Appendix 2, Spence, 2015 | N-EU | Trials GAP: 1 x 750 g as/ha, BBCH 32, outdoor  2 x <0.01 |
| Overall supporting data for cGAP | N-EU | 4 x <0.01, 6 x <0.02, <0.04, 11 x <0.05 | 0.045 | 0.05 | 0.05 | 2 | Yes |
| Wheat  (straw) | RAR (Greece, 2013) | N-EU | Cereals (wheat, barley and oats)  Trials GAPs: 1 x 720-1303 g/ha, BBCH 28-32, outdoor  Barley straw: <0.02, 5 x <0.05, <0.1, 0.19  Oat straw: <0.05  Wheat straw: 2 x <0.02, 2 x<0.05, 0.025, 0.06, 0.08, <0.1, 0.28, 0.65, 1.4 | N/A | | | | |
| New – see Appendix 2, Spence, 2015 | N-EU | Trials GAP: 1 x 750 g as/ha, BBCH 32, outdoor  0.538 – 1.48 |
| Overall supporting data for cGAP | N-EU | 3 x<0.02, 11 x <0.05, 0.025, 0.06, 0.08, 2 x <0.1, 0.19, 0.28, 0.538, 0.65, 1.4, 1.48 | 0.05 | 1.48 | 1.928 | - | - |

\* Reg. (EU) 2022/1363 (03 August 2022)

#### Conclusion on the magnitude of residues in plants

Wheat is a major crop in northern Europe (SANTE/2019/12752) and therefore, generally requires eight trials in the residue region where residues in the edible commodity are >LOQ.

The intended critical GAP for ADM.09250.H.1.A is 1 x 750 g as/ha, at BBCH 15-25 which is less critical than the GAP used to confirm the MRL in wheat (EFSA, 2011), which was 1 x 1250 g as/ha, at BBCH 30-31. A total of 20 trials conducted on range of cereals (wheat, barley and oat) at an exaggerated rate ( 1 x 720 - 1303 g as/ha, at BBCH 28-32) were submitted for wheat during the renewal process (Greece, 2014). According to SANTE/2019/12752, extrapolation from other cereals is considered possible because the application was performed before forming the edible part. Additionally, two new trials conducted at 1 x 750 g as/ha, BBCH 32 are also available. These trials are in the 25% tolerance rule and could be used to support the cGAP.

Considering these trials, the data provided to support the use of ADM.09250.H.1.A on spring wheat are sufficient. These trials can be used to support the intended GAP. Therefore, sufficient trials are available to support the proposed use on spring wheat grain. The available submitted data show that no exceedance of the MRL will occur. The use is considered acceptable.

### Magnitude of residues in livestock

#### Dietary burden calculation

The use of ADM.09250.H.1.A may result in residues of 2,4-D in animal feed items. Indeed, wheat straw and grain may be fed to livestock. Therefore, the possible transfer of residues in animal commodities from the proposed uses should be considered.

New animal dietary burden calculations are deemed necessary, the values reported in the peer review of the risk assessment of 2,4-D (EFSA, 2014) were used to calculate the animal dietary burdens using the EFSA animal model 2017. All input values, livestock in-take calculations and feeding studies undertaken are provided below.

The input values for all relevant commodities have been selected according to the recommendations of JMPR (FAO, 2009). Under the generic name of cereals, wheat, barley, oat and rye were considered. As a worst case, residues in wheat grain and straw from trials with a latest application timing were taken into account to derive STMR and HR for animal burden calculations. For cereal bran, default processing factors of 7 has been included in the calculation in order to consider potential concentration of residues in these commodities. For apple pomace, no default processing factor was applied because 2,4-D is applied early in the growing season and residues are expected to be below the LOQ.

Table 7.2‑8: Input values for the dietary burden calculation

| Feed Commodity | Median dietary burden | | Maximum dietary burden | |
| --- | --- | --- | --- | --- |
| Input value (mg/kg) | Comment | Input value (mg/kg) | Comment |
| Risk assessment residue definition: sum of 2,4-D, its salts, esters and conjugates expressed as 2,4-D | | | | |
| Maize forage | 0.02 | STMR (EFSA, 2014) | 0.76 | HR (EFSA, 2014) |
| Apple pomace | 0.01 | STMR (EFSA, 2011) | 0.01 | STMR (EFSA, 2011) |
| Cereal grain | 0.05 | STMR (EFSA, 2014) | 0.05 | STMR (EFSA, 2014) |
| Maize grain | 0.035 | STMR (EFSA, 2014) | 0.05 | STMR (EFSA, 2014) |
| Cereal bran | 0.40 | STMR x 7 (EFSA, 2014) | 0.40 | STMR x 7 (EFSA, 2014) |
| Cereal straw | 0.05\* | STMR | 1.48\* | HR |

\* Input values (STMR and HR) from residue studies presented in this document.

The results of the calculations are reported in Table 7.2‑9. The calculated dietary burdens for cattle, dairy sheep, lamb, swine and poultry were found to exceed the trigger value of 0.004 mg/kg bw/d. Further investigation of residues is therefore required in these groups of livestock.

Table 7.2‑9: Results of the dietary burden calculation

| Animal species | Median  dietary burden (mg/kg bw/d) | Maximum dietary burden  (mg/kg bw/d) | Highest contributing commodity | Max dietary burden (mg/kg DM) | Trigger exceeded (Y/N) |
| --- | --- | --- | --- | --- | --- |
| Risk assessment residue definition: sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D | | | | | |
| Beef cattle\* | 0.004 | 0.038 | Corn forage/silage | 1.60 | Y |
| Dairy cattle\* | 0.006 | 0.049 | Corn forage/silage | 1.27 | Y |
| Ram/ewe | 0.006 | 0.039 | Barley straw | 1.16 | Y |
| Lamb | 0.010 | 0.049 | Barley straw | 1.16 | Y |
| Breeding swine | 0.005 | 0.014 | Corn forage/silage | 0.60 | Y |
| Finishing swine\* | 0.007 | 0.007 | Corn forage/silage | 0.23 | Y |
| Broiler poultry | 0.008 | 0.008 | Corn forage/silage | 0.12 | Y |
| Layer poultry\* | 0.009 | 0.021 | Corn forage/silage | 0.31 | Y |
| Turkey | 0.008 | 0.008 | Corn forage/silage | 0.12 | Y |

\* These categories correspond to those (formerly) assessed at EU level.

#### Livestock feeding studies (KCA 6.4.1-6.4.3)

Reference EFSA, 2011

“During the peer review of Directive 91/414/EEC the magnitude of 2,4-D residues in livestock was investigated in a feeding study on lactating cows (Greece, 2000). Four groups of lactating cows, each consisting of three animals, were dosed for 28 days with 2,4-D at levels of 52, 105, 210 and 312 mg a.s./kg bw/d. Results of the livestock feeding study for the three lowest doses are summarized in Table 3-6.

Residues of 2,4-D were detected in most milk and tissues samples analysed. The highest relative residue level of the various cattle matrices analysed was found in kidney, followed by liver, fat muscle and milk. The magnitude of residues was generally found to be dose-dependent.

The storage stability of 2,4-D in animal products was evaluated under the peer review of Directive 91/414/EEC (Greece, 2000). Studies demonstrated storage stability of 2,4-D in milk and beef tissues for up to 4 months when stored deep frozen. Samples of the livestock feeding study were stored less than 1 month according to the RMS; degradation of residues during storage of the samples is therefore not expected”.

The metabolic patterns identified for goats and hens were consistent with the rat metabolism and therefore considered applicable to pigs as well. Therefore, results from the ruminant / lactating dairy cattle feeding study can be considered representative for pigs without a separate feeding study being conducted in pigs.

A feeding study in poultry was not previously required. However, a metabolism study on laying hens was previously evaluated (Reference). According to this study in poultry, where three groups of hens, each consisting of five animals, were dosed for 7 days with 2,4-D at levels of 1.4 mg a.s./kg bw/d corresponding to 66N rate based on current estimated dietary intakes, 2,4-D was extensively excreted in urine and faeces and less than 0.1% of the administered radioactivity was recovered in eggs and tissues. . Results of the metabolism study are summarised in Table 3-6. This metabolism study is considered sufficient to assess and quantify the possible transfer of 2,4-D in animal tissues and eggs.

Table 7.2‑12: Overview of feeding studies

| Commodity | Dietary burden | | Results of the livestock feeding study | | | | | | Median residue  (mg/kg) | Highest residue  (mg/kg) | Calculated MRL  (mg/kg) | ****Establi-shed MRL (mg/kg)(d)**** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Med. (mg/kg bw/d) | Max. (mg/kg bw/d) | Dose Level (mg/kg bw/d) | No | Result for enforcement | | Result for RA | |
| Mean (mg/kg) | Max. (mg/kg) | Mean (mg/kg) | Max. (mg/kg) |
| **EU reviewed data** | | | | | | | | | | | | |
| Enforcement residue definition : 2,4-DB and its conjugates, expressed as 2,4-DB  Risk assessment residue definition : 2,4-DB, its conjugates and 2,4-dichlorophenol,expressed as 2,4-DB | | | | | | | | | | | | |
| **Pig meat (a)** | 0.005 | 0.014 | 52.58 | 3 | 0.21 | 0.24 | 0.21 | 0.24 | 0.05 | 0.05 | 0.05\* | 0.2 |
| 105.10 | 3 | 0.41 | 0.51 | 0.41 | 0.51 |
| 210.10 | 3 | 0.76 | 1.10 | 0.76 | 0.76 |
| **Pig fat (a)** | 52.58 | 3 | 0.42 | 0.51 | 0.42 | 0.51 | 0.05 | 0.05 | 0.05\* | 0.2 |
| 105.10 | 3 | 0.59 | 0.75 | 0.59 | 0.75 |
| 210.10 | 3 | 2.50 | 3.60 | 2.50 | 2.50 |
| **Pig liver (a)** | 52.58 | 3 | 0.12 | 0.20 | 0.23 | 0.39 | 0.05 | 0.05 | 0.05\* | 5 |
| 105.10 | 3 | 1.90 | 2.40 | 3.69 | 4.66 |
| 210.10 | 3 | 3.00 | 3.50 | 5.82 | 11.29 |
| **Pig kidney (a)** | 52.58 | 3 | 3.80 | 6.50 | 10.91 | 18.66 | 0.05 | 0.097 | 0.1 (d) | 5 |
| 105.10 | 3 | 14 | 18 | 40.18 | 51.66 |
| 210.10 | 3 | 17 | 29 | 48.79 | 140.03 |
| **Ruminant meat** | 0.006 | 0.049 | 52.58 | 3 | 0.21 | 0.24 | 0.21 | 0.24 | 0.05 | 0.05 | 0.05\* | 0.2 |
| 105.10 | 3 | 0.41 | 0.51 | 0.41 | 0.51 |
| 210.10 | 3 | 0.76 | 1.10 | 0.76 | 0.76 |
| **Ruminant fat** | 52.58 | 3 | 0.42 | 0.51 | 0.42 | 0.51 | 0.050 | 0.054 | 0.1 | 0.2 |
| 105.10 | 3 | 0.59 | 0.75 | 0.59 | 0.75 |
| 210.10 | 3 | 2.50 | 3.60 | 2.50 | 2.50 |
| **Ruminant liver** | 52.58 | 3 | 0.12 | 0.20 | 0.23 | 0.39 | 0.050 | 0.050 | 0.05\* | 5 |
| 105.10 | 3 | 1.90 | 2.40 | 3.69 | 4.66 |
| 210.10 | 3 | 3.00 | 3.50 | 5.82 | 11.29 |
| **Ruminant kidney** | 52.58 | 3 | 3.80 | 6.50 | 10.91 | 18.66 | 0.195 | 0.689 | 1 | 5 |
| 105.10 | 3 | 14 | 18 | 40.18 | 51.66 |
| 210.10 | 3 | 17 | 29 | 48.79 | 140.03 |
| **Poultry muscle** | 0.009 | 0.021 | 1.4 | 15 | 0.006 | 0.08 | 0.006 | 0.08 | 0.01 | 0.01 | 0.01\* | 0.05 |
| **Poultry fat** | 1.4 | 15 | 0.028 | 0.032 | 0.028 | 0.032 | 0.01 | 0.01 | 0.01\* | 0.05 |
| **Poultry liver** | 1.4 | 15 | 0.030 | 0.046 | 0.030 | 0.046 | 0.01 | 0.01 | 0.01\* | 0.05 |
| **Milk** | 0.006 | 0.049 | 52.58 | 3 | 0.04(b) | 0.07(b) | 0.04(b) | 0.07(b) | 0.010 | 0.010 | 0.01\* | 0.01\* |
| 105.10 | 3 | 0.12(c) | 0.18(c) | 0.12(c) | 0.18(c) |
| 210.10 | 3 | 0.29(c) | 0.59(c) | 0.29(c) | 0.59(c) |
| **Eggs** | 0.009 | 0.021 | 1.4 | 15 | 0.02 | 0.018 | 0.02 | 0.018 | 0.01 | 0.01 | 0.01\* | 0.05 |

n.a.: Not analysed,

(\*): Indicates that the MRL is set at the limit of analytical quantification.

(a): The feeding studies were carried out with ruminants, according to the metabolism pathway, an extrapolation between ruminant and pig is acceptable.

(b) Mean residue level from day 7 until day 28 (3 cows, 7 sampling days).

(c) Mean residue level from day 1 until day 28 (3 cows, 9 sampling days).

(d) Established MRL in Regulation (EU) 2022/1363.

Summary of livestock feeding studies

Reference EFSA, 2011

“Based on the available livestock feeding study, MRLs and risk assessment values in ruminant and pig products were calculated in compliance with the latest international recommendations on this matter (FAO, 2009). The feeding doses were exaggerated, and it can be concluded that significant residues in edible matrices of ruminants and pigs are not expected except in ruminant fat and kidney as well as pig kidney. It is therefore concluded that MRLs for these commodities can be established at the LOQ, except for ruminant fat, ruminant kidney and pig kidney where higher MRLs are proposed.”

Based on the residue levels in edible tissues in the poultry metabolism study, inputs for risk assessment and MRL determination in poultry products were calculated. The dose rate was exaggerated (estimated 66N) based on current anticipated dietary burden, and it can be concluded that residues of 2,4-D in edible matrices of poultry are not expected. At a realistic estimation of dietary intake, it is extremely unlikely that there would be an exceedance of the current MRL (Regulation (EU) 2022/1363).

### Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

No new data submitted in the framework of this application. As residues in cereal grains were all below 0.1 mg/kg, processing studies to investigate the magnitude of the residues were not required. No further studies have been performed.

### Magnitude of residues in representative succeeding crops

No new data submitted in the framework of this application.

Spring wheat may be grown in rotation but, according to the soil degradation studies evaluated in the framework of the peer review, the DT90 value calculated of 2,4-D, was 24.8 days which is below the trigger value of 100 days (RAR, Vol. 3, Revised Annex B.7, 2014, Greece). Relevant soil metabolites were also not identified. Further investigation of residues in rotational crops is not required and relevant residues in this crop are not expected.

### Other / special studies (KCA 6.10, 6.10.1)

According to SANTE/11956/2016 rev. 9 (Commission Services, 2018), wheat (spring) is not considered melliferous. Therefore, as the production of honey directly from the target crop is not possible, any residues of 2,4-D which would come directly from the treated crop cannot be transferred to honey.

After soil preparation for sowing spring wheat, any broadleaf flowering weeds are generally mechanically or chemically removed. The time between soil preparation and the application of ADM.09250.H.1.A on spring cereal can be estimated in central Europe at approximately 1.5 months. In this time, spring wheat will reach a growth stage between BBCH 15 and BBCH 25. Any new broadleaf weeds, which will develop in the field would be closer to a rosette stage (BBCH 30-39). 2,4-D will avoid the development of these pests. They would not reach the flowering growth stage; therefore, residues of 2,4-D are not expected in nectar or honey coming directly from any broadleaf weeds present in the field.   
Additionally, although the active substance is systemic, it is not considered to be persistent, therefore residues of 2,4-D are not expected in nectar or honey coming directly from any broadleaf weeds present in the field.

The typical period of ADM.09250.H.1.A application would be between March and early May so theoretically some adjacent melliferous crops to fields may be flowering at the time of application although this is considered to be early for the principal melliferous crops such as oilseed rape in central Europe. Furthermore, by following good agricultural practice, the application of herbicides is directed towards the ground and also limiting the edges of the fields as much as possible by the use of buffer zones. So it can be concluded that significant spray drift to the adjacent crop is very limited. The potential for any transfer of residues of 2,4-D to honey after applications to spring wheat could be considered as negligible.

The intended uses of ADM.09250.H.1.A on spring wheat can be approved without specific data to address this point as no unacceptable risks for consumption of honey are expected and the default MRL in honey of 0.05 mg/kg can be applied.

### Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population (EFSA, 2018).

#### Input values for the consumer risk assessment

The input values used for the chronic TMDI risk assessments are the current EU MRLs contained in Reg. (EU) 2022/1363 (03 August 2022). All crop and animal commodities with a specified MRL were considered in the risk assessments with no refinements. As TMDI was above 100%, IEDI chronic risk assessment is necessary. The input values used for the IEDI chronic risk assessments are the current EU MRLs contained in Reg. (EU) 2022/1363 (03 August 2022), and all data relevant to the consumer exposure assessment collected from JMPR evaluations in order to include the CXLs in the calculations. The STMR and HR from wheat residue studies presented in this document were less critical than the one used in the Art 12 (EFSA, 2011) review. All inputs for the IEDI assessment are detailed in Table 7.2-15.

All MRLs for 2,4-D are based on the residue definition for monitoring/enforcement of sum of 2,4-D, its salts, esters and conjugates, expressed as 2,4-D, which is also the residue definition for risk assessment. CXLs for 2,4-D have been established for 2,4-D only. Nevertheless, according to EFSA (2011), the difference in residues definition proposed by JMPR and EFSA is not expected to impact on the outcome of the risk assessment. Indeed, although not explicitly mentioned in the residue definitions, CXLs for 2,4-D also include all salts, esters and conjugates and analytical methods reported by JMPR hydrolyse esters, conjugates and salts of 2,4-D into the acid form. No conversion factor is required to account for the residue definitions and no processing factors are required.

Table 7.2‑15: Input values for the consumer risk assessment

| Commodity | Chronic risk assessment | | Acute risk assessment | |
| --- | --- | --- | --- | --- |
| Input value (mg/kg) | Comment | Input value (mg/kg) | Comment |
| IEDI Risk assessment residue definition 2,4-D (sum of 2,4-D, its salts, its esters and its conjugates, expressed as 2,4-D) | | | | |
| Citrus fruits whole group | 0.31 | STMR (CXL) | - | - |
| Tree nuts, except chestnuts | 0.05 | STMR (CXL) | - | - |
| Chestnuts | 0.05 | STMR (CXL) | - | - |
| Pome fruits whole group | 0.01 | STMR (<LOQ) | - | - |
| Stone fruits whole group | 0.01 | STMR (<LOQ) | - | - |
| Berries and small fruits | 0.05 | STMR (CXL) | - | - |
| Potatoes | 0.05 | STMR (CXL) | - | - |
| Sweet corn | 0.05 | STMR (CXL) | - | - |
| Asparagus | 0.05 | STMR (=LOQ) | - | - |
| Soya bean | 0.05\* | (Reg. (EU) 2022/1363) | - | - |
| Barley | 0.22\*\* | STMR (CXL) | 1.40\*\* | HR (CXL) |
| Buckwheat | 0.05\* | (Reg. (EU) 2022/1363) | - | - |
| Maize/Corn | 0.05 | STMR (=LOQ) | - | - |
| Common millet/proso millet | 0.05 | STMR (=LOQ) | - | - |
| Oat | 0.22\*\* | STMR (CXL) | 1.40\*\* | HR (CXL) |
| Rice | 0.01 | STMR (CXL) |  |  |
| Rye | 0.22\*\* | STMR (CXL) | 1.40\*\* | HR (CXL) |
| Sorghum | 0.05 | STMR (=LOQ) | - | - |
| Wheat | 0.22 | STMR (CXL) | 1.40 | HR (CXL) |
| Sugar cane | 0.01 | STMR (<LOQ) | - | - |
| Swine muscle | 0.13 | STMR (CXL) | - | - |
| Swine fat | 0.13 | STMR (CXL) | - | - |
| Swine liver | 2.75 | STMR (CXL) | - | - |
| Swine kidney | 2.75 | STMR (CXL) | - | - |
| Ruminant meat | 0.13 | STMR (CXL) | - | - |
| Ruminant fat | 0.13 | STMR (CXL) | - | - |
| Ruminant liver | 2.75 | STMR (CXL) | - | - |
| Ruminant kidney | 2.75 | STMR (CXL) | - | - |
| Poultry meat | 0.05 | STMR (CXL) | - | - |
| Poultry fat | 0.01 | STMR (CXL) | - | - |
| Poultry liver | 0.01 | STMR (CXL) | - | - |
| Milk | 0.01 | STMR (=LOQ) | - | - |
| Bird eggs | 0.01 | STMR (CXL) | - | - |
| \* corresponding to LOQ value  \*\* according to SANTE/2019/12752, extrapolation from wheat data as a worst case scenario | | | | |

#### Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.2‑16: Consumer risk assessment

|  |  |
| --- | --- |
| TMDI (% ADI) according to EFSA PRIMo 3.1 | 114% (based on DK child) |
| IEDI (% ADI) according to EFSA PRIMo 3.1 | 31 % (based on NL toddler) |
| IESTI RAC (% ARfD) according to EFSA PRIMo 3.1 | Wheat: 1 % (based on UK 4-6 years)  Rye: 0.5 % (based on UK infant)  Barley: 0.4 % (based on UK 7-10 years) |
| IESTI Processed (% ARfD) according to EFSA PRIMo 3.1 | Wheat /milling (flour): 0.9 % (based on DE child)  Wheat /milling (wholemeal): 0.4 % (based on NL child)  Rye/boiled: 0.3 % (based on NL child) |

The proposed uses of 2,4-D in the formulation ADM.09250.H.1.A do not represent unacceptable acute and chronic risks for the consumer.

## Active substance 2

Not relevant. The product contains only one active substance.

## Combined exposure and risk assessment

Not relevant. The product contains only one active substance.

## References

|  |
| --- |
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| Greece, 2000. Addendum to the draft assessment report on the active substance 2,4-DB prepared by the rapporteur Member State Greece in the framework of Council Directive 91/414/EEC, October 2000. |
| Greece, 2002. Addendum to the draft assessment report on the active substance 2,4-DB prepared by the rapporteur Member State Greece in the framework of Council Directive 91/414/EEC, April 2002. |
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| 2,4-DB: |
| EFSA (European Food Safety Authority), 2016. Peer review of the pesticide risk assessment of the active substance 2,4-DB. 13 May 2016, j.efsa.2016.4500. |

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 |
| --- | --- | --- | --- | --- | --- |
| KCA 6.3/01 | Spence, C. | 2015  2016 | Residues of 2,4-D DMA in spring wheat following a single application of LAF-74 – Northern and Southern European zones – 2014.  Charles River, Tranent, Edinburgh, EH33 2NE, UK; Report No. 36122, DAS Study ID 140657.  XXXX Report No. 90019777  GLP: yes  Unpublished  Residues of 2,4-D DMA in spring wheat following a single application of LAF-74 – Northern and Southern European zones – 2014.  Charles River, Tranent, Edinburgh, EH33 2NE, UK; Report No. 36122, DAS Study ID 140657.  XXXX Report No. 90019777 – report amendment 1  GLP: yes  Unpublished | N | EU 2,4-D Task Force |

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 |
| --- | --- | --- | --- | --- | --- |
| KCA 6.1 | Barker, W. | 1995 | Determination of Frozen Storage Stability for 2.4-Dichlorophenoxy Acetic Acid (2,4-D) in/on Crops" Report/file No EN-CAS Project # 93-0044  GLP  Not published | N | EU 2,4-D Task Force |
| KCA 6.1 | Krautter, G.R.  &  Downs, J.H. W. | 1996 | 2,4-D: Magnitude of Residue in Meat and Milk of Lactating Dairy Cows Report No.: PTRL Project # 886  GLP  Not published | N | EU 2,4-D Task Force |
| KCA 6.1 | Rawle, N. W. | 2002 | Storage Stability of Residues of 2,4-DCP, 2,4-D, 2,4-DB and 2,4-DP-p in Cereal Whole Plant, Grain and Straw  Report No. CEMR-1397 (AHM R 99 142)  GLP  Not published | N | EU 2,4-D Task Force |
| KCA 6.2.1 | Puvanesarajah, V. | 1992a | Metabolism of 14C-ring labelled (2,4-Dichlorophenoxy)acetic acid, 2-ethylhexyl ester in Wheat, ABC Laboratories, Report No. 38076  GLP  Not published | N | EU 2,4-D Task Force |
| KCA 6.2.1 | Puvanesarajah, V. | 1992b | Supplemental data for the study: Metabolism of uniformly 14C-ring labelled (2,4-Dichlorophenoxy) acetic acid, 2-ethylhexyl ester in Wheat, ABC Laboratories, Report No. 38076-01  GLP  Not published | N | EU 2,4-D Task Force |
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| KCA 6.2.1 | Smith, G.A. | 1991 | Metabolism of 14C-(2,4-Dichloro phenoxy)acetic acid, Dimethyl amine salt in Apples, ABC Laboratories, Report No. 38072  GLP  Not published | N | EU 2,4-D Task Force |
| KCA 6.2.2 | Puvanesarajah, V.  & Bliss | 1992 & 2001 | Metabolism of Uniformly Ring Labeled [14C] 2,4-Dichloro phenoxyacetic Acid in Poultry ABC Laboratories Report 38077  GLP  Not published | Y | EU 2,4-D Task Force |
| KCA 6.2.3 | *Anonymous* | 1993  & 19941 | Metabolism of Uniformly 14C-ring Labeled 2,4-Dichlorophenoxyacetic acid in Lactating Goats, ABC Laboratories Report 40630  and supplementary report Supplemental Data for the Study, Metabolism of Uniformly 14C-ring Labeled 2,4-  Report 40630-01  GLP  Not published  1see Barnekow et.al published in J. Agric. Food Chem. 2001, 49, 156 – 163 | Y | EU 2,4-D Task Force |
| KCA 6.3.1 | Róẑalski, K. | 2009 | Residues of 2,4-D and Dicamba after one application of Aminopielik D 450 SL applied at two dose rates in spring barley and wheat, Poland 2008  GAB Poland Sp. z.o.o.  S08-02158  GLP  Unpublished | N | EU 2,4-D Task Force |
| KCA 6.3.1 | Zmijowska, A. | 2008  2010 | Aminopielik D 450 SL. Determination of residues of 2,4-D and Dicamba in grain, straw and soil  Institute of Industrial Organic Chemistry  C/09/08  GLP  Unpublished  Amendment No 1 to the final report Aminopielik D 450 SL. Determination of residues of 2,4-D and Dicamba in grain, straw and soil  Institute of Industrial Organic Chemistry  C/09/08  GLP  Unpublished | N | EU 2,4-D Task Force |
| KCA 6.3.1 | Róẑalski, K. | 2008a | Residues of 2,4-D and Dicamba after one application of Aminipielik D 450 SL in spring barley, one site in Poland 2007  GAB Poland Sp. z.o.o.  20074502/PL1-FPSH  GLP  Unpublished | N | EU 2,4-D Task Force |
| KCA 6.3.1 | Róẑalski, K. | 2008b | Residues of 2,4-D, Dicamba and Mecoprop after one application of Aminipielik Tercet 500 SL in winter wheat, one site in Poland 2007  GAB Poland Sp. z.o.o.  20074503/PL1-FPSH  GLP  Unpublished | N | EU 2,4-D Task Force |
| KCA 6.3.1 | Klimmek S., Tanguy M. | 2011 | Determination of residues of 2,4-D in spring wheat after one application of 2,4-D DMA 600 g/L and 2,4-D 2EHE 600 g/L at 4 sites in Northern Europe in 2010.  Eurofins Agroscience Services Chem GmbH, 21079 Hamburg, Germany; Report No. S10-02109.  XXXX Report No. 90018697  GLP: yes  Unpublished | N | EU 2,4-D Task Force |

1. Detailed evaluation of the additional studies relied upon
   1. 2,4-D
      1. Stability of residues

No new data submitted.

* + 1. Nature of residues in plants, livestock and processed commodities

No new data submitted.

* + 1. Magnitude of residues in plants
       1. Spring wheat

Table A 19: Comparison of intended and critical EU GAPs

| Type of GAP | Number of applications | Application rate per treatment  (precise unit) | Interval between application | Growth stage at last application | PHI (days) |
| --- | --- | --- | --- | --- | --- |
| cGAP N-EU (Art. 12, EFSA, 2011) | 1 | 1250 g a.s./ha | - | BBCH 30-31 | - |
| cGAP N-EU (Greece, 2014) | 1 | 750 g a.s./ha | - | BBCH 21-32 | - |
| Intended cGAP (1\*) | 1 | 750 g a.s./ha | - | BBCH 15-25 | - |

\* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0

* + - * 1. Study 1 - 36122

|  |  |
| --- | --- |
| Comments of zRMS: | The study has been accepted.  The target application rate of 750 g as/ha of 2,4-D was applied. The analysis with MS detection was used (transitions 218.9 →160.9 m/z and 221.0 →162.9 m/z). The average recovery at the 0.10 mg/kg level exceeded protocol acceptance criteria of 70-110% however this deviation is considered to have no significant impact on the integrity of the study. |

|  |  |
| --- | --- |
| Reference: | KCA 6.3/01 |
| Report | Residues of 2,4-D DMA in spring wheat following a single application of LAF-74 – Northern and Southern European zones – 2014. Spence C., 2015; Report No. 36122, DAS Study ID 140657 |
| Guideline(s): | Yes  OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).  General recommendation for the design, preparation and realisation of residue trials (7029/VI/95 rev. 5) |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

**Materials and methods**

**Field phase:**

In the growing season of 2014, 2,4-D DMA 600 (SL formulation, containing 600 g/L 2,4-D) was applied to spring wheat at two test sites in Northern Europe (Northern France, and the UK) under practical field conditions. At each site, one magnitude of residue trial was carried out one treated plots and an untreated control plot. 2,4-D DMA 600 was applied once at a rate of ca. 1.25 L/ha, corresponding to 750 g of a.s./ha. The application rates are within the allowed range of 25% deviation of the critical annual load. The application was performed at BBCH stage 32. Samples of wheat grain and straw were collected from the untreated and treated plots by hand at harvest (63-83 DAA). In the decline trials, additional whole plant samples were taken at 0, 7 (±1), 14, and 21 days after the application (DAA). The specimens were stored deep-frozen until analysis. Detailed summaries of relevant weather parameters are included in the original report.

**Analytical phase**:

2,4-D residues were quantified following the method 698838.01, which is based on Dow AgroSciences Analytical Method 130886. This method determines 2,4-D as free acid, including its salts, esters and conjugates. Residues of 2,4-D were extracted from wheat (whole plant, grain and straw) samples by homogenizing and by shaking with methanol/1.0 N sodium hydroxide (90:10). An aliquot is removed and acidified using 0.2M hydrochloric acid. The acidified aliquot is then cleaned up using a Strata-X polymeric sorbent reversed phase SPE cartridge (30mg,1 mL). Once the sample is eluted it is then diluted using 13C6-2,4-D stable isotope internal standard solution prior to LC-MS/MS analysis. The quantification was performed by liquid chromatography with tandem mass spectrometry detection (LC-MS/MS). The limit of quantification (LOQ) was 0.01 mg/kg.

**Results and discussion**

The method for 2,4-D was validated in wheat (whole plant, grain and straw) within this study. To confirm the validity of results during analysis, procedural recovery was performed on each matrix at the LOQ (0.01 mg/kg). Additionally, fortifications were performed at 0.1 mg/kg and 50 mg/kg in whole plant, 0.1 mg/kg in grain, 0.1 mg/kg and 5.0 mg/kg in straw. Mean recoveries were in the intended range of 70-110 % (91 to 105 %) with RSD below 20% (4 to 5%).

In addition to immature wheat whole plant, grain and straw taken from treated and untreated field plots at commercial harvest (BBCH 89) were analysed for residues of 2,4-D as free acid, including its salts, esters and conjugates. No residues of 2,4-D were found above the respective limit of quantification (LOQ), i.e., 0.01 mg/kg in any wheat grain specimens.

A summary of relevant trial data is provided in **Table A 2**.

**Conclusion:**

In two trials conducted in Northern Europe, no residues of 2,4-D were found above the respective limit of quantification (LOQ), 0.01 mg/kg. The application rates are within the critical GAP for the uses of ADM.09250.H.1.A on spring wheat in Northern Zone.

Table A 2: Summary of the study 1 trials

| Trial No./  Location/  EU zone/  Year | Commodity/ Variety | Date of  1.Sowing or planting  2.Flowering  3. Harvest | Application rate per treatment | | | Dates of treatment or no. of treatments and last date | Growth stage at last treatment or date | Portion analysed | Residues (mg/kg) | PHI (days) | Details on trial |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| g a.s./ ha | Water (L/ha) | g a.s./hL | aminopyralid |
|  | (a) | (b) |  |  |  | (c) |  |  |  | (d) | (e) |
| Trial: 698822 A  North Yorkshire, YO17 6QA, UK  Northern Europe  2014 | Spring Wheat /  Mulika | 1. 18/03/2014  2. -  3. 04/09/2014 | 754 | 301 | 250 | 13/06/2014 | BBCH 32 | Whole plant | 15.7 | 0 | LOQ = 0.01 mg/kg  Max. storage (sampling to analyse): 269 days |
| Whole plant | 7.84 | 7 |
| Whole plant | 5.38 | 14 |
| Whole plant | 4.85 | 21 |
| Grain | <0.01 | 83 |
| Straw | 1.48(f)  (1.54, 1.54, 1.69, 1.24, 1.41) | 83 |
| 698822 C  Nord-Pas de Calais, 59500, France  Northern Europe  2014 | Spring Wheat /  Lennox | 1. 08/04/2014  2. -  3. 19/08/2014 | 778 | 311 | 250 | 02/06/2014 | BBCH 32 | Grain | <0.01 | 78 |
| Straw | 0.0613 | 78 |

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

(f) Sample re-extracted in duplicate to confirm result. In addition the spare sample was also extracted in duplicate. The average of all five values is reported (1.48 mg/kg).

* + 1. Magnitude of residues in livestock

No new data submitted.

* + 1. Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No new data submitted.

* + 1. Magnitude of residues in representative succeeding crops

No new data submitted.

* + 1. Other/Special Studies

No new data submitted.

1. Pesticide Residue Intake Model (PRIMo)
   1. TMDI calculations



* 1. IEDI calculations



* 1. IESTI calculations - Raw commodities



* 1. IESTI calculations - Processed commodities

