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| FINAL REGISTRATION REPORT  Part B  Section 5  Analytical Methods  Detailed summary of the risk assessment |
| Product code: 054-01-05  Product name(s): MESO-IODO OD-LIFE  Chemical active substances:  Mesosulfuron-methyl, 10 g/L  Iodosulfuron-methyl-sodium, 2 g/L  Safener: Mefenpyr-diethyl, 30 g/L |
| Central Zone  Zonal Rapporteur Member State: Poland  Concerned Member State: Germany |
| CORE ASSESSMENT  (Application) |
| Applicant: Life Scientific Ltd  Submission date: Q1 2023  Update: November 2023; April 2024  Finalisation date: November 2023; April 2024 |

Version history

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| --- | --- |
| When | What |
| Q1 2023 | Submission date |
| November 2023 | Following a request by IOS the applicant has provided a full dRR part B5. In addition to the full dRR, the applicant has submitted an updated bridging validation report including precision and recovery data for iodosulfuron, report number VAL-18-035-Rev 2, (Ilie, N. 2023). |
| November 2023 | zRMS assessment |
| April 2024 | At the request of the zRMS the applicant has updated the dRR to include a description of methods for the analysis of active ingredient in body fluids and tissues. |
| April 2024 | Final Report after commenting period |

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# Analytical methods

This application is being submitted to register the product Meso-Iodo OD-Life (containing 10 g/L mesosulfuron-methyl, 2 g/L iodosulfuron-methyl-sodium and 30 g/L mefenpyr-diethyl OD) in the central zone according to Article 34 of Regulation (EC) No. 1107/2009. It is requested that Poland act as zRMS for this application. As the applicant also intends to register the product in Germany, they have been listed as the ‘concerned’ Member State (cMS). Meso-Iodo OD-Life will be referred to as product 054-01-05 for the remainder of this document.

Product 054-01-05 is a professional use herbicide formulated as an oil dispersion containing 10 g/L mesosulfuron-methyl, 2 g/L iodosulfuron-methyl-sodium and 30 g/L mefenpyr-diethyl. The product has not previously been evaluated in Poland according to Uniform Principles.

As part of this application, Life Scientific Ltd. wishes to have the proposed formulation assessed for comparability to the Polish reference product Atlantis 12 OD (10 g/L mesosulfuron-methyl, 2 g/L iodosulfuron-methyl-sodium and 30 g/L mefenpyr-diethyl, OD, authorisation number R-98/2009) of Bayer AG. The applicant considers product 054-01-05 to be comparable, if not identical to Atlantis 12 OD (full details of the composition can be found in the dRR Part C). The uses and claims for which approval is being sought are the same as those already approved for Atlantis 12 OD. Consequently, the applicant requests that the zRMS refers to the analytical method data presented in the renewal of Atlantis 12 OD in order to support the authorisation of 054-01-05. At the request of the zRMS, the applicant has provided the underlying data out of protection from the re-registration report of Atlantis 12 OD (authorisation number R-98/2009) in order to present a full dRR. As new data is being submitted in this application relating to the toxicity of 054-01-05 to bees, the details of the methods supporting these studies have been included. Additionally, methods used to determine the active substance content in the formulation have also been included in this dRR Part B5.

## Conclusion and summary of assessment

State whether submitted data are sufficient for evaluation. There are no data gaps.

Sufficiently sensitive and selective analytical methods are available for the active substances in the plant protection product.

Sufficiently sensitive and selective analytical methods are available for all analytes included in the residue definitions.

There are no data gaps outstanding relating to analytical methods.

It is considered that all commodities under consideration are supported.

NOTE: The data protection for Atlantis 12 OD should be confirmed by the relevant authority at national level before registration.

| Commodity/crop | Supported/ Not supported |
| --- | --- |
| Cereals | Supported |

## Methods used for the generation of pre-authorization data (KCP 5.1)

### Analysis of the plant protection product (KCP 5.1.1)

#### Determination of active substance and/or variant in the plant protection product (KCP 5.1.1)

An overview of the acceptable methods and possible data gaps for analysis of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in the plant protection product 054-01-05 (10 g/L mesosulfuron-methyl, 2 g/L iodosulfuron-methyl-sodium and 30 g/L mefenpyr-diethyl OD) is provided below.

An analytical method was originally developed for quantitative determination of these active substances in a similar formulation (054-02-01; mesosulfuron/iodosulfuron/mefenpyr 7.5/7.5/22.5 g/L OD, VAL-17-017-Rev1). In order to show that this method is also suitable for determination of active substance content in 054-01-05 (mesosulfuron/iodosulfuron/mefenpyr 10/2/30 g/L OD), a bridging method, VAL-18-035-Rev2 was developed and validated. Since method precision and accuracy were already established in VAL-17-017-Rev1, it can be safely inferred that the method will also be precise and accurate for product 054-01-05, provided that there is no interference from matrix components in the product i.e. specificity/non-analyte interference (NAI). Nevertheless, accuracy and precision were presented for iodosulfuron in VAL-18-035-Rev2.

Furthermore, in VAL-17-017-Rev2 linearity was established for all three analytes. The linear range established for mesosulfuron and mefenpyr is sufficient for product 054-01-05. Report VAL-18-035-Rev2 includes the linearity results for iodosulfuron to demonstrate that a suitable range was encompassed for all analytes.

Therefore, to assess active content in 054-01-05, two reports are presented below. VAL-17-017-Rev1 and VAL-18-035-Rev2.

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| Comments of zRMS: | Analytical method HPLC - UV for determination of active substances: mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in plant protection product MESO-IODO OD-LIFE has been validated and meet criteria of specificity, linearity, precision and accuracy according to the requirement SANCO 3030/99 rev. 5. Method is considered acceptable. |

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| Reference: | KCP 5.1.1/01 |
| Report | Validation of a HPLC method for the quantitative determination of mesosulfuron methyl, iodosulfuron methyl sodium and mefenpyr diethyl in mesosulfuron/iodosulfuron/mefenpyr 7.5/7.5/22 g/L OD. Cooney, G. 2017. VAL-17-017-Rev1 |
| Guideline(s): | Yes, SANCO/3030/99 rev.5, 22/03/2019 |
| Deviations: | No |
| GLP: | No |
| Acceptability: | Yes |

Materials and methods

The objective of this study was to validate a HPLC-UV analytical method for the quantitative determination of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in product 054-02-01 (mesosulfuron-methyl/iodosulfuron-methyl-sodium/mefenpyr-diethyl 7.5/7.5/22 g/L OD). Validation was performed according to SANCO/3030/99 rev.5, 22 March 2019.

Stock standard preparations of mesosulfuron-methyl and iodosulfuron-methyl-sodium (0.75 mg/mL) were prepared by weighing approximately 20 mg of reference standard into a 25 mL volumetric flask. This was dissolved in and made to volume with diluent (100:900 v/v pH 9 borate buffer: acetonitrile).

Working standard preparations of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl (0.075, 0.075, 0.22 mg/mL) were prepared in duplicate by weighing approximately 22 mg of mefenpyr-diethyl reference standard into a 100 mL volumetric flask. 10 mL of each stock standard solution (mesosulfuron-methyl, iodosulfuron-methyl-sodium) were added to the 100 mL volumetric flask containing 22 mg of mefenpyr-diethyl. The contents were dissolved in and made up to volume with diluent.

Samples (10 mg/mL) were prepared by weighing approximately 500 mg of product 054-02-01 into a 50 mL volumetric flask. This was made up to volume with diluent. Prior to analysis samples were filtered through 0.45 µm filters.

The active substances were analysed by HPLC with UV detection.

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| **HPLC details:** |

**Results**

Refer to Table 5.2‑1.

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| Reference: | KCP 5.1.1/02 |
| Report | Bridging validation of a HPLC method for the quantitative determination of mesosulfuron methyl, iodosulfuron methyl sodium and mefenpyr diethyl in mesosulfuron/iodosulfuron/mefenpyr 10/2/30 g/L OD. Ilie, N. 2023. VAL-18-035-Rev 2. |
| Guideline(s): | Yes, SANCO/3030/99 rev.5, 22/03/2019 |
| Deviations: | No |
| GLP: | No |
| Acceptability: | Yes |

Materials and methods

The objective of this study was to demonstrate that the analytical method developed for the quantitative determination of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in product 054-02-01 is also fit for purpose for analysis of product 054-01-05. Validation was performed according to SANCO/3030/99 rev.5, 22 March 2019.

Stock standard preparations of mesosulfuron-methyl (1 mg/mL) were prepared by weighing approximately 20 mg of reference standard into a 20 mL volumetric flask. This was dissolved in approximately 10 mL of diluent (100:900 *v/v* pH 9 borate buffer: acetonitrile) and made to volume with diluent following sonification.

Stock standard preparations of iodosulfuron-methyl-sodium (0.2 mg/mL) were prepared by weighing approximately 10 mg of reference standard into a 50 mL volumetric flask. This was dissolved in approximately 25 mL of diluent (100:900 *v/v* pH 9 borate buffer: acetonitrile) and made to volume with diluent following sonification.

A working standard preparation of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl (0.1, 0.02, 0.3 mg/mL) was prepared by weighing approximately 30 mg of mefenpyr-diethyl reference standard into a 100 mL volumetric flask. Using a pipette, 10 mL of each stock standard solution (mesosulfuron-methyl, iodosulfuron-methyl-sodium) was added to the 100 mL volumetric flask. The flask was sonicated until the mixture was dissolved and made up to volume with diluent (100:900 v/v pH 9 borate buffer: acetonitrile).

Samples (10 mg/mL) were prepared in duplicate by weighing approximately 500 mg of product 054-01-05 into a 50 mL volumetric flask. This was made up to volume with diluent. Prior to analysis samples were filtered through 0.45 µm filters.

The active substances were analysed by HPLC with UV detection.

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| **HPLC details:** |

**Results**

Refer to Table 5.2‑1.

Validation - Results and discussions

Table 5.2‑1: Methods suitable for the determination of active substances mesosulfuron, iodosulfuron and mefenpyr in plant protection product 054-01-05 (mesosulfuron/iodosulfuron/mefenpyr 10/2/30 g/L OD)

|  | Mesosulfuron  validation  (054-02-01) | Mesosulfuron  bridging validation  (054-01-05) | Iodosulfuron  validation  (054-02-01) | Iodosulfuron  bridging validation  (054-01-05) | Mefenpyr  validation  (054-02-01) | Mefenpyr  bridging validation  (054-01-05) |
| --- | --- | --- | --- | --- | --- | --- |
| Author(s), year | Cooney, G. 2017 | Ilie, N. 2023 | Cooney, G. 2017 | Ilie, N. 2023 | Cooney, G. 2017 | Ilie, N. 2023 |
| Principle of method | HPLC-UV | HPLC-UV | HPLC-UV | HPLC-UV | HPLC-UV | HPLC-UV |
| Linearity  (linear between  mg/L / % range of the declared content)  (correlation coefficient, expressed as r) | Linear over a range of 0.049783 mg/mL to 0.124458 mg/mL  (5.0-12.5 g/L of product)  ~~66% to 166% of the nominal sample concentration~~  n = 5  y=24456911x+13672  r = 1.0000 | Since linearity has already been established for mesosulfuron-methyl in (Cooney, G. 2017), this will also be linear over a suitable range for 054-01-05. | Linear over a range of 0.049967 mg/mL to 0.124918 mg/mL  (5.0-12.5 g/L of product)  ~~67% to 167% of the nominal sample concentration~~  n = 5  y=33087387x+8619  r = 1.0000 | Linear over a range of 0.010146 mg/ml to 0.030438 mg/mL. (1.0 – 3.0 g/L of product) ~~50.7-152.2% of the nominal sample concentration.~~  n = 5  y=29843963x+7989  r = 0.9999 | Linear over a range of 0.149115 mg/mL to 0.372789 mg/mL.  (15.3-38.8 g/L of product) ~~68% to 169% of the nominal sample concentration~~  n = 5  y=7326680x+7441  r = 1.0000 | Since linearity has already been established for mefenpyr-diethyl in (Cooney, G. 2017), this will also be linear over a suitable range for 054-01-05. |
| Precision  n = xx  Mean content  (Hr ≤ 1) | Precision measured over 5 replicates.  0.745% w/w (7.4 g/L)  n = 5  %RSD = 1.60  %RSDr (Horwitz) = 2.80  Hr = 0.57 | Since precision has already been established for 054-02-01 (Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. | Precision measured over 5 replicates.  0.752% w/w (7.5 g/L)  n = 5  %RSD = 1.49  %RSDr (Horwitz) = 2.80  Hr = 0.53 | Precision measured over 6 replicates.  0.19% w/w (1.9 g/L)  n = 6  %RSD = 0.6  %RSDr (Horwitz) = 3.4  Hr = 0.176 | Precision measured over 5 replicates.  2.227% w/w (22.3 g/L)  n = 5  %RSD = 1.48  %RSDr (Horwitz) = 2.38  Hr = 0.62 | Since precision has already been established for 054-02-01 (Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. |
| Recovery  Level  n = xx (% Recovery)  Total recovery (blank matrix fortified) | Fortification level = 7.5 g/L  Mean % Recovery = 102% (n=2) | Since recovery has already been established for 054-02-01(Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. | Fortification level = 7.5 g/L  Mean % recovery = 101% (n=2) | Fortification level = 2.0 g/L  Mean % recovery = 101% (n=2) | Fortification level = 22.4 g/L  Mean % recovery = 101% (n=2) | Since recovery has already been established for 054-02-01 (Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. |
| Interference/ Specificity | No significant interference was detected. | Since specificity has already been established for 054-02-01 (Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. | No significant interference was detected. | No significant interference was detected. | No significant interference was detected. | Since specificity has already been established for 054-02-01 (Cooney, G. 2017), it can be inferred that 054-01-05 will also comply with precision requirements. |

Conclusion

The method for the determination of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in 054-02-01 was found to be valid. A bridging method was developed which shows that there is no interference from the matrix components in 054-01-05, meaning that it can be safely inferred that the method is precise and accurate for 054-01-05. VAL-18-035-Rev2 also includes linearity results for iodosulfuron-methyl-sodium in 054-01-05 in order to demonstrate that the method is also valid for this formulation.

#### Description of analytical methods for the determination of relevant impurities (KCP 5.1.1)

Not applicable as the preparation does not contain relevant impurities which are formed during manufacturing or storage of the product (see dRR Part C).

#### Description of analytical methods for the determination of formulants (KCP 5.1.1)

With respect to toxicological, eco-toxicological or environmental aspects the product 054-01-05 does not contain any relevant formulants. Therefore, a special analytical method and validation is not needed.

#### Applicability of existing CIPAC methods (KCP 5.1.1)

Not applicable, as no CIPAC method currently exist for the determination of actives in the plant protection product (OD).

### Methods for the determination of residues (KCP 5.1.2)

**Iodosulfuron-methyl-sodium**

An overview on the acceptable methods and possible data gaps for analysis of residues of iodosulfuron-methyl-sodium for the generation of pre-authorization data is given in the following tables. For the detailed evaluation of new studies relating to the toxicity of 054-01-05 to bees, please refer to Appendix 2.

All other data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

Table 5.2‑2: Validated methods for the generation of pre-authorization data

| Component of residue definition: iodosulfuron-methyl-sodium | | | | |
| --- | --- | --- | --- | --- |
| Matrix type | Method type | Method LOQ | Principle of method  (i.e. GC-MS or HPLC-UV) | Author(s), year / missing / EU agreed |
| Wheat grain (Residues) | Primary  Method  AL008/96-0 | 0.01 mg/kg | HPLC-UV | Wrede A., 1997; [M-141767-02-1](dart://dart/edition?ed_no=M-141767-02-1)  DAR, Germany, 2000;  EU agreed |
| Amendment  Method  AL008/96-0 | 0.01 mg/kg | HPLC-UV | Wrede A., 1998;  [M-141767-02-1](dart://dart/edition?ed_no=M-141767-02-1)  DAR, Germany, 2000;  EU agreed |
| Confirmatory  Method  AL008/96-0 | 0.01 mg/kg | HPLC-UV | Wrede A., 1998;  [M-182662-01-1](dart://dart/edition?ed_no=M-182662-01-1)  DAR, Germany, 2000;  EU agreed |
| ILV  Method  AL008/96-0 | 0.01 mg/kg | HPLC-UV | Taylor N., 1998;  [M-181323-02-1](dart://dart/edition?ed_no=M-181323-02-1)  DAR, Germany, 2000;  EU agreed |
| Wheat straw (residues) | Primary  Method  AL121/96-0 | 0.05 mg/kg | HPLC-UV | Wrede A., 1997;  [M-143342-01-1](dart://dart/edition?ed_no=M-143342-01-1)  DAR, Germany, 2000;  EU agreed |
| Wheat shoot (residues) | Primary  Method  AL120/96-0 | 0.05 mg/kg | HPLC-UV | Wrede A., 1997;  [M-142974-01-1](dart://dart/edition?ed_no=M-142974-01-1)  DAR, Germany, 2000;  EU agreed |
| Wheat shoot and  straw (Residues) | Radiovalidation of  methods AL120/96-0  (shoot) and  AL121/96-0 (straw) | 0.05 mg/kg | HPLC-UV | Wrede A., 1998;  [M-182685-01-1](dart://dart/edition?ed_no=M-182685-01-1)  DAR, Germany, 2000  EU agreed |
| Cereal grain  Cereal shoot  Cereal straw | Primary  Method EM  F08/99 renamed  00815 | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg | LC-MS/MS | Wrede A., 2000;  [M-194528-01-1](dart://dart/edition?ed_no=M-194528-01-1)  DAR, Germany, 2000;  EU agreed |
| Cereal grain Cereal shoot  Cereal straw | Validation  Method EM F08/99-0 | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg | LC-MS/MS | Wrede A., 2000; [M-194531-01-1](dart://dart/edition?ed_no=M-194531-01-1)  DAR, Germany, 2000; EU agreed |
| Lemon  Tomato  Maize kernel | Validation of EM  Method  F08/99-0 | 0.01 mg/kg 0.01 mg/kg  0.01 mg/kg | LC-MS/MS | Wrede A., 2002;  [M-212674-01-1](dart://dart/edition?ed_no=M-212674-01-1)  RAR, Sweden, 2015;  EU agreed |
| Wheat grain | ILV  Method EM  F08/99-0 | 0.01 mg/kg | LC-MS/MS | Anspach T., 2001;  [M-200884-01-1](dart://dart/edition?ed_no=M-200884-01-1)  RAR, Sweden, 2015;  EU agreed |
| Tomato  Citrus | ILV  Method EM  F08/99-0 | 0.01 mg/kg | LC-MS/MS | Reichert N., Klimmek S., 2002;  [M-215456-01-1](dart://dart/edition?ed_no=M-215456-01-1)  RAR, Sweden, 2015;  EU agreed |
| Cereal grain  Cereal shoot  Cereal straw Flax (grain, pomace,wet, oil) Flax | Primary  Method  00815/M001  (modification of  EM F08/99-0) | 0.01 mg/kg 0.05 mg/kg 0.05 mg/kg  0.01 mg/kg    0.05 mg/kg | LC-MS/MS | Heinemann, O., 2004;  [M-226888-01-1](dart://dart/edition?ed_no=M-226888-01-1)  RAR Dec.2015  EU agreed |
| Wheat grain Wheat green material Wheat straw  Rape seed | Primary method 01376/M002 | 0.01 mg/kg | LC-MS/MS  (2 MRM transitions validated) | Kaussmann M.; 2017,  [M-587949-01-1](dart://dart/edition?ed_no=M-587949-01-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Wheat grain Wheat green material Wheat straw  Barley grain Barley green material Barley straw | Primary method 01514 | 0.01 mg/kg (metabolites: AE  F059411 and AE  0031838) | LC-MS/MS  (2MRM transitions validated) | Kaussmann M., 2017  [M-583894-01-1](dart://dart/edition?ed_no=M-583894-01-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Soil  (Environmental fate) | Primary  Method 01115 | 0.01 mg/kg | HPLC-MS/MS | Freitag T., Wolters A., 2013; Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Primary  Report  BY98R004 | 0.0005 ppm | HPLC-MSD GC-NPD | Norris F., 2000;  [M-238505-01-1;](dart://dart/edition?ed_no=M-238505-01-1)  Appendix 2 |
| Water  (Environmental fate) | Primary  Method 01387 | Iodosulfuronmethyl-sodium: 0.05 µg/L Metsulfuronmethyl:  0.05 µg/L | HPLC-MS/MS | Krebber R., Braune M., 2013;  (refer to post authorisation for summary) |
| ILV  Method 01387 | Iodosulfuronmethyl-sodium: 0.05 µg/L Metsulfuronmethyl: 0.05 µg/L | DI-HPLC-MS/MS | Stanislowski, 2013;  Previously reviewed during Atlantis OD 12 re-registration (R-98/2009) |
| Sediment  (Environmental fate) | Primary  Method 01115 | 0.01 mg/kg | HPLC-MS/MS | Freitag T., Wolters A., 2013;  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Primary  Report  BY98R004 | 0.0005 ppm | HPLC-MSD GC-NPD | Norris, F., 2000;  [M-238505-01-1;](dart://dart/edition?ed_no=M-238505-01-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Soil, water,... (Efficacy) | Not relevant | | | |
| Air  (Exposure) | Primary  Report  RESID/98/27 | 1.05 µg/m3 | GC-ECD | Everitt, S. L., 1998;  [M-181311-03-1](dart://dart/edition?ed_no=M-181311-03-1)  Monograph (22 May 2000);  EU agreed |
| Soil  (Ecotoxicology) | Primary  Report IF100/21283-00 | 1.6 µg/m3 | LC-UV | Reichert, N., 2000, ammended by  Zietz, E., 2009;  [M-199299-02-1](dart://dart/edition?ed_no=M-199299-02-1)  Addendum to Monograph (18  June 2001);  EU agreed |
| Primary  Method 01115 | 0.01 mg/kg | HPLC-MS/MS | Freitag T., Wolters A., 2013;  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Water  (Ecotoxicology) | Primary  Method 01387 | Iodosulfuronmethyl-sodium: 0.05 µg/L Metsulfuronmethyl: 0.05 µg/L | HPLC-MS/MS | Krebber R., Braune M., 2013;  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| ILV  Method 01387 | Iodosulfuronmethyl-sodium: 0.05 µg/L Metsulfuronmethyl: 0.05 µg/L | DI-HPLC-MS/MS | Stanislowski, 2013;  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009) |
| Bee  (acute and oral) | Primary | 2 mg/kg (sucrose)  20 μg/ml (triton X-100) | HPLC-UV (DAD) | Wilkins, S., 2020a  New study, see appendix 2 |
| Bee  (chronic) | Primary | 2 mg/kg (sucrose)  20 μg/ml (triton X-100) | HPLC-UV (DAD) | Wilkins, S., 2020b  New study, see appendix 2 |
| Bee  (larvae) | Primary | Method M1 (analyte in stock solutions):  2 mg/kg (sucrose)  20 μg/ml (triton X-100)  Method M2 (feed in the larval study):  0.2014 mg kg | HPLC-UV (DAD)  and  HPLC-MS/MS | Wilkins, S., 2020c  New study, see appendix 2 |

**Mesosulfuron-methyl**

An overview on the acceptable methods and possible data gaps for analysis of residues of mesosulfuron-methyl for the generation of pre-authorization data is given in the following table. All data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.2‑3: Validated methods for the generation of pre-authorization data**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Component of residue definition: mesosulfuron-methyl** | | | | | | | |
| **Matrix type** | **Method type / Method No** | | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | | | **Author(s), year / missing / EU agreed** |
| Wheat grain  Wheat straw  Wheat shoot  (Residues) | Primary  DGM F02/99-0 | | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg | LC-MS/MS | | | Wrede, A., 1999,  M-191437-01-1  DAR Dec.2001  EU agreed |
| Cereal grain  Cereal shoot  Cereal straw | Primary  EM F08/99 re-named 00815 | | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg | LC-MS/MS | | | Wrede, A., 2000,  M-194528-01-1  RAR Dec.2015  EU agreed |
| Cereal grain  Cereal shoot  Cereal straw | Validation of EM F08/99-0  renamed 00815 | | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg | LC-MS/MS | | | Wrede, A., 2000,  M-194531-01-1  RAR Dec.2015  EU agreed |
| Lemon  Tomato  Maize kernel | Validation of EM F08/99-0  renamed 00815 | | 0.01 mg/kg | LC-MS/MS | | | Wrede, A., 2002,  M-212674-01 -1  RAR Dec.2015  EU agreed |
| Wheat grain | ILV of EM F08/99-0  renamed 00815 | | 0.01 mg/kg | LC-MS/MS | | | Reichert, N., 2000,  M-198857-01-1  RAR Dec.2015  EU agreed |
| Tomato  Citrus | ILV of EM F08/99-0  renamed 00815 | | 0.01 mg/kg | LC-MS/MS | | | Reichert, N., Klimmek, S.;2002;  M-215456-01-1  RAR Dec.2015  EU agreed |
| Cereal grain  Cereal shoot  Cereal straw  Flax (grain, pomace,wet, oil)  Flax (plant without root) | Primary  Method 00815/M001 (modification of EM F08/99-0) | | 0.01 mg/kg  0.05 mg/kg  0.05 mg/kg  0.01 mg/kg  0.05 mg/kg | LC-MS/MS | | | Heinemann, O., 2004;  M-226888-01-1  RAR Dec.2015  EU agreed |
| Cereal green  material,  Cereal grain,  Cereal straw | Primary  Method 00815/M001 Additional validation in the residue study  13-2127 | | 0.05 mg/kg  0.01 mg/kg  0.05 mg/kg | LC-MS/MS | | | Stuke, S., 2017 M-503498-03-1  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 |
| Primary  Method 00815/M001 **Additional validation in the residue study**  13-2129 | | 0.05 mg/kg  0.01 mg/kg  0.05 mg/kg | LC-MS/MS | | | Freitag T., Wolters A., 2013;  M-310074-03-1 RAR, France, 2015;  EU agreed |
| Soil, water,...  (Efficacy) | Not relevant | | | | | | |
| Air  (Exposure) | Primary | 12 μg/m3 | | | LC-UV | Reichert, N., 2000, ammended by Zietz, E., 2009;  M-198860-01-1  Addendum to Monograph (18 June 2001);  EU agreed | |
| Water (Ecotoxicology) | Primary  Method 01542  M-602768-01-1 | BCS-CV14885  0.05 μg/L | | | HPLC-MS/MS | Krebber, R.; Ruttmann, F.; 2017  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009 | |
| Water (Ecotoxicology) | Primary  Method 01387 | 0.05 μg/L | | | HPLC-MS/MS | Krebber R., Braune M., 2013;  M-466732-01-1  RAR, France, 2015;  EU agreed | |

**Mefenpyr-diethyl (safener)**

An overview on the acceptable methods and possible data gaps for analysis of residues of mefenpyr-diethyl for the generation of pre-authorization data is given in the following tables. Mefenpyr-diethyl has not yet been assessed at EU level, however a Draft Assessment Report has been prepared by Austria and France in 2011 and is available to all Member States. Only data from studies considered valid are reported.

**Table 5.2-4: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892) and metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid (AE F094270) expressed as Mefenpyr-diethyl** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Crops (grain) (Residues) | Primary/Confirmatory | 0.01 mg/kg | LC-MS/MS | Jooss, 2010  (Mefenpyr-diethyl DAR Addendum 1) |
| Crops (green material)  (Residues) | Primary/Confirmatory | 0.01 mg/kg | LC-MS/MS | Jooss, 2010  (Mefenpyr-diethyl DAR Addendum 1) |
| Crops (wheat straw)  (Residues) | Primary/Confirmatory | **-** | GC-MSD | Neuss and Losse, 1999  (Mefenpyr-diethyl DAR) |
| Crops (cereal grain)  (Residues) | Primary/Confirmatory | 0.01 mg/kg | HPLC-MS/MS | Preu and Philipowski, 2004  (Mefenpyr-diethyl DAR) |
| Crops (wheat grain)  (Residues) | Primary/Confirmatory | 0.01 mg/kg | LC-MS/MS | Richter and Class, 2005  (Mefenpyr-diethyl DAR) |

**Table 5.2-5: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892) and metabolite 1-(2,4-dichlorophenyl)-5-ethoxycarbonyl-5-methyl-2-pyrazoline-3-carboxylic acid (AE F113225) expressed as Mefenpyr-diethyl** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Food of animal origin (fat, milk, meat, kidney and liver)  (Residues) | Primary/Confirmatory | 0.01 mg/kg | HPLC-MS/MS | Zimmer and Stucke, 2007  (Mefenpyr-diethyl DAR) |
| Food of animal origin (fat, milk, meat, kidney and liver)  (Residues) | Primary/Confirmatory | 0.01 mg/kg | HPLC-MS/MS | Rzepka and Rotzoll (2007)  (Mefenpyr-diethyl DAR) |

**Table 5.2-6: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892)** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Soil  (Environmental fate) | Primary/Confirmatory | 5 µg/kg | HPLC-MS/MS | Brumhard and Schneider, 2007  (Mefenpyr-diethyl DAR) |

**Table 5.2-7: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892) and its metabolite 1-(2,4-dichlorophenyl)-5-ethoxycarbonyl-5-methyl-2-pyrazoline-3-carboxylic acid (AE F113225)** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Surface water  (Environmental fate) | Primary/Confirmatory | 0.5 µg/L | GC-MSD | Kaune, 2001  (Mefenpyr-diethyl DAR) |

**Table 5.2-8: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892) and its metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid (AE F094270)** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Groundwater  (Environmental fate) | Primary/Confirmatory | 0.05 µg/L | GC-MSD | Kaune, 2001  (Mefenpyr-diethyl DAR) |

**Table 5.2-9: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892)** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Surface water  (Environmental fate) | Primary/Confirmatory | 0.05 µg/L | HPLC-MS/MS | Krebber and Leppelt, 2007.  (Mefenpyr-diethyl DAR) |

**Table 5.2-10: Validated methods for the generation of pre-authorisation data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component residue definition: Mefenpyr-diethyl (AE F107892)** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year / missing / EU agreed** |
| Air  (Environmental fate) | Primary/Confirmatory | 8 μg/m3 | HPLC-UV | Class, 1994 (Mefenpyr-diethyl DAR) |

## Methods for post-authorization control and monitoring purposes (KCP 5.2)

### Analysis of the plant protection product (KCP 5.2)

Analytical methods for the determination of the active substance in the plant protection product are available. Please refer to point 5.2.1 above.

### Description of analytical methods for the determination of residues of iodosulfuron methyl-sodium (KCP 5.2)

#### Overview of residue definitions and levels for which compliance is required

Compared to the residue definition proposed in the Draft Assessment Report the current legal residue definition is identical.

**Table 5.3-1: Relevant residue definitions for monitoring/enforcement and levels for which compliance is required**

|  |  |  |  |
| --- | --- | --- | --- |
| **Matrix** | **Residue definition** | **MRL / limit** | **Reference for MRL/level Remarks** |
| Plant, high water content | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuronmethyl | 0.01\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Plant, high acid content | 0.01\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Plant, high protein/high starch content (dry commodities) | 0.01\* mg/kg / LOQ | EFSA Journal, 2012;  10(11):2974  Reg. (EU) 289/2014 |
| Plant, high oil content | 0.02\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Plant, difficult matrices (hops, spices, tea) | 0.05\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Muscle | Not defined (EFSA, 2016) | 0.02\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Milk |
| Eggs |
| Fat |
| Liver, kidney |
| Soil  (Ecotoxicology) | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuronmethyl | 0.01 µg/kg / LOQ |  |
| Drinking water  (Human toxicology) | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuronmethyl and metsulfuronmethyl (AE F075736) | 0.05 µg/L / LOQ (both analytes) | general limit for drinking water: 0.1 µg/L |
| Surface water (Ecotoxicology) | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuron- methyl and metsulfuronmethyl (AE F075736) | 0.05 µg/L / LOQ (both analytes) |  |
| Air | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuronmethyl | 1.05 µg/m3 / LOQ  1.6 µg/m3 / LOQ |  |
| Body fluids | Sum of iodosulfuronmethyl and its salts, expressed as iodosulfuronmethyl | Not set / LOQ 0.05 mg/L | Not classified as T / T+ |

\* indicates lower limit of analytical quantification

#### Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of iodosulfuron-methyl-sodium in plant matrices is given in the following tables. These data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009). For the detailed evaluation of new/additional studies, refer to Appendix 2 of the B5, R-98/2009.

**Table 5.3-2: Validated methods for food and feed of plant origin**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Component of residue definition: iodosulfuron-methyl-sodium** | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year, Document No (report) / missing / EU agreed** |
| High water content (sugar  beet leaf)    High acid content (lemon  fruit)    High oil content  (oilseed rape)    High protein/high starch content (dry) (wheat straw/sugar beet body) | Primary  Method 01360 | 0.01 mg/kg | LC-MS/MS  (2 MRM validated) | Stuke, S., Ballmann, C.,  2013;  [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  EU reviewed, EFSA, 2016 |
| ILV  Method 01360 | 0.01 mg/kg | LC-MS/MS  (2 MRM validated) | Konrad, S., 2013;  [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  EU reviewed, EFSA, 2016 |
| Confirmatory method is not required. The primary method was confirmed by validation of two different mass transitions. | | | |
| High starch content (dry) (wheat grain) | Primary  Method  01360/M001 | 0.01 mg/kg | LC-MS/MS  (2 MRM validated) | Stuke, S., 2015;  [M-537921-01-1;](dart://dart/edition?ed_no=M-537921-01-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009) |
| ILV - not required as available for the 4 other matrix types | | | |
| Confirmatory method is not required. The primary method was confirmed by validation of two different mass transitions. | | | |

**Table 5.3-4: Statement on extraction efficiency**

|  |  |
| --- | --- |
|  | **Method for products of plant origin** |
| Available from: | Stuke, S., 2015, [M-525863-01-1,](dart://dart/edition?ed_no=M-525863-01-1) RAR, Sweden, Dec.2015, EU agreed |
| Not required, because: | As residues are not expected to be ≥LOQ in cereal grain, extraction efficiency is not required according to SANCO/825/00 rev. 8.1. |

#### Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

An overview on the acceptable methods for analysis of iodosulfuron-methyl-sodium in animal matrices is given in the following table. In matrices of animal origin, no residue definition was proposed during the Annex I Renewal since no residues are anticipated. Although not required for iodosulfuron-methylsodium by the current EU regulations, some analytical methods for matrices of animal origin were developed for sulfonylureas.

**Table 5.3-5: Validated methods for food and feed of animal origin (if appropriate)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component of residue definition: iodosulfuron-methyl-sodium\*** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method (*i.e.* GCMS or HPLC-UV)** | **Method No / Author(s), year / missing** |
| Milk, eggs, muscle, fat, kidney, liver | Primary  Method  01208/M001 | 0.01 mg/kg | LC-MS/MS  (2 MRM validated) | Pross, S.;  [M-389788-04-1;](dart://dart/edition?ed_no=M-389788-03-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009) |
| ILV  Method  01208/M001 | 0.01 mg/kg | LC-MS/MS  (2 MRM validated) | Moore, S., 2010;  [M-398300-02-1;](dart://dart/edition?ed_no=M-398300-02-1)  Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009) |

\* refers to the analyte relevant to the method as no residue definition is proposed for matrices of animal origin.

**Table 5.3-6: Statement on extraction efficiency**

|  |  |
| --- | --- |
|  | **Method for products of animal origin** |
| Required, available from: | - |
| Not required, because: | Methods for products of animal origin are not required (no residue definition). Residues are not expected to be ≥LOQ in animal matrices, so extraction efficiency is not required. |

#### Description of methods for the analysis of body fluids and tissues (KCP 5.2)

~~An overview on the acceptable methods and possible data gaps for analysis of iodosulfuron-methyl-sodium in body fluids and tissues is given in the following table. This data was submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).~~

At the request of the zRMS, the applicant has submitted new data supporting the analysis of iodosulfuron-methyl-sodium in body fluids and tissues with an LOQ of 0.01 mg/kg in accordance with SANTE 2020/12830 rev. 2.

**Table 5.3-7: Methods for body fluids and tissues (if appropriate)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Component of residue definition: iodosulfuron-methyl** | | |
| **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| ~~Primary~~  ~~Method 01478~~ | ~~50 µg/L~~ | ~~HPLC-MS/MS~~  ~~(2 transitions)~~ | ~~Kaussmann, M.; 2016;~~  [~~M-551992-01-1;~~](dart://dart/edition?ed_no=M-551992-01-1)  ~~Previously summarised and evaluated during Atlantis OD 12 re-registration (R-98/2009)~~ |
| Primary method | 0.01 mg/kg | HPLC-MS/MS  (2 transitions) | Kaiser, M., 2022; S22-05738  This submission |
| Confirmatory | Not required | | |

#### Description of methods for the analysis of soil (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of iodosulfuron-methylsodium in soil is given in the following table. This data was submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.3-8: Validated methods for soil (if appropriate)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Component of residue definition: iodosulfuron-methyl-sodium** | | | |
| **Method type** | **Method LOQ** | **Principle of method (*i.e.* GC-MS or HPLC-UV)** | **Author(s), year / missing** |
| Primary | 0.01 µg/kg | HPLC-MS/MS | Freitag, T., Wolters, A.,  2013,  [M-310074-03-1](dart://dart/edition?ed_no=M-310074-03-1)  RAR, France, 2016;  EU agreed |

#### Description of methods for the analysis of water (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of iodosulfuron-methylsodium and its metabolite metsulfuron-methyl (AE F075736) in surface and drinking water is given in the following table.

**Table 5.3-9: Validated methods for water (if appropriate)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Component of residue definition: iodosulfuron-methyl-sodium (and metabolite metsulfuron-methyl (AE F075736))** | | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| Drinking water | Primary | 0.05 μg/L (for both substances) | HPLC-MS/MS | Krebber, R., Braune, M., 2013,  [M-466732-01-1](dart://dart/edition?ed_no=M-466732-01-1)  RAR, Sweden, 2015;  EU agreed |
| ILV to [M-](dart://dart/edition?ed_no=M-466732-01-1)  [466732-01-1](dart://dart/edition?ed_no=M-466732-01-1) | 0.05 μg/L (for both substances) | DI-HPLC-MS/MS | Stanislowski, 2013, [M-](dart://dart/edition?ed_no=M-470714-02-1)  [470714-02-1](dart://dart/edition?ed_no=M-470714-02-1)  RAR, Sweden, 2015;  EU agreed |
| Surface water | Primary | 0.05 μg/L (for both substances) | HPLC-MS/MS | Krebber, R., Braune, M., 2013,  Previously reviewed during Atlantis OD 12 re-registration (R-98/2009) |
| ILV to [M-](dart://dart/edition?ed_no=M-466732-01-1)  [466732-01-1](dart://dart/edition?ed_no=M-466732-01-1) | 0.05 μg/L (for both substances) | DI-HPLC-MS/MS | Stanislowski, 2013  Previously reviewed during Atlantis OD 12 re-registration (R-98/2009) |

#### Description of methods for the analysis of air (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of iodosulfuron-methylsodium in air is given in the following table. These data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.3-10: Validated methods for air (if appropriate)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Component of residue definition: iodosulfuron-methyl-sodium** | | | |
| **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| Primary | 1.05 μg/m3 | GC-ECD | Monograph (22 May 2000),  [M-181311-03-1,](dart://dart/edition?ed_no=M-181311-03-1) EU agreed |
| Primary | 1.6 µg/m3 | LC-UV | Addendum to Monograph (18 June 2001), EU agreed |

For any special comments or remarkable points concerning the analytical methods for air it is referred to Appendix 2.

#### Other studies/ information

None.

### Description of analytical methods for the determination of residues of mesosulfuron-methyl (KCP 5.2)

#### Overview of residue definitions and levels for which compliance is required

Compared to the residue definition proposed in the Assessment Report (incl. its addenda) the current legal residue definition is identical.

**Table 5.3-11: Relevant residue definitions for monitoring/enforcement and levels for which compliance is required**

|  |  |  |  |
| --- | --- | --- | --- |
| **Matrix** | **Residue definition** | **MRL / limit** | **Reference for MRL/level Remarks** |
| Plant, high water content | Mesosulfuron-methyl | 0.01\* mg/kg | Reg. (EU) 289/2014 |
| Plant, high acid content | 0.01\* mg/kg | Reg. (EU) 289/2014 |
| Plant, high protein/high starch content (dry commodities) | 0.01\* mg/kg | EFSA Journal, 2012;  10(11):2974  Reg. (EU) 289/2014 |
| Plant, high oil content | 0.02\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Plant, difficult matrices (hops, spices, tea) | 0.05\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Muscle  Milk  Eggs  Fat  Liver, kidney | Mesosulfuron-methyl | 0.02\* mg/kg / LOQ | Reg. (EU) 289/2014 |
| Soil  (Ecotoxicology) | Mesosulfuron-methyl | 0.01 µg/kg / LOQ |  |
| Drinking water  (Human toxicology) | Mesosulfuron-methyl | 0.05 µg/L / LOQ | general limit for drinking water: 0.1 µg/L |
| Surface water (Ecotoxicology) | Mesosulfuron-methyl | 0.05 µg/L / LOQ |  |
| Air | Mesosulfuron-methyl | 12 µg/m3 / LOQ |  |
| Body fluids | Mesosulfuron-methyl | Not set / LOQ 0.05 mg/L | Not classified as T / T+ |

#### Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of residues of mesosulfuron-methyl for the generation of pre-authorization data is given in the following table.

**Table 5.3-12: Validated methods for food and feed of plant origin**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Component of residue definition: mesosulfuron-methyl** | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLC-UV)** | **Author(s), year, Document No (report) / missing / EU agreed** |
| High water content | Primary EM 01360 | 0.01 mg/kg | LC-MS/MS | Stuke, S., Ballmann, C., 2013,  [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  EU agreed RAR 2016 |
| ILV | 0.01 mg/kg | LC-MS/MS | Konrad, S., 2013,  [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  EU agreed RAR 2016 |
| High acid content | Primary EM 01360 | 0.01 mg/kg | LC-MS/MS | Stuke, S., Ballmann, C., 2013,  [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  EU agreed RAR 2016 |
| ILV | 0.01 mg/kg | LC-MS/MS | Konrad, S., 2013,  [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  EU agreed RAR 2016 |
| High oil content | Primary EM 01360 | 0.01 mg/kg | LC-MS/MS | Stuke, S., Ballmann, C., 2013  [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  EU agreed RAR 2016 |
| ILV | 0.01 mg/kg | LC-MS/MS | Konrad, S., 2013,  [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  EU agreed RAR 2016 |
| High protein/high starch content (dry): straw | Primary EM 01360 | 0.01 mg/kg | LC-MS/MS | Stuke, S., Ballmann, C., 2013,  [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  EU agreed RAR 2016 |
| ILV | 0.01 mg/kg | LC-MS/MS | Konrad, S., 2013,  [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  EU agreed RAR 2016 |
| Dry commodities: cereal grain | Primary EM  01360/M001  (MR-15/090) | 0.01 mg/kg | LC-MS/MS | Stuke, S., 2015, [M-537921-01-1](dart://dart/edition?ed_no=M-537921-01-1)  Previously reviewed during Atlantis OD 12 re-registration (R-98/2009) |

**Table 5.3-13: Statement on extraction efficiency**

|  |  |
| --- | --- |
|  | **Method for products of plant origin** |
| Available from: | Stuke, S., 2015, [M-525863-01-1,](dart://dart/edition?ed_no=M-525863-01-1) RAR, Sweden, Dec.2015, EU agreed |
| Not required, because: | As residues are not expected to be ≥LOQ in cereal grain, extraction efficiency is not required according to SANCO/825/00 rev. 8.1. |

#### Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

An overview on the acceptable methods for analysis of mesosulfuron-methyl in animal matrices is given in the following table. In matrices of animal origin, no residue definition was proposed during the Annex I Renewal since no residues are anticipated. Although not required for iodosulfuron-methyl-sodium by the current EU regulations, some analytical methods for matrices of animal origin were developed for sulfonylureas. These data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.3-14: Validated methods for food and feed of animal origin (if appropriate)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Component of residue definition: mesosulfuron-methyl** | | | |
| **Matrix type** | **Method type /**  **Method No /**  **Document No**  **(report)** | **Method LOQ** | **Principle of method**  **(*i.e.* GC-MS or HPLC-UV)** | **Author(s), year / Document No (report) / missing** |
| Milk | Primary  01208/M001 | 0.01 mg/kg | LC-MS/MS | Schmeer, K., 2011,  [M-389788-03-1](dart://dart/edition?ed_no=M-389788-03-1)  EU agreed RAR 2016  Amended in 2018 by Pross, S. ([M389788-04-1)](dart://dart/edition?ed_no=M-389788-04-1), no impact on the evaluation |
| ILV | 0.01 mg/kg | LC-MS/MS | Moore, S., 2010,  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1)  EU agreed RAR 2016 |
| Eggs | Primary  01208/M001 | 0.01 mg/kg | LC-MS/MS | Schmeer, K., 2011,  [M-389788-03-1](dart://dart/edition?ed_no=M-389788-03-1)  EU agreed RAR 2016  Amended in 2018 by Pross, S. ([M389788-04-1)](dart://dart/edition?ed_no=M-389788-04-1), no impact on the evaluation |
| ILV  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1) | 0.01 mg/kg | LC-MS/MS | Moore, S., 2010,  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1)  EU agreed RAR 2016 |
| Muscle | Primary  01208/M001 | 0.01 mg/kg | LC-MS/MS | Schmeer, K., 2011,  [M-389788-03-1](dart://dart/edition?ed_no=M-389788-03-1)  EU agreed RAR 2016  Amended in 2018 by Pross, S. ([M389788-04-1)](dart://dart/edition?ed_no=M-389788-04-1), no impact on the evaluation |
| ILV | 0.01 mg/kg | LC-MS/MS | Moore, S., 2010,  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1)  EU agreed RAR 2016 |
| Fat | Primary  01208/M001 | 0.01 mg/kg | LC-MS/MS | Schmeer, K., 2011,  [M-389788-03-1](dart://dart/edition?ed_no=M-389788-03-1)  EU agreed RAR 2016  Amended in 2018 by Pross, S. ([M389788-04-1)](dart://dart/edition?ed_no=M-389788-04-1), no impact on the evaluation |
| ILV | 0.01 mg/kg | LC-MS/MS | Moore, S., 2010,  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1)  EU agreed RAR 2016 |
| Kidney, liver | Primary  01208/M001 | 0.01 mg/kg | LC-MS/MS | Schmeer, K., 2011,  [M-389788-03-1](dart://dart/edition?ed_no=M-389788-03-1)  EU agreed RAR 2016  Amended in 2018 by Pross, S. ([M389788-04-1)](dart://dart/edition?ed_no=M-389788-04-1), no impact on the evaluation |
| ILV  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1) | 0.01 mg/kg | LC-MS/MS | Moore, S., 2010,  [M-398300-01-1](dart://dart/edition?ed_no=M-398300-01-1)  EU agreed RAR 2016 |

**Table 5.3-15: Statement on extraction efficiency**

|  |  |
| --- | --- |
|  | **Method for products of animal origin** |
| Required, available from: | - |
| Not required, because: | Methods for products of animal origin are not required (no residue definition). Residues are not expected to be ≥LOQ in animal matrices, so extraction efficiency is not required. |

#### Description of methods for the analysis of body fluids and tissues (KCP 5.2)

~~An overview on the acceptable methods and possible data gaps for analysis of mesosulfuron-methyl in body fluids and tissues is given in the following table. These data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).~~

At the request of the zRMS, the applicant has submitted new data supporting the analysis of mesosulfuron-methyl in body fluids and tissues with an LOQ of 0.01 mg/kg in accordance with SANTE 2020/12830 rev. 2.

**Table 5.3-16: Methods for body fluids and tissues**

|  |  |  |  |
| --- | --- | --- | --- |
| **Component of residue definition: mesosulfuron-methyl** | | | |
| **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| ~~Primary~~  ~~Method 01478~~ | ~~50 µg/L~~ | ~~HPLC-MS/MS~~  ~~(2 transitions)~~ | ~~Kaussmann, M.; 2016,~~  [~~M-551992-01-1~~](dart://dart/edition?ed_no=M-551992-01-1)  ~~Previously reviewed during Atlantis OD 12 re-registration (R-98/2009)~~ |
| Primary method | 0.01 mg/kg | HPLC-MS/MS  (2 transitions) | Wien, J., 2024;  S23-105500  This submission |
| Confirmatory | Not required | | |

#### Description of methods for the analysis of soil (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of mesosulfuron-methyl in soil is given in the following table. These data were submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.3-17: Validated methods for soil (if appropriate)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Component of residue definition: mesosulfuron-methyl** | | |
| **Method type** | **Method LOQ** | **Principle of method (*i.e.* GC-MS or HPLC-UV)** | **Author(s), year / missing** |
| Primary  Method 01115 | 0.1 µg/kg | HPLC-MS/MS | Freitag, T., Wolters, A.,  2013,  [M-310074-03-1](dart://dart/edition?ed_no=M-310074-03-1)  RAR, France, 2016;  EU agreed |

#### Description of methods for the analysis of water (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of mesosulfuron-methyl in surface and drinking water is given in the following tables.

**Table 5.3-18: Validated methods for water (if appropriate)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Component of residue definition: mesosulfuron-methyl** | | | |
| **Matrix type** | **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| Drinking water | Primary  Method 01387 | 0.05 μg/L | HPLC-MS/MS | Krebber, R., Braune, M., 2013,  [M-466732-01-1](dart://dart/edition?ed_no=M-466732-01-1)  RAR; France, 2016  EU agreed |
| ILV to [M-](dart://dart/edition?ed_no=M-466732-01-1)  [466732-01-1](dart://dart/edition?ed_no=M-466732-01-1) | 0.05 μg/L | DI-HPLC-MS/MS | Stanislowski, 2013, [M-](dart://dart/edition?ed_no=M-470714-02-1)  [470714-02-1](dart://dart/edition?ed_no=M-470714-02-1)  RAR; France, 2016  EU agreed |
| Surface water | Primary | 0.05 μg/L | HPLC-MS/MS | Krebber, R., Braune, M., 2013,  RAR; France, 2016  EU agreed |
| ILV to [M-](dart://dart/edition?ed_no=M-466732-01-1)  [466732-01-1](dart://dart/edition?ed_no=M-466732-01-1) | 0.05 μg/L | DI-HPLC-MS/MS | Stanislowski, 2013,  RAR; France, 2016  EU agreed |

#### Description of methods for the analysis of air (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of mesosulfuron-methyl in air is given in the following table. This data was submitted and previously evaluated during the re-registration of Atlantis 12 OD (authorisation number R-98/2009).

**Table 5.3-19: Validated methods for air (if appropriate)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Component of residue definition: mesosulfuron-methyl** | | | |
| **Method type** | **Method LOQ** | **Principle of method**  **(i.e. GC-MS or HPLCUV)** | **Author(s), year / missing** |
| Primary | 1.6 µg/m3 | LC-UV | Addendum to Monograph (18 June 2001), EU agreed |

#### Other studies/ information

None.

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 |
| --- | --- | --- | --- | --- | --- | --- |
| KCP 5.1.1/01 | | Cooney, G. | 2017 | Validation of a HPLC Method for the quantitative determination of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in mesosulfuron/iodosulfuron/mefenpyr 7.5/7.5/22 g/L OD.  Report No: VAL-17-017 Rev1  Life Scientific Ltd.  Non GLP  Unpublished | N | Life Scientific Ltd |
| KCP 5.1.1/02 | | Ilie, N. | 2023 | Bridging validation of a HPLC method for the quantitative determination of mesosulfuron-methyl, iodosulfuron-methyl-sodium and mefenpyr-diethyl in mesosulfuron/iodosulfuron/mefenpyr 10/2/30 g/L  Report No: VAL-18-035 Rev2  Life Scientific Ltd.  Non GLP  Unpublished | N | Life Scientific Ltd |
| KCP 5.1.2/57  KCP 10.3.1.1/01 | | Wilkins, S. | 2020a | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: Acute contact and oral toxicity to adult worker honeybees (*Apis mellifera* L.)  Company Report No.: FR/001918-06  GLP  Unpublished | N | Life Scientific Ltd. |
| KCP 5.1.2/58  KCP 10.3.1.2/01 | | Wilkins, S. | 2020b | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: 10 Day chronic oral toxicity test (repeated dose) for adult honey bees (*Apis mellifera* L.)  Company Report No.: FR/001918-10  GLP  Unpublished | N | Life Scientific Ltd. |
| KCP 5.1.2/03  KCP 10.3.1.3/01 | | Wilkins, S. | 2020c | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: In vitro 22 day toxicity test - repeated exposure to larval stage honeybees (*Apis mellifera* L.)  Company Report No.: FR/001918-11  GLP  Unpublished | N | Life Scientific Ltd. |
| KCP 5.1.2 / 01 | Stuke, S.;  Kerkering, S. | 2018 | Amendment no. 2: Determination of the residues of BYH 18636 , iodosulfuron-methyl-sodium, mefenpyr-diethyl and mesosulfuron-methyl in/on winter wheat after spraying of IMS & MSM & MPR  WG 12.6 and thiencarbazone-methyl WG 70 in the field in Germany, Spain and Portugal  Report No.: 13-2127, Edition Number: [M-503498-03-1](dart://dart/edition?ed_no=M-503498-03-1)  Bayer AG, Crop Science Division, Monheim, Germany | No | Bayer |
| ... amended: 2018-08-31 |
| GLP/GEP: Yes unpublished |
| KCP 5.1.2 / 02 | Stuke, S.;  Kerkering, S. | 2018 | Amendment no. 2: Determination of the residues of mefenpyr-diethyl, BYH 18636, iodosulfuronmethylsodium and mesosulfuron-methyl in/on winter wheat after spraying of IMS & MSM & MPR  WG 15 and thiencarbazone-methyl WG 70 in the field in Belgium, the Netherlands and Italy  Report No.: 13-2129, Edition Number: [M-506719-03-1](dart://dart/edition?ed_no=M-506719-03-1)  Bayer AG, Crop Science Division, Monheim, Germany | No | Bayer |
| ... amended: 2018-08-31 |
| GLP/GEP: Yes unpublished |
| KCP 5.1.2 / 03 | Mahlo, C.;  Gabriel, E.; Vagt, I.; Meyer, M. | 2017 | Determination of the residues of amidosulfuron and iodosulfuron-methyl-sodium in/on wheat and barley after spray application of AMS & IMS & MPR OD 375 in Germany, Denmark, Poland and the United Kingdom  Report No.: 16-2030, Edition Number: [M-612290-01-1](dart://dart/edition?ed_no=M-612290-01-1)  SGS Institut Fresenius GmbH, Taunusstein, Germany  GLP/GEP: Yes unpublished | No | Bayer |
| KCP 5.1.2 / 04 | Kaussmann, M. | 2017 | Modification M002 of the residue analytical method 01376 for the determination of foramsulfuron, iodosulfuron-methyl, metsulfuron-methyl and AE F153745 in/on plant material by HPLC-MS/MS  Report No.: 01376/M002, Edition Number: [M-587949-01-1](dart://dart/edition?ed_no=M-587949-01-1)  Bayer AG, Crop Science Division, Monheim, Germany  GLP/GEP: Yes unpublished | No | Bayer |
| KCP 5.1.2 / 05 | Kaussmann, M. | 2017 | Analytical method 01514 for the determination of AE F092944, AE F059411 and AE 0031838 in/on plant by HPLC-MS/MS  Report No.: P602166508, Edition Number: [M-583894-01-1](dart://dart/edition?ed_no=M-583894-01-1)  Bayer AG, Crop Science Division, Monheim, Germany  GLP/GEP: Yes unpublished | No | Bayer |
| KCP 5.1.2.1 / 01 | Norris, F. A. | 2000 | Dissipation of AE F115008 and AE F130360 in soil following application of AE F115008 WDG and AE F122006 WDG or AE F130060 WDG and AE F107892 WDG to a bare plot at the maximum proposed rates, USA, 1998: AE F115008  Report No.: B002785, Edition Number: [M-238505-01-1](dart://dart/edition?ed_no=M-238505-01-1)  Aventis CropScience USA LP, RTP, NC, USA  GLP/GEP: Yes unpublished | No | Bayer |
| KCP 5.1.2.6 / 01 | Krebber, R.; Ruttmann, F. | 2017 | Analytical method 01542 for the determination of BCS-CV14885 in test water from aquatic toxicity tests by HPLC-MS/MS  Report No.: P 604 177052, Edition Number: [M-602768-01-1](dart://dart/edition?ed_no=M-602768-01-1)  Bayer AG, Crop Science Division, Monheim, Germany  GLP/GEP: No unpublished | No | Bayer |
| KCA  4.2/25 | Kaiser, M. | 2022 | Validation of an Analytical Method for the Determination of Iodosulfuron-methyl in Different Matrices of Animal Origin  Report no.: S22-05738  GLP/GEP: Yes  Unpublished | N | Life Scientific Ltd. |
| KCA  4.2/26 | Wien, J. | 2024 | Validation of an analytical Method for the Determination of Mesosulfuron-methyl in Body Fluids and Animal Matrices  Report no.: S23-105500  GLP/GEP: Yes  Unpublished | N | Life Scientific Ltd. |

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

Please note that all data mentioned as part of DAR, RAR, or EFSA journals are considered as relied on.

**Iodosulfuron-Methyl-Sodium**

| **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 4.1.2 /01 | Wrede, A. | 1997 | Analytical method, validation Determination of residues in straw by HPLC Code: AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: A59678,  Report includes Trial Nos.: CR96/027,  Edition Number: [M-143342-01-1](dart://dart/edition?ed_no=M-143342-01-1)  Date: 1997-12-02  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.1.2 /02 | Wrede, A. | 1997 | Analytical method and validation Determination of residues in shoot by HPLC Code: AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: A59290, Edition Number: [M-142974-01-1](dart://dart/edition?ed_no=M-142974-01-1)  Report includes Trial Nos.: CR96/028  Date: 1997-09-04  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.1.2 /03 | Wrede, A. | 1997 | Aged residue in wheat straw and shoot. Radio validation of the residue analytical method AL121/96-0 (straw) and AL120/96-0 (shoot) Code: AE F115008  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C001460, Edition Number: [M-182685-01-1](dart://dart/edition?ed_no=M-182685-01-1)  Date: 1998-11-09  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.1.2 /04 | Wrede, A. | 1997 | Aged residue of AE F115008 and its metabolite AE F075736 in soil. - Radio validation of the residue analytical method DGM F 06/97 - 0 - Code: AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C001581,  Edition Number: [M-182982-01-1](dart://dart/edition?ed_no=M-182982-01-1)  EPA MRID No.: 45108718  Date: 1998-11-26  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /01 | Wrede, A. | 1997 | Analytical method, validation Determination of residues in grain by HPLC Code: AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: A58043, Edition Number: [M-141767-02-1](dart://dart/edition?ed_no=M-141767-02-1)  Report includes Trial Nos.: CR96/019  Date: 1997-04-28  ...Amended: 1998-06-29  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /02 | Wrede, A. | 1998 | Validation of the analytical method AL - 008/96 -0 for the determination of residues of AE F115008 in grain by HPLC with two different HPLC columns Code: AE F115008  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C001452, Edition Number: [M-182662-01-1](dart://dart/edition?ed_no=M-182662-01-1)  Date: 1998-11-05  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /03 | Taylor, N. W. | 1998 | Independent laboratory validation (ILV) of the Analytical Method (AL-008/96-0) for the determination of AE F115008 residues in cereal grain - Final Report AE F115008 analytical grade Code: AE F115008 AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom  Bayer CropScience,  Report No.: C000836, Report includes Trial Nos.: 200/07/001  Edition Number: [M-181323-01-1](dart://dart/edition?ed_no=M-181323-01-1)  Date: 1998-09-28  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /04 | Stan, H. J.;  Schwarzer, F.;  Brockmeyer, R. | 1992 | Practical application of methods for the analysis of sulfonylurea herbicides and their metabolites in foodstuffs  Techn. Universitaet Berlin, DEU;Institut fuer Lebensmittelchemie  Report No.: C005929,  Edition Number: [M-131964-01-2](dart://dart/edition?ed_no=M-131964-01-2)  Date: 1992-04-30  GLP/GEP: no, unpublished | N | Bayer |
| KCA 4.2  /05 | Wrede, A. | 1998 | Multi-residue method for the determination of AE F115008 in grain (statement) Code: AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C001451,  Edition Number: [M-182660-01-1](dart://dart/edition?ed_no=M-182660-01-1)  Date: 1998-11-06  GLP/GEP: no, unpublished | N | Bayer |
| KCA 4.2  /06 | Wrede, A. | 1998 | Analytical method and validation for the determination of residues of AE F115008 and its metabolite AE  F075736 in soil using HPLC (method and validation) Code: AE F115008  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: A67461,  Report includes Trial Nos.: CR97/032  Edition Number: [M-147842-01-1](dart://dart/edition?ed_no=M-147842-01-1)  EPA MRID No.: 45108717  Date: 1998-07-14  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /07 | Wrede, A. | 2000 | Enforcement Method for Soil by LC-MS/MS Metsulfuron-methyl (AE F075736) Iodosulfuron-methylsodium (AE F115008)  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C006394,  Edition Number: [M-193807-01-1](dart://dart/edition?ed_no=M-193807-01-1)  EPA MRID No.: 45108502  Date: 2000-02-04  GLP/GEP: no, unpublished | N | Bayer |
| KCA  4.2/08 | Wrede, A. | 2000 | Validation of the enforcement method EM F13/99-0 in soil by LC-MS/MS - Metsulfuron-methyl - Iodosulfuron-methyl-sodium - Code: AE F075736, AE F115008 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience,  Report No.: C006396, Edition Number: [M-193814-01-1](dart://dart/edition?ed_no=M-193814-01-1)  EPA MRID No.: 45108720  Date: 2000-02-04  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/09 | Wrede, A. | 1998 | Analytical method and validation for the determination of residues of AE F115008 and its metabolite AE F075736 in water using HPLC Code: AE F115008  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C000710, Report includes Trial Nos.: CR98/002  Edition Number: [M-181134-01-1](dart://dart/edition?ed_no=M-181134-01-1)  EPA MRID No.: 45108721  Date: 1998-09-22  GLP/GEP: no, unpublished | N | Bayer |
| KCA  4.2/10 | Wrede, A. | 2000 | Enforcement method of iodosulfuron-methyl-sodium and its metabolite metsulfuron-methyl in surface water by HPLC incl. validation. Extension of the enforcement method EM F 01/98-0 for iodosulfuronmethyl-sodium in drinking water to its metabolite metsulfuron-methyl incl. validation Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C006395, Report includes Trial Nos.: CR99/029  Edition Number: [M-193810-01-1](dart://dart/edition?ed_no=M-193810-01-1)  EPA MRID No.: 45108722  Date: 2000-02-08  GLP/GEP: no, unpublished | N | Bayer |
| KCA  4.2/11 | Wrede, A. | 1999 | Data generation method and validation for cereal by LC-MS/MSCode: AE F130060  Hoechst Schering AgrEvo GmbH; Rueckstaende und Verbrauchersicherheit, Frankfurt  Document No: C005129**,** M-191437-01-1  GLP / GEP  unpublished | N | Bayer |
| KCA  4.2/12 | Reichert, N. | 2000 | Development and validation of an analytical method for the determination of iodosulfuron methyl sodium in air Institut Fresenius Chem.und Biolog. Lab. AG, Taunusstein, Germany Bayer CropScience,  Report No.: IF-100/21283-00, Edition Number: [M-199299-02-1](dart://dart/edition?ed_no=M-199299-02-1)  Date: 2000-11-22  ...Amended: 2009-06-19  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/13 | Wrede, A. | 2000 | Enforcement Method for Cereal Grain, Straw and Shoot by LC-MS/MS Amidosulfuron (AE F075032) Metsulfuron-methyl (AE F075736) Iodosulfuron-methyl-sodium (AE F115008) AE F130060 AE F130360  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C006734, Edition Number: [M-194528-01-1](dart://dart/edition?ed_no=M-194528-01-1)  Date: 2000-03-02  GLP/GEP: no, unpublished | N | Bayer |
| KCA  4.2/14 | Wrede, A. | 2000 | Validation of the Enforcement Method EM F08/99-0 of cereal grain, straw and shoot by LC-MS/MS - Amidosulfuron (AE F075032) - Metsulfuron-methyl (AE F075736) Iodosulfuron-methyl-sodium (AE F115008) - AE F130060 - AE F 130360  Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C006735, Edition Number: [M-194531-01-1](dart://dart/edition?ed_no=M-194531-01-1)  Date: 2000-03-02  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/15 | Wrede, A. | 2002 | Validation of the enforcement method EM F08/99-0 for lemon, tomato and maize kernel by LC-MS/MS - Amidosulfuron (AE F075032) - Iodosulfuron-methyl-sodium (AE F115008) - Mesosulfuron-methyl (AE F130060) - Foramsulfuron (AE F130360) Aventis CropScience GmbH, Frankfurt am Main, Germany  Bayer CropScience,  Report No.: C022220, Edition Number: [M-212674-01-1](dart://dart/edition?ed_no=M-212674-01-1)  Date: 2002-04-30  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /16 | Heinemann, O. | 2004 | Modification M001 to method 00815 for the determination of residues of amidosulfuron, iodosulfuronmethyl-sodium including metabolite metsulfuron-methyl, foramsulfuron and mesosulfuron-methyl in/on flax and wheat matrices by HPLC-MS/MS  Bayer CropScience,  Report No.: 00815/M001, Report includes Trial Nos.: P602033000  Edition Number: [M-226888-01-1](dart://dart/edition?ed_no=M-226888-01-1)  Date: 2004-01-30  GLP/GEP: yes, unpublished  ...also filed: KCA 6.1 /06 | N | Bayer |
| KCA  4.2/17 | Anspach, T. | 2001 | Independent laboratory validation of the enforcement method for the determination of residues of iodosulfuron-methyl-sodium (AE F115008) and amidosulfuron (AE F075032) in wheat (grain) Dr. Specht & Partner, Chemische Laboratorien GmbH, Germany  Bayer CropScience,  Report No.: C015636, Edition Number: [M-200884-01-1](dart://dart/edition?ed_no=M-200884-01-1)  Date: 2001-08-28  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /18 | Reichert, N.; Klimmek, S. | 2002 | Independent laboratory validation of the analytical method EM F08/99-0 for the residue analysis of Amidosulfuron (AE F075032), Iodosulfuron-methyl-sodium (AE F115008), Mesosulfuron-methyl (AE  F130060), Foramsulfuron (AE F130360) in tomato and citrus  Institut Fresenius Chem.und Biolog. Lab. AG, Taunusstein, Germany  Bayer CropScience,  Report No.: C023679,  Edition Number: [M-215456-01-1](dart://dart/edition?ed_no=M-215456-01-1)  Date: 2002-06-06  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 4.2  /19 | Stuke, S.; Ballmann, C. | 2013 | Analytical method 01360 for the determination of amidosulfuron, metsulfuron-methyl, iodosulfuronmethyl-sodium, mesosulfuron-methyl, and foramsulfuron in samples from plant origin by HPLC-MS/MS Bayer CropScience,  Report No.: MR-13/007,  Edition Number: [M-455564-01-1](dart://dart/edition?ed_no=M-455564-01-1)  Method Report No.: MR-13/007  Date: 2013-05-28  GLP/GEP: yes, unpublished  ...also filed: KCA 6.1 /07 | N | Bayer |
| KCA 4.2/20 | Stuke, S. | 2015 | Cross validation of enforcement method 01360 for the determination of sulfonylureas vs. extraction procedure applied in 14C-metabolism studies using incurred residues in plant matrices analysed by  HPLC-MS/MS | N | Bayer |
| KCA  4.2/21  ...also filed: KCA 6.1 /08 | Konrad, S. | 2013 | Independent lab validation of BCS method 01360 for the determination of residues of amidosulfuron, metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl and foramsulfuron in samples from plant origin by HPLC-MS/MS Currenta GmbH & Co. OHG, Leverkusen, Germany BCS,  Report No.: 2013/0060/01,  Edition Number: [M-470160-01-1](dart://dart/edition?ed_no=M-470160-01-1)  Date: 2013-10-18  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/22 | Krebber, R.; Braune, M. | 2013 | Analytical method 01387 for the determination of various pesticides in drinking and surface water by  HPLC-MS/MS  Bayer CropScience,  Report No.: MR-13/085, Edition Number: [M-466732-01-1](dart://dart/edition?ed_no=M-466732-01-1)  Method Report No.: MR-13/085  Date: 2013-10-09  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/23 | Stanislowski, T. | 2013 | Independent laboratory validation of BCS analytical methods 01333 and 01387 for determination of various pesticides in surface water by Di-HPLC-MS/MS  PTRL Europe, Ulm, Germany  Bayer CropScience,  Report No.: P3117 G, Edition Number: [M-470714-02-1](dart://dart/edition?ed_no=M-470714-02-1)  Date: 2013-12-13  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  4.2/24 | Freitag, T. | 2013 | Amendment no. 0001 to report no.: MR-08/138 - Analytical Method 01115 for the determination of residues of amidosulfuron,iodosulfuron-methyl-sodium, metsulfuron-methyl, mesosulfuron-methyl and foramsulfuron in soil by HPLC-MS/MS  Bayer CropScience,  Report No.: [M-310074-03-1,](dart://dart/edition?ed_no=M-310074-03-1) Edition Number: [M-310074-03-1](dart://dart/edition?ed_no=M-310074-03-1)  Method Report No.: MR-08/138  Date: 2008-10-27 (original report by Freitag & Wolters)  ...Amended: 2013-08-08  GLP/GEP: yes, unpublished | N | Bayer |
| KCA  5.3/01 | B A Mallyon | 2000 | Analytical method for the determination of test material in diet by HPLC RESID/93/34  [M-198511-01-1](dart://dart/edition?ed_no=M-198511-01-1)  GLP | N | Bayer |
| / | / | / | Hoe 130060 Determination of concentrations in dietary formulations by high performance liquid chromatography  Report 96.0191  [M-143016-01-1](dart://dart/edition?ed_no=M-143016-01-1)  GLP | N | Bayer |
| KCA 5.6.2/04 | xxxxxxxxxxx | 2004 | AE F130060; substance technical Code: AE F130060 00 1C95 0001 Rabbit oral developmental toxicity (teratogenicity) study  Report 98.0254  [M-181336-02-1](dart://dart/edition?ed_no=M-181336-02-1)  GLP | N | Bayer |
| KCA 5.1.1/10 | Solà, J. |  | [Pyrimidyl-2-14C]mesosulfuron-methyl: Metabolic stability and profiling in liver microsomes from rats and humans for Inter-Species Comparison  Harlan Laboratories S.A. Centro Industrial Santiga, c/Argenters, Mogoda, Spain Bayer CropScience,  Report No.: EnSa-13-0829,  Edition Number: [M-470477-01-1](dart://dart/edition?ed_no=M-470477-01-1)  Date: 2013-11-15  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.2.6 /02 | Leidenfrost, P. | 2003 | 1st amentment to report no.: AT00537 of July 10.2003 - Study for the skin sensitization effect in guinea pigs (Guinea pig maximization test according to Magnusson and Kligman)  Bayer Pharma AG, Wuppertal, Germany  Bayer CropScience,  Report No.: T3072716, | N | Bayer |

**Mesosulfuron Methyl**

| **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** |
| --- | --- | --- | --- | --- | --- |
| / | / | / | Analytical method for the determination of AE F130060 in dog diet by High Performance liquid chromatography (HPLC)  Report 98.0289  Document M-147837-01-1  GLP  Edition Number: M-235831-02-1  Date: 2003-07-10  ...Amended: 2016-02-29  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.2.7 /01 | xxxxxxxxxxxx. | 2014 | Mesosulfuron-methyl (AE F130060) technical: Cytotoxicity assay in vitro with BALB/c3T3 c31 cells: Neutral Red (NR) test during simultaneous irradiation with artificial sunlight xxxxxxxxxx  Report No.: 1592100,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.4.1 /05 | Sokolowski, A. | 2016 | Mesosulfuron-methyl (AE F130060): Salmonella typhimurium reverse mutation assay Envigo CRS GmbH, Rossdorf, Germany  Bayer CropScience,  Report No.: 1744700,  Edition Number: [M-547488-01-1](dart://dart/edition?ed_no=M-547488-01-1)  Date: 2016-02-12  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /01 | Sokolowski, A. | 2012 | Salmonella typhimurium reverse mutation assay with AE F147447  Harlan CCR, Rossdorf, Germany  Bayer CropScience,  Report No.: 1462101,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /02 | xxxxxxxxxxxx | 2015 | Report amendment - In vitro chromosome aberration test in Chinese hamster V79 cells with AE F147447 xxxxxxxxxxxxxxxx  Report No.: 1462102,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /03 | xxxxxxxxxxxxxxxx | 2012 | Gene mutation assay in Chinese hamster V79 cells in vitro (V79 / HPRT) - AE F147447 xxxxxxxxxxxxx  Report No.: 1462103,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /04 | Sokolowski, A. | 2012 | Salmonella typhimurium reverse mutation assay with AE F160460  Harlan CCR, Rossdorf, Germany  Bayer CropScience,  Report No.: 1462301,  Edition GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /05 | xxxxxxxxxxxx | 2015 | Report amendment - In vitro chromosome aberration test in Chinese hamster V79 cells with AE F160460 x  Report No.: 1462302,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /06 | xxxxxxxxxxxxx | 2015 | Report amendment no. 1 - Gene mutation assay in Chinese hamster V79 cells in vitro (V79 / HPRT) - AE F160460 xxxxxxxxxx  Report No.: 1462303,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /07 | Sokolowski, A. | 2012 | Salmonella typhimurium reverse mutation assay with BCS-CV14885  Harlan Cytotest Cell Research GmbH (Harlan CCR), Rossdorf, Germany Bayer CropScience,  Report No.: 1490201,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /08 | xxxxxxxxx | 2015 | Report amendment - In vitro chromosome aberration test in Chinese hamster V79 cells with BCS-  CV14885  x  Report No.: 1490202,  GLP/GEP: yes, unpublished | N | Bayer |
| KCA 5.8.1 /09 | xxxxxxxxxxxx | 2015 | Report amendment no. 1 - Gene mutation assay in Chinese hamster V79 cells in vitro (V79/HPRT) - BCSCV14885 xxxxxxxxxx  Report No.: 1490203,  GLP/GEP: yes, unpublished | N | Bayer |
| / | / | / | Analytical method for the determination of AE F130060 in dog diet by High Performance liquid chromatography (HPLC)  Report 98.0289  Document [M-147837-01-1](dart://dart/edition?ed_no=M-147837-01-1)  GLP | N | Bayer |

**Mefenpyr-diethyl**

| **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 4.1.2/47 | Jooss, S. | 2010 | Validation of analytical BCS method 01300/M001 for the determination of residues of mefenpyr-diethyl and its metabolite AE F094270 (using QuEChERS and LC/MS/MS) in/on plant materials  Report No.: 01300/M001  KCA 4.3.9/01 – mefenpyr-diethyl DAR addendum 1  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/48 | Neuss B., Losse K. | 1999 | Mefenpyr-diethyl Code: AE F107892 Bridging data between the Residue Analytical Methods AL001/92-5 and EM F03/98-0  Report No.: CR98/025  KCA 4.3.9 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/49 | Preu, T., Philipowski, C | 2004 | Residue Analytical Method 00814 for the Determination of Residues of Mefenpyr-diethyl (AE F107892) and its Metabolites in/on Wheat and Barley (Green Material, Grain and Straw) by HPLC-MS/MS  Report No.: C039456  KCA 4.2.1/01 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/50 | Richter, M., Class, T. | 2005 | Independent laboratory validation of method 00814/M001 for the determination of residues of mefenpyr-diethyl (AE F107892) and AE F094270 in/on matrices of plant origin by HPLC-MS/MS. Demonstration of a LC/MS/MS confirmation method  Report No.: C046787  KCA 4.2.1/04 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/51 | Zimmer, D., Stuke, S. | 2007 | Analytical Method 01027 for the Determination of Residues of the Active Item Mefenpyr-diethyl and its Metabolites AE F113225 and AE F094270 in/on Animal Tissues and Milk by HPLC-MS/MS  Report No.: 01027  KCA 4.2.1/06 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/52 | Rzepka, S., Rotzoll, N. | 2007 | Independent laboratory validation of Bayer CropScience analytical method No. 01027 for the determination of residues of Mefenpyr-diethyl and its metabolites AE F113225 and AE F094270 in/on animal tissues and milk by HPLC-MS/MS  Report No.: BAY-0701V  KCA 4.2.1/07 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/53 | Brumhard, B. & Schneider, U. | 2007 | Analytical Method 00996 for the Determination of Residues of Mefenpyr-diethyl (AE F107892) in Soil by HPLC-MS/MS  Report No.: 00996  KCA 4.2.2/01 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/54 | Kaune, A. | 2001 | Validation of the analytical method EM F02/01-0 for the determination of AE F107892 and its metabolites AE F113225, AE F109453 and AE F094270 in water and storage stability in water  Report No.: 01F004  KCA 4.2.2 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/55 | Krebber, R., Leppelt, L. | 2007 | Analytical method 01059 for the determination of mefenpyr-diethyl in drinking and surface water by HPLC-MS/MS  Report Number: 01059  KCA 4.2.3/01 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |
| KCA 4.1.2/56 | Class T. | 1994 | Validation of an Analytical Method for the Determination of Diethyl 1-(2,4-dichlorophenyl)-5-rnethyl-2-pyrazoline-3,5-dicarboxylate in Air  Report No.: A52415  KCA 4.2.4/02 – mefenpyr-diethyl DAR  GLP  Unpublished | N | Bayer |

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 |
| --- | --- | --- | --- | --- | --- |
| KCP XX | Author | YYYY | Title  Company Report N  Source  GLP/non GLP/GEP/non GEP  Published/Unpublished | 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 |
| --- | --- | --- | --- | --- | --- |
| KCP XX | Author | YYYY | Title  Company Report N  Source  GLP/non GLP/GEP/non GEP  Published/Unpublished | Y/N | Owner |
|  |  |  |  |  |  |

1. Detailed evaluation of submitted analytical methods
   1. Analytical methods for Iodosulfuron-methyl sodium and mesosulfuron-methyl
      1. Methods used for the generation of pre-authorization data (KCP 5.1)
         * 1. Analytical method 1

Method validation

zRMS: Method is accepted.

|  |  |
| --- | --- |
| Reference: | KCP 5.1.2/01 (Cross reference KCP 10.3.1.1/01) |
| Report | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: Acute contact and oral toxicity to adult worker honeybees (*Apis mellifera* L.). Wilkins. S., 2020a. Report number FR/001918-06 |
| Guideline(s): | OECD 213 and 214, SANCO/3029/99 rev.4, 11/07/00. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

Materials and methods

For this dose verification testing a single constituent active substance of the formulation was selected as the target indicator analyte – iodosulfuron-methyl-sodium. It was considered appropriate to use a single component and assume that if this was within ± 20% of expected concentration, that the other component active substance (mesosulfuron-methyl) would also be, this reasoning being based upon the fact that this is an off the shelf product and has to meet required manufacturing standards and the active substance content is declared (and will have been checked with analysis during the manufacturing process). An analytical method for determination of the active substance in the final dosing solutions (water plus Triton X-100 for contact dosing and 50% w/v aqueous sucrose) was developed and validated according to SANCO3029/99 rev4.0.

Stock solution: iodosulfuron-methyl sodium was prepared at nominal concentration of 500 to 1000 µg/mL in acetonitrile.

Sample preparation: an aliquot of 1 mL was weighed in 2 mL vial and dilutions were performed as needed using an autosampler (please refer to Table 1 – dilution protocol for sample aliquots in page 110 of the study report for further information).

The active substance was analysed by high performance liquid chromatography (HPLC) with UV (DAD) detection.

**Results and discussions**

Table A 1: Recovery results from method validation of iodosulfuron-methyl-sodium using the analytical method.

| Matrix | Analyte | Fortification Level | Number of  Samples | Mean  Recovery (%) | RSD (%) |
| --- | --- | --- | --- | --- | --- |
| 50% (w/w) sucrose + 5% Triton X-100 | Iodosulfuron-methyl-sodium | 1.2 mg/ml | 5 | 102 | 2.27 |
| 30 mg/ml | 5 | 105 | 1.48 |
| Triton X-100 | Iodosulfuron-methyl-sodium | 10 mg/ml | 5 | 102 | 3.91 |
| 280 mg/ml | 5 | 101 | 2.00 |
| 50% (w/w) sucrose in water | Iodosulfuron-methyl-sodium | 1000 mg/kg | 5 | 103 | 1.73 |
| 30000 mg/kg | 5 | 102 | 1.56 |
| Water | Iodosulfuron-methyl-sodium | 80 mg/ml | 5 | 99.5 | 4.20 |
| 550 mg/ml | 5 | 102 | 0.765 |

Table A 2: Characteristics for the analytical method used for validation of iodosulfuron-methyl-sodium residues in test solutions.

|  | Iodosulfuron-methyl sodium |
| --- | --- |
| Specificity | The analytical method was shown to be sufficiently specific. There were no interfering peaks in those fortified controls at the retention times of the analyte, so the analyte can be determined in the presence of either sample matrix, or by inference: any mixture of them. |
| Calibration | Six points were tested at concentrations ranging from 0.1 to 2 μg/mL with a correlation coefficient >0.99. |
| Assessment of matrix effects is presented | No |
| Limit of quantification | 2 mg/kg (sucrose)  20 μg/ml (Triton X-100) |

Conclusion

The method was successfully validated for the determination of iodosulfuron-methyl-sodium in test solutions, in accordance with the requirements of SANCO/3029/99 rev. 4.

* + - * 1. Analytical method 2

Method validation

zRMS: Method is accepted.

|  |  |
| --- | --- |
| Reference: | KCP 5.1.2/02 (Cross reference KCP 10.3.1.2/01) |
| Report | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: 10 Day chronic oral toxicity test (repeated dose) for adult honey bees (*Apis mellifera* L.) Wilkins. S., 2020b. Report number FR/001918-10 |
| Guideline(s): | OECD 245, SANCO/3029/99 rev.4. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

The stock solutions from this study were analysed using method FR/001918-M1 which was validated in the report presented under KCP 5.1.2/01 (Cross reference KCP 10.3.1.1/01): “Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: Acute contact and oral toxicity to adult worker honeybees (*Apis mellifera* L.). Wilkins. S., 2020a. Report number FR/001918-06”. Please refer to the method summarised under Analytical method 1.

Conclusion

The method was successfully validated for the determination of iodosulfuron-methyl-sodium in test solutions, in accordance with the requirements of SANCO/3029/99 rev. 4.

* + - * 1. Analytical method 3

Method validation

zRMS: Method is accepted.

|  |  |
| --- | --- |
| Reference: | KCP 5.1.2/03 (Cross reference KCP 10.3.1.3/01) |
| Report | Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: In vitro 22 day toxicity test - repeated exposure to larval stage honeybees (*Apis mellifera* L.) Wilkins. S., 2020c. Report number FR/001918-11 |
| Guideline(s): | OECD 239, SANCO/3029/99 rev.4. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

Two methods were presented in the report no.: FR/001918-11. Method FR/001918-M1 was validated in the report presented under KCP 5.1.2/01 (Cross reference KCP 10.3.1.1/01): “Formulated iodosulfuron-methyl-sodium and mesosulfuron-methyl: Acute contact and oral toxicity to adult worker honeybees (*Apis mellifera* L.). Wilkins. S., 2020a. Report number FR/001918-06”. Please refer to the method summarised under Analytical method 1. Additionally for this study, a method was developed to determine the analyte in the larval diet (FR/001918-11-M2). This method is described below.

Materials and methods

For this dose verification testing a single constituent active substance of the formulation was selected as the target indicator analyte – iodosulfuron-methyl-sodium. component and assume that if this was within ± 20% of expected concentration, that the other component active substance (mesosulfuron-methyl) would also be, this reasoning being based upon the fact that this is an off the shelf product and has to meet required manufacturing standards and the active substance content is declared (and will have been checked with analysis during the manufacturing process). Analysis was validated to SANCO/3029/99 rev4.0 guidelines. The stock solutions were analysed using method FR/001918-M1 which was validated under study with the report number FR/001918-06 (see KCP 5.1.2/01 (Cross reference KCP 10.3.1.1/01)). The larval diet samples were validated as part of this study using method FR/001918-M2.

Stock solution: iodosulfuron-methyl sodium was prepared at nominal concentration of 500 to 1000 µg/mL in acetonitrile.

Sample preparation: an aliquot of 0.05 mL was weighed in 2 mL vial and dilutions were performed as needed using an autosampler (please refer to Table 1 – dilution protocol for sample aliquots in page 72 of the study report for further information).

The active substance was analysed by HPLC with MS/MS detection.

**Results and discussions**

Table A 3: Recovery results from method validation of iodosulfuron-methyl-sodium using the analytical method.

| Matrix | Analyte | Fortification Level | Number of  Samples | Mean  Recovery (%) | RSD (%) |
| --- | --- | --- | --- | --- | --- |
| Larval diet | Iodosulfuron-methyl-sodium | 0.2014 mg/kg | 5 | 99.6 | 2.71 |
| 11.102 mg/kg | 5 | 99.7 | 7.00 |

Table A 4: Characteristics for the analytical method used for validation of iodosulfuron-methyl-sodium residues in larval diet.

|  | Iodosulfuron-methyl sodium |
| --- | --- |
| Specificity | The analytical method was shown to be sufficiently specific. There were no interfering peaks in those fortified controls at the retention times of the analyte, so the analyte can be determined in the presence of either sample matrix, or by inference: any mixture of them. |
| Calibration | Five points were tested at concentrations ranging from 0.25 to 5 ng/mL with a correlation coefficient > 0.997. |
| Assessment of matrix effects is presented | No |
| Limit of quantification | 0.2014 mg/kg |

Conclusion

The method was successfully validated for the determination of iodosulfuron-methyl-sodium in larval diet, in accordance with the requirements of SANCO/3029/99 rev. 4.

* + 1. Methods for post-authorization control and monitoring purposes (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Soil (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Water (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Air (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)

~~No new or additional studies have been submitted.~~

An analytical method for the determination of solutions concentrations of iodosulfuron-methyl-sodium for the test “matrices of animal origin” to cover the analysis of body fluids and tissues is provided as follows:

|  |  |
| --- | --- |
| Comments of zRMS: | Method is accepted |

|  |  |
| --- | --- |
| Reference: | KCA 4.2/25 |
| Report | Validation of an Analytical Method for the Determination of Iodosulfuron-methyl in Different Matrices of Animal Origin, Kaiser, M., 2022, Report no.: S22-05738 |
| Guideline(s): | Yes, SANTE/2020/12830, rev. 1 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

Multi-residue method QuEChERS

Matrices: bovine meat and synthetic urine

**Materials and methods**

Stock solution(s) of the analyte were prepared by dissolving a weight of the test item with the aid of an ultrasonic bath. Solutions for fortification and calibration were obtained by (serial) dilution of the stock solution(s). Matrix-matched calibration solutions were prepared using final sample extracts of control (untreated) samples of a respective matrix which were then fortified with solvent standard solutions. All solutions were stored at typically 1 °C to 10 °C in a brown glass vial in the dark.

In case of meat, the sample was homogenised via cutter using dry ice. Meat and urine samples were extracted with acetonitrile after addition of water. The samples were cleaned up using dispersive SPE with primary/secondary amine (PSA) and measured via LC-MS/MS. A reagent blank and two (2) control samples per matrix were extracted and analysed according to the method to investigate the presence of residue and/or background interference at the retention time of the analyte.

LC-MS/MS determination was conducted on a Shimadzu HPLC fitted with a pre-column (Phenomenex UHPLC guard 2.1 mm C18) and column (Phenomenex Kinetex® 2.6 um XB-C18 100 Å, 100 mm x 4.6 mm, 2.6 μm). The mobile phase used was (A) water with 0.5% formic acid and (B) methanol. Two mass transitions were evaluated, *m/z* 508-167 (quantifier) and *m/z* 508-141 (qualifier).

**Validation - Results and discussions**

**Table A 5: Recovery results from method validation of iodosulfuron-methyl using the analytical method.**

| **Matrix** | **Analyte** | **Mass Transition** | **Fortification Level (mg/kg)** | **Number of  Samples** | **Mean  Recovery (%)** | **RSD (%)** |
| --- | --- | --- | --- | --- | --- | --- |
| Meat | Iodosulfuron-methyl | Quantifier (m/z 508 – 167) | 0.01 | 5 | 89 | 2 |
| 0.1 | 5 | 79 | 3 |
| Qualifier (m/z 508 - 141) | 0.01 | 5 | 89 | 5 |
| 0.1 | 5 | 79 | 7 |
| Urine | Iodosulfuron-methyl | Quantifier (m/z 508 – 167) | 0.01 | 5 | 92 | 2 |
| 0.1 | 5 | 88 | 2 |
| Qualifier (m/z 508 - 141) | 0.01 | 5 | 89 | 3 |
| 0.1 | 5 | 86 | 4 |

**Table A 6: Method suitable for the determination of active substance iodosulfuron-methyl in body fluids and tissues**

|  | **Iodosulfuron** |
| --- | --- |
| Specificity | Confirmation of identity was demonstrated by determining the recovery and precision for both MS/MS transitions. HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary. The blank values of all control samples were below the LOD. |
| Calibration | Matrix-matched calibration standards at a minimum of five (5) concentration levels ranging from 0.1 ng/mL to 10 ng/mL for meat and 0.3 ng/mL to 20 ng/mL for urine.  Linear regression was performed with 1/x-weighting for urine samples. In meat samples, quadratic regression with 1/x-weighting was chosen, as the best fit of detector response was second order. |
| Assessment of matrix effects is presented | Yes, matrix effects were ≥ 20 % and deemed to be significant in meat matrix. Therefore, matrix-matched standards were used for quantification throughout the study.  Matrix effects were < 20 % in urine matrix and thus deemed to be insignificant. Nevertheless, matrix-matched standards were used for quantification throughout the study. |
| Standard stability | The difference of stored stock solution compared to  freshly prepared stock solution was 0.8%. Therefore, standard stability has been demonstrated. |
| Stability of final extracts | The final extracts of samples fortified at the 10x LOQ level together with two control sample extracts were stored at typically 1 °C to 10 °C in the dark. After storage (13 days) the final extracts were analysed against freshly prepared calibration standards.  For meat, the mean recovery after storage was 92 %.  For urine, the mean recovery after storage was 82 %.  Therefore, stability of final extracts was demonstrated. |
| Limit of quantification | 0.01 mg/kg in meat and 0.01 mg/L in urine |

**Conclusion**

Validation data was generated for linearity, repeatability, accuracy, and specificity criterions were achieved. As all criteria were met, the method is considered validated.

* + - 1. A.2.A.9 Other Studies/ Information

No new or additional studies have been submitted.

* 1. Analytical methods for Mesosulfuron-methyl

Please refer to Section A 2.1.

* + 1. Methods for post-authorization control and monitoring purposes (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Soil (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Water (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Air (KCP 5.2)

No new or additional studies have been submitted.

* + - 1. Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)

~~No new or additional studies have been submitted.~~

An analytical method for the determination of solutions concentrations of mesosufluron-methyl for the test “animal matrices and body fluids” to cover the analysis of body fluids and tissues is provided as follows:

|  |  |
| --- | --- |
| Comments of zRMS: | Method is accepted |

|  |  |
| --- | --- |
| Reference: | KCA 4.2/26 |
| Report | Validation of an analytical Method for the Determination of Mesosulfuron-methyl in Body Fluids and Animal Matrices, Wien, J., 2024. Report no.: S23-105500 |
| Guideline(s): | Yes, SANTE/2020/12830, rev. 2 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

Multi-residue method QuEChERS

Matrix:

Body Fluids (Urine)

Animal Matrices (Bovine meat)

**Materials and methods**

Stock solution(s) of the analyte were prepared by dissolving a weight of the test item with the aid of an ultrasonic bath. Solutions for fortification and calibration were obtained by (serial) dilution of the stock solution(s). Matrix-matched calibration solutions were prepared using final sample extracts of control (untreated) samples of a respective matrix which were then fortified with solvent standard solutions. All solutions were stored at typically 1 °C to 10 °C in a brown glass vial in the dark.

Control (untreated) samples were fortified prior to extraction at 0.01 mg/L and 0.1 mg/L in urine, and 0.01 mg/kg and 0.1 mg/kg in meat. For the low level fortified urine sample, fortification solution (50 µL, 1000 ng/mL) was added to urine (5 mL) giving a concentraion of 0.01 mg/L. For the low level fortified meat sample, fortification solution (50 µL, 1000 ng/mL) was added to meat (5 g) giving a concentraion of 0.01 mg/kg.

In brief, samples of urine or meat were extracted with acetonitrile after addition of water and after liquid-liquid partitioning with QuEChERS salt mixture diluted in water containing 0.1 % formic acid.

LC-MS/MS determination was conducted on a Agilent HPLC fitted with a pre-column (AJ0-9000, Phenomenex with 2.1 mm C18 cartridge) and column ( Agilent, ZORBAX Eclipse XDB-C18, 600 bar, 50 mm x 4.6 mm, 1.8 μm). The mobile phase used was (A) water with 0.1% formic acid and (B) methanol with 0.1% formic acid. Two mass transitions were evaluated, *m/z* 504-182 (quantifier) and *m/z* 504-139 (qualifier).

**Validation - Results and discussions**

**Table A 7: Recovery results from method validation of mesosulfuron-methyl using the analytical method.**

| **Matrix** | **Analyte** | **Mass Transition** | **Fortification Level (mg/kg)** | **Number of  Samples** | **Mean  Recovery (%)** | **RSD (%)** |
| --- | --- | --- | --- | --- | --- | --- |
| Meat | Mesosulfuron-methyl | Quantifier (m/z 504-182) | 0.01 | 5 | 92 | 6.4 |
| 0.1 | 5 | 103 | 10.7 |
| Qualifier (m/z 504-139) | 0.01 | 5 | 90 | 4.3 |
| 0.1 | 5 | 100 | 12.5 |
| Urine | Mesosulfuron-methyl | Quantifier (m/z 504-182) | 0.01 | 5 | 93 | 3.7 |
| 0.1 | 5 | 95 | 2.5 |
| Qualifier (m/z 504-139) | 0.01 | 5 | 92 | 4.9 |
| 0.1 | 5 | 95 | 2.1 |

**Table A 8: Method suitable for the determination of active substance mesosulfuron-methyl in body fluids and tissues**

|  | **Mesosulfuron-methyl** |
| --- | --- |
| Specificity | Confirmation of identity was demonstrated by determining the recovery and precision for both MS/MS transitions. HPLC-MS/MS method is highly specific, and an additional confirmatory method is not necessary. The blank values of all control samples were below the LOD. |
| Calibration | Matrix-matched calibration standards at a minimum of five (5) concentration levels ranging from 0.075 ng/mL to 7.5 ng/mL. This range corresponds to a mass fraction level of 0.003 mg/kg to 0.3 mg/kg for animal matrices and 0.003 mg/L to 0.3 mg/L for body fluids.  Linear regression was performed with 1/x-weighting. The calibration curves obtained for both ion mass transitions were linear since the regression residuals were randomly distributed on visual inspection.  Furthermore, correlation coefficients (R) were ≥ 0.99. |
| Assessment of matrix effects is presented | Yes, mean measured matrix effects were < 20 % and deemed to be insignificant in meat (+5%) and urine (-1%). Nevertheless, matrix-matched standards were used for quantification throughout the study. |
| Standard stability | The difference of stored stock solution compared to  freshly prepared stock solution was 5%. Therefore, standard stability has been demonstrated. |
| Stability of final extracts | The final extracts of samples fortified at the 10x LOQ level together with two control sample extracts were stored at typically 1 °C to 10 °C in the dark. After storage the final extracts were analysed against freshly prepared calibration standards.  For meat, the mean recovery after storage was 104 %.  For urine, the mean recovery after storage was 97 %.  Therefore, stability of final extracts was demonstrated. |
| Limit of quantification | 0.01 mg/kg in meat and 0.01 mg/L in urine |

**Conclusion**

Validation data was generated for linearity, repeatability, accuracy, stability, and specificity criterions were achieved. As all criteria were met, the method is considered validated.

* + - 1. A.2.A.9 Other Studies/ Information

No new or additional studies have been submitted.