Modification of the existing maximum residue level for cycloxydim in strawberries

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Abstract
In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Landwirtschaftliches Technologiezentrum Augustenberg submitted a request to the competent national authority in Germany, to modify the existing maximum residue level (MRL) for the active substance cycloxydim in strawberries. The data submitted in support of the request were found to be sufficient to derive an MRL proposal for strawberries. Adequate analytical methods for enforcement are available to control the residues of cycloxydim on the commodity under consideration at the validated limit of quantification (LOQ) of 0.05 mg/kg. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of cycloxydim according to the reported agricultural practice is unlikely to present a risk to consumer health.

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Keywords: cycloxydim, strawberries, pesticide, MRL, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Landwirtschaftliches Technologiezentrum Augustenberg submitted an application to the competent national authority in Germany (evaluating Member State, EMS), to modify the existing maximum residue level (MRL) for the active substance cycloxydim in strawberries. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 26 April 2018. To accommodate for the intended use of cycloxydim, the EMS proposed to raise the existing MRL from 3 mg/kg to 4 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under a previous MRL assessment and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of cycloxydim following foliar application was investigated in crops belonging to the groups of root crops, cereals and pulses/oilseeds.

Studies investigating the effect of processing on the nature of cycloxydim (hydrolysis studies) demonstrated that the active substance is almost completely degraded to a number of degradation products that are covered by the common moiety analytical methods.

EFSA concluded that for the crop assessed in this application, metabolism of cycloxydim in primary and in rotational crops and the possible degradation in processed products has been sufficiently addressed and that the previously derived residue definitions are applicable.

Sufficiently validated analytical methods based on high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) are available to quantify residues in the crop assessed in this application according to the enforcement residue definition at the limit of quantification (LOQ) of 0.05 mg/kg.

The available residue trials are sufficient to derive a MRL proposal of 4 mg/kg for strawberries.

Specific processing studies investigating the magnitude of residues in processed strawberry commodities are not required, considering the low contribution of residues in strawberries to the total long-term exposure.

The occurrence of cycloxydim residues in rotational crops was investigated in the framework of the European Union (EU) pesticides peer review. Based on the available information on the nature and magnitude of residues, it was concluded that significant residue levels are unlikely to occur in rotational crops, provided that the active substance is used according to the proposed good agricultural practice (GAP).

Residues of cycloxydim in commodities of animal origin were not assessed since the crop under consideration in this MRL application is normally not fed to livestock.

The toxicological profile of cycloxydim was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.07 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 2 mg/kg bw.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The highest long-term dietary intake accounted for maximum 32% of the ADI (UK toddler). The contribution of strawberries to the total consumer exposure of cycloxydim residues was < 1% of the ADI.

No acute consumer risk was identified in relation to the MRL proposed in the current assessment.

EFSA concluded that the proposed use of cycloxydim on strawberries will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers’ health.

EFSA proposes to amend the existing MRL as reported in the summary table below.

Full details of all endpoints and the consumer risk assessment can be found in Appendices B–D.
| Code<sup>(a)</sup> | Commodity   | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                                                 |
|------------------|-------------|-------------------------|-------------------------|---------------------------------------------------------------------------------------|
| 0152000          | Strawberries | 3                       | 4                       | The submitted data are sufficient to derive a MRL proposal for the NEU outdoor use. Risk for consumers unlikely |

**Enforcement residue definition:** cycloxydim including degradation and reaction products which can be determined as 3-(3-thianyl)glutaric acid S-dioxide (BH 517-TGSO2) and/or 3-hydroxy-3-(3-thianyl)glutaric acid S-dioxide (BH 517-5-OH-TGSO2) or methyl esters thereof, calculated in total as cycloxydim

<sup>(a):</sup> Commodity code number according to Annex I of Regulation (EC) No 396/2005.
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Modification of existing MRL for cycloxydim in strawberries

Assessment

The detailed description of the intended use of cycloxydim in strawberries, which is the basis for the current maximum residue level (MRL) application, is reported in Appendix A. Cycloxydim is the ISO common name for (5RS)-2-[(EZ)-1-(ethoxyimino)butyl]-3-hydroxy-5-[(3RS)-thian-3-yl]cyclohex-2-en-1-one (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Cycloxydim was evaluated in the framework of Directive 91/414/EEC with Austria designated as rapporteur Member State (RMS) for the representative uses as outdoor foliar applications against perennial grasses in oilseed rape, sugar beet, potato, bean and tolerant maize (derived by natural plant breeding). The draft assessment report (DAR) prepared by the RMS has been peer reviewed by European Food Safety Authority (EFSA, 2010). Cycloxydim has been approved for the use as herbicide on 1 June 2011.

The European Union (EU) MRLs for cycloxydim are established in Annex III of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has not yet been completed. EFSA has issued one reasoned opinion on the modification of MRLs for cycloxydim in various crops (EFSA, 2015). The proposals from this reasoned opinion have been considered in a regulation amending the EU MRL legislation.

In accordance with Article 6 of Regulation (EC) No 396/2005, Landwirtschaftliches Technologiezentrum Augustenberg submitted an application to the competent national authority in Germany (evaluating Member State, EMS), to modify the existing maximum residue level (MRL) for the active substance cycloxydim in strawberries. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA on 26 April 2018. To accommodate for the intended use of cycloxydim, the EMS proposed to raise the existing MRL from 3 mg/kg to 4 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation.

EFSA based its assessment on the evaluation report submitted by the EMS (Germany, 2018), the DAR (Austria, 2009) prepared under Council Directive 91/414/EEC, the confirmatory data submitted under the peer review (Austria, 2013), the Commission review report on cycloxydim (European Commission, 2014), the conclusion on the peer review of the pesticide risk assessment of the active substance cycloxydim (EFSA, 2010) as well as the conclusions from a previous EFSA opinion on cycloxydim (EFSA, 2015).

For this application, the data requirements established in Regulation (EU) No 544/2011 and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a–g, 2000, 2010a,b, 2017; OECD, 2011). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011.

As the review of the existing MRLs under Article 12 of Regulation 396/2005 is not yet finalised, the conclusions reported in this reasoned opinion should be taken as provisional and might need to be reconsidered in the light of the outcome of the MRL review.

A selected list of endpoints of the studies assessed by EFSA in the framework of this MRL application including the endpoints of relevant studies assessed previously, submitted in support of the current MRL application, are presented in Appendix B.

The evaluation report submitted by the EMS (Germany, 2018) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.

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1 Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1–32.
2 Commission Directive 2011/4/EU of 20 January 2011 amending Council Directive 91/414/EEC to include cycloxydim as active substance and amending Decision 2008/934/EC. OJ L 18, 21.1.2011, p.30–33.
3 Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.03.2005, p. 1–16.
4 For an overview of all MRL Regulations on this active substance, please consult: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN.
5 Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.
6 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
1. **Residues in plants**

1.1. **Nature of residues and methods of analysis in plants**

1.1.1. **Nature of residues in primary crops**

The nature of residues in primary crops resulting from the use of cycloxydim has been investigated in root (sugar beet), pulses/oilseeds (soybean) and cereal (maize) crops using a single foliar application and $^{13}$C-labelling on the cyclohexanone moiety (EFSA, 2010). The active substance is rapidly and intensively metabolised and the parent cycloxydim is never detected in plants except in trace amounts when samples are collected just after application. The metabolism proceeds first by oxidation to the sulfoxide and sulfone metabolites BH 517-TSO and BH 517-TSO2. Further loss of the alkyl side chain at the oxime group gives the imine metabolites BH 517-T1SO and BH 517-T1SO2, and the oxazole metabolites BH 517-T2SO and BH 517-T2SO2 are formed by Beckman rearrangement. All these metabolites are also found in their hydroxylated forms. In addition, cleavage of the cyclohexenone ring results in substituted glutaric acid derivative metabolites (BH 517-TGSO, BH 517-TGSO2).

1.1.2. **Nature of residues in rotational crops**

Degradation studies show that cycloxydim exhibits a very low persistence in soil (DT$_{90 \text{ lab}}$ = 8.6 days). The major soil metabolite is the sulfoxide metabolite BH 517-TSO, which exhibits also a low persistence in soil (max DT$_{90 \text{ field}}$ = 46 days). Considering the fast degradation of cycloxydim and its metabolite in the soil, no further studies investigating the nature and magnitude of the compound uptake in rotational crops are required (European Commission, 1997c).

Although not required, a metabolism study of cycloxydim in rotational crops was provided in the framework of the peer review and it was concluded that the metabolic pathway in succeeding crops is similar to the primary crop metabolism and that the same residue definition applies. Moreover, the total radioactive residue (TRR) observed in crops grown as rotational crop were low, confirming that no residues of cycloxydim or its metabolites above the LOQ are expected in rotational crops (EFSA, 2010).

1.1.3. **Nature of residues in processed commodities**

The effect of processing on the nature of cycloxydim was investigated under standard hydrolysis conditions. The studies were reported in the DAR and in the conclusion on the peer review (Austria, 2009; EFSA, 2010). Cycloxydim was almost totally degraded under the standard hydrolysis conditions, mainly to the oxazole metabolite BH 517-T2S (75–94% TRR) and to a lesser extent to its sulfoxide BH 517-T2SO (EFSA, 2010).

1.1.4. **Methods of analysis in plants**

A common moiety analytical methods for the determination of cycloxydim residues including all nonhydroxylated metabolites that can be oxidised to BH 517-TGSO2 and its metabolite BH 517-5-OH-TSO2 that can be oxidised to BH 517-5-OH-TGSO2 in plant commodities were assessed during the peer review (Austria, 2009). It was concluded that fully validated methods of analysis for products of plant origin were not available and had to be submitted (EFSA, 2010).

In 2013, the applicant submitted the required data which were assessed as confirmatory data by the RMS (Austria, 2013). With these confirmatory data, the applicant submitted validation data to prove the applicability of the primary method for the determination of further nonhydroxylated metabolites of cycloxydim, such as BH 517-TSO, BH 517-T1SO and BH 517-T2SO, and a hydroxylated metabolite BH 517-5-OH-TSO (Austria, 2013). The principle of the method involves the extraction of metabolites using isopropanol/distilled water mixture, oxidation of parent compound and relevant metabolites with H$_2$O$_2$ under alkaline conditions to BH 517-TGSO2 and BH 517-5-OH-TGSO2. The final determination is performed using HPLC-MS/MS. According to the EU review report (European Commission, 2014), the submitted methods were found to be adequate to determine residues of cycloxydim in plant matrices according to the proposed enforcement residue definition.

The validation data indicate that the method is sufficiently validated to control residues of cycloxydim according to the enforcement residue definition in high water-, high acid-, high oil content and dry commodities at the LOQ of 0.05 mg/kg for each analyte.
1.1.5. Stability of residues in plants

The storage stability of cycloxydim in primary crops was investigated in the DAR under Directive 91/414/EEC (Austria, 2009). The storage stability studies were conducted using samples spiked with the parent cycloxydim, BH 517-TSO, BH 517-T2SO2 and BH 517-5-OH-TSO2; these compounds were regarded as representative for the hydroxylated and nonhydroxylated metabolites identified in plants. The metabolites BH 517-TSO, BH 517-T2SO2 and BH 517-5-OH-TSO2 were stable for up to 2 years in high acid, high water (pineapple, sugar beet) and high oil (rapeseed) content matrices. Cycloxydim and metabolite BH 517-5-OH-TSO2 were found to be stable for up to 2 years in high starch (maize), high oil (oilseed), high water (pea) and high acid (strawberry) content matrices, using a common moieties analytical method (EFSA, 2010).

1.1.6. Proposed residue definitions

Based on the metabolism in primary and rotational crops and considering the ability of the available analytical methods to quantify a significant part of the residues in plants, the following general definition was proposed by the peer review for monitoring and risk assessment:

- cycloxydim including degradation and reaction products which can be determined as 3-(3-thianyl)glutaric acid S-dioxide (BH 517-TGSO2) and/or 3-hydroxy-3-(3-thianyl)glutaric acid S-dioxide (BH 517-5-OH-TGSO2) or methyl esters thereof, calculated in total as cycloxydim (EFSA, 2010).

The same residue definition applies to rotational crops and processed commodities. The current residue definition set in Regulation (EC) No 396/2005 is identical to the residue definition for enforcement derived in the peer review. For the uses on the crop under consideration, EFSA concludes that the metabolism of cycloxydim is sufficiently addressed and the residue definitions for enforcement and risk assessment agreed in the peer review are applicable.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

The Northern Europe (NEU) outdoor good agricultural practice (GAP) for strawberries assessed in the reasoned opinion is reported in Appendix A.

The applicant submitted eight residues trials on strawberries conducted in Germany in 2011 and 2012. The samples were analysed in accordance with the residue definition for enforcement and risk assessment. The analytical methods used were sufficiently validated and fit for purpose. The samples of the residue trials were stored under conditions for which integrity of the samples have been demonstrated.

All trials were conducted in compliance with the GAP. The growth stages of mono- and dicotyledonous plants (BBCH) were in the acceptable $\pm$ 25% range of deviation from the critical GAP (cGAP) in some cases. Strawberries are considered a major crop in NEU; therefore, eight trials are sufficient to derive an MRL proposal. The residue data allow to derive an MRL proposal of 4 mg/kg for strawberries accommodating for the NEU use.

1.2.2. Magnitude of residues in rotational crops

No further information is required (see Section 1.1.2).

1.2.3. Magnitude of residues in processed commodities

In the framework of the peer review, processing studies were provided and processing factors (PF) were derived for various potato, pea and rapeseed fractions (EFSA, 2010). Additional processing studies on rapeseeds and carrots were evaluated under a subsequent EFSA reasoned opinion (EFSA, 2015).

No additional information on processing was submitted under the current application. Specific processing studies investigating the magnitude of cycloxydim residues in processed strawberry commodities are not required, considering the low contribution of residues in strawberries to the total long-term exposure.
1.2.4. Proposed MRLs

The available data are considered sufficient to derive a MRL proposal of 4 mg/kg to accommodate for the NEU outdoor use on strawberries.

2. Residues in livestock

Not relevant as strawberries are not used for feed purposes.

3. Consumer risk assessment

The toxicological profile of the active substance cycloxydim was assessed in the framework of the peer review under Directive 91/414/EEC (EFSA, 2010). The data were sufficient to derive an acceptable daily intake (ADI) of 0.07 mg/kg body weight per day and an acute reference dose (ARfD) of 2 mg/kg body weight. The metabolites included in the residue definition were found to be of similar or lower toxicity than the parent active substance, therefore are considered to be covered by toxicological reference values of the parent. EFSA performed a dietary risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different subgroups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016).

The long-term exposure was performed taking into account the supervised trials median residue (STMR) values derived for strawberries. For the remaining crops, the input values derived in previous assessments, JMPR evaluations (for crops where Codex MRLs have been taken over in the EU legislation) or the existing EU MRLs were used to estimate the overall long-term exposure. The estimated long-term dietary intake of cycloxydim residues was in the range of 4.32% of the ADI (highest, UK toddler). The contribution of strawberries to the total consumer exposure of cycloxydim residues were < 1% of the ADI.

The acute exposure assessment was performed only with regard to the commodity under consideration assuming the consumption of a large portion of the food item as reported in the national food surveys and that these items contained residues at the highest level as observed in supervised field trials (EFSA, 2007). The calculated maximum exposure in percentage of the ARfD accounted for 1.7% for strawberries.

For further details on the exposure calculations, a screenshot of the Report sheet of the PRIMo is presented in Appendix C.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for strawberries.

EFSA concluded that the proposed use of cycloxydim on strawberries will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers’ health.

The MRL recommendation is summarised in Appendix B.4.

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Abbreviations

a.s. active substance
ADI acceptable daily intake
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
cGAP critical GAP
DAR draft assessment report
DAT days after treatment
DT<sub>90</sub> period required for 90% dissipation (define method of estimation)
EMS evaluating Member State
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
HPLC-MS/MS high performance liquid chromatography with tandem mass spectrometry
HR highest residue
IEDI international estimated daily intake
IESTI international estimated short-term intake
ISO International Organisation for Standardisation
IUPAC International Union of Pure and Applied Chemistry
JMPR Joint FAO/WHO Meeting on Pesticide Residues
LOQ limit of quantification
MRL maximum residue level
MW molecular weight
NEU northern Europe
OECD Organisation for Economic Co-operation and Development
PBI plant back interval
PF processing factor
PHI preharvest interval
| Abbreviation | Description |
|--------------|-------------|
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| RA           | risk assessment |
| RD           | residue definition |
| RD-Mo        | Plant residue definition for monitoring |
| RD-RA        | Plant residue definition for risk assessment |
| RMS          | rapporteur Member State |
| SANCO        | Directorate-General for Health and Consumers |
| SC           | suspension concentrate |
| SEU          | southern Europe |
| STMR         | supervised trials median residue |
| TRR          | total radioactive residue |
| WHO          | World Health Organization |
## Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, MS or country | F G or I(a) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|-------------------------|------------|-----------------------------------|-------------|-------------|-------------------------------|--------------|---------|
|                       |                         |            |                                   | Type(b)     | Conc. a.s.  | Method kind                   | Range of growth stages & season(c) | Number min-max | Interval between application (min) | g a.s./hL min-max | Water L/ha min-max | Rate | Unit  |
| Strawberries          | NEU                     | F          | Annual monocotyledonous weeds, volunteer cereals (except: annual bluegrass) | SC          | 100 g/L    | Spraying                              | up to BBCH 71, After emergence of weeds | 1            | –                           | 125–250 | 200–400 | 500   | g/ha | 14  | –    |

NEU: northern Europe; SEU: southern Europe; MS: Member State.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.
Appendix B – List of endpoints

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/Source |
|-----------------------------------|-------------|---------|----------------|----------------|----------------|
| Root crops                        | Sugar beet  |         | Nutrient solution: 1 × 200 g/ha | 7, 22, 46, 77, 119 | Root uptake 14C-label on cyclohexanone moiety EFSA, 2010 |
|                                   |             |         | Foliar treatment: 1 × 650 g/ha | 1, 94 | 14C-label on cyclohexanone moiety EFSA, 2010 |
| Cereals/grass                     | Maize       |         | Foliar: 1 × 400 g/ha (BBCH 22-23) | 72, 96 | Naturally tolerant maize 14C-label on cyclohexanone moiety EFSA, 2010 |
|                                   |             |         | Foliar: 1 × 800 g/ha (BBCH 61-67) | 54 |  |
| Pulses/oilseeds                   | Soybean     |         | Foliar treatment: 1 × 200 g/ha at fruit setting or at 3 leaf or 2 leaf stage | 45 or 71 or 82 | 14C-label on cyclohexanone moiety EFSA, 2010 |
|                                   |             |         | Foliar treatment: 1 × 1,000 g/ha (at flowering) | 69 |  |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
|--------------------------------------|-------------|---------|----------------|-----------|----------------|
| Root/tuber crops                     | Radish      |         | Bare soil 1 × 650 g/ha | 30, 135, 365 | EFSA (2010) |
| Leafy crops                          | Lettuce     |         | Bare soil 1 × 650 g/ha | 30, 135, 365 | EFSA (2010) |
| Cereal (small grain)                 | Wheat       |         | Bare soil 1 × 650 g/ha | 30, 135, 365 | EFSA (2010) |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)      | no         |         | EFSA (2010) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | no | EFSA (2010) |
| Sterilisation (20 min, 120°C, pH 6)      | no         |         | EFSA (2010) |
Can a general residue definition be proposed for primary crops?

|           | EFSA (2010) |
|-----------|-------------|
| Rotational crop and primary crop metabolism similar? | EFSA (2010) |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | Yes | Cycloxydim almost totally degraded to BH517-T2S and BH517-TSO under standard hydrolysis conditions; the degradation products are similar to metabolites in primary crops. They are all covered by the proposed residue definition and the common moiety analytical methods |

Plant residue definition for monitoring (RD-Mo)

Cycloxydim including degradation and reaction products which can be determined as 3-(3-thianyl)glutaric acid S-dioxide (BH 517-TGSO2) and/or 3-hydroxy-3-(3-thianyl)glutaric acid S-dioxide (BH 517-5-OH-TGSO2) or methyl esters thereof, calculated in total as cycloxydim

Plant residue definition for risk assessment (RD-RA)

Cycloxydim including degradation and reaction products which can be determined as 3-(3-thianyl)glutaric acid S-dioxide (BH 517-TGSO2) and/or 3-hydroxy-3-(3-thianyl)glutaric acid S-dioxide (BH 517-5-OH-TGSO2) or methyl esters thereof, calculated in total as cycloxydim

Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)

Matrices with high water-, high acid-, high oil content and dry commodities at the LOQ of 0.05 mg/kg, HPLC–MS/MS, LOQ 0.05 mg/kg

Confirmatory method not required as two ion transitions are considered highly specific

Method fully validated (Austria, 2013)

LOQ: limit of quantification; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry.

**B.1.1.2. Stability of residues in plants**

| Plant products (available studies) | Category | Commodity | T (°C) | Stability period | Compounds covered | Comment/Source |
|-----------------------------------|----------|-----------|--------|------------------|-------------------|---------------|
| Infrequent rain                   | High water content | Pea       | –20    | 2 Years          | Cycloxydim and BH 517-5-OH-TSO2 | EFSA (2010) |
|                                   |          | Sugar beet| –20    | 2 Years          | BH 517-TSO, BH 517-T2SO2 and BH 517-5-OH-TSO2 | EFSA (2010) |
| Frequent rain                    | High oil content | Rapeseed  | –20    | 2 Years          | BH 517-TSO, BH 517-T2SO2 and BH 517-5-OH-TSO2 | EFSA (2010) |
|                                   |          | Oilseed   | –20    | 2 Years          | Cycloxydim and BH 517-5-OH-TSO2 | EFSA (2010) |
| Desert                             | Dry/High starch | Maize     | –20    | 2 Years          | Cycloxydim and BH 517-5-OH-TSO2 | EFSA (2010) |
| Mountain                            | High acid content | Strawberry| –20    | 2 Years          | Cycloxydim and BH 517-5-OH-TSO2 | EFSA (2010) |
| Mediterranean                      |          | Pineapple | –20    | 2 Years          | BH 517-TSO, BH 517-T2SO2 and BH 517-5-OH-TSO2 | EFSA (2010) |
B.1.2. Magnitude of residues in plants

B.1.2.1. Summary of residues data from the supervised residue trials

| Commodity   | Region/Indoor<sup>(a)</sup> | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                        | Calculated MRL (mg/kg) | HR<sup>(b)</sup> (mg/kg) | STMR<sup>(c)</sup> (mg/kg) |
|-------------|-----------------------------|---------------------------------------------------------------|----------------------------------------|------------------------|--------------------------|---------------------------|
| Strawberry  | NEU                         | 2 × 0.72, 0.84, 0.93, 0.94, 1.4, 2.0, 2.2                    | Residue trials on strawberries compliant with GAP. | 4                      | 2.2                      | 0.94                      |

(a): NEU: Outdoor trials conducted in northern Europe.
(b): Highest residue.
(c): Supervised trials median residue.
B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | No | EFSA (2010) |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | No | EFSA (2010) |

B.1.2.3. Processing factors

No processing studies were submitted in the framework of the present MRL application.

B.2. Residues in livestock

Not relevant as the crop under consideration is not fed to livestock.

B.3. Consumer risk assessment

| ARfD | 2 mg/kg bw (EFSA, 2010) |
| Highest IESTI, according to EFSA PRIMo | Strawberries 1.7% of ARfD |
| Assumptions made for the calculations | The calculation is based on the highest residue levels expected in raw agricultural commodity |

| ADI | 0.07 mg/kg bw per day (EFSA, 2010) |
| Highest IEDI, according to EFSA PRIMo | 32% ADI (UK toddler) |
| Assumptions made for the calculations | The calculation is based on the median residue level derived for raw agricultural commodity from the NEU residue trials. For the remaining crops, the input values derived in previous assessments, JMPR evaluations or the existing EU MRLs were used to estimate the overall long-term exposure |

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level.

B.4. Recommended MRLs

| Code(a) | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------|-----------|------------------------|------------------------|-----------------------|
| 0152000 | Strawberries | 3 | 4 | The submitted data are sufficient to derive a MRL proposal for the NEU use. Risk for consumers unlikely |

Modification of existing MRL for cycloxydim in strawberries

Enforcement residue definition: Cycloxydim including degradation and reaction products which can be determined as 3-(3-thianyl)glutaric acid S-dioxide (BH 517-TGSO2) and/or 3-hydroxy-3-(3-thianyl)glutaric acid S-dioxide (BH 517-5-OH-TGSO2) or methyl esters thereof, calculated in total as cycloxydim

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
Appendix C – Pesticide Residue Intake Model (PRIMo)

### Cycloxydim

| Status of the active substance: | Included | Code no. |
|---------------------------------|----------|----------|
| LOQ (mg/kg bw):                 | 0.05     | Proposed LOQ |

#### Toxicological endpoints

- **ADI (mg/kg bw per day):** 0.07
- **ARfD (mg/kg bw):** 2

- **Source of ADI:** EFSA
- **Source of ARfD:** EFSA
- **Year of evaluation:** 2010
- **Year of evaluation:** 2010

| Highest calculated TMDI values in % of ADI | Commodity/ group of commodities | 2nd contributor to MS diet in % of ADI | Commodity/ group of commodities | 3rd contributor to MS diet in % of ADI |
|-------------------------------------------|----------------------------------|--------------------------------------|----------------------------------|--------------------------------------|
| 39 | UK Toddler | Sugar beet (root) | 6 | Peas (without pods) |
| 39 | UK Infant  | Soya bean | 3 | Peas |
| 39 | WHO Cluster diet B | Peas (without pods) | 7 | Sugar beet (root) |
| 39 | NL child | Soya bean | 3 | Peas |
| 39 | FR toddler | Peas (without pods) | 6 | Potatoes |
| 39 | FR cluster diet F | Peas | 4 | Peas (without pods) |
| 39 | IE adult | Peas (without pods) | 5 | Potatoes |
| 39 | WHO regional European diet | Peas (without pods) | 6 | Potatoes |
| 39 | Toddler | Peas (without pods) | 4 | Potatoes |
| 39 | WHO cluster diet D | Soya bean | 7 | Potatoes |
| 39 | DE child | Peas (without pods) | 3 | Potatoes |
| 39 | NL general | Peas (without pods) | 3 | Potatoes |
| 39 | UK vegetarian | Peas (without pods) | 3 | Sugar beet (root) |
| 39 | SE general population 90th percentile | Peas (without pods) | 2 | Peas (without pods) |
| 39 | UK adult | Sugar beet (root) | 3 | Peas (without pods) |
| 39 | ES child | Peas (without pods) | 2 | Lentils |
| 39 | ES adult | Peas (without pods) | 1 | Potatoes |
| 39 | IT children/holding | Peas (without pods) | 1 | Lentils |
| 39 | DK child | Peas (without pods) | 1 | Potatoes |
| 39 | FR all population | Peas | 3 | Lentils |
| 39 | PL general population | Peas | 4 | Lentils |
| 39 | DK adult | Peas (without pods) | 2 | Potatoes |
| 39 | LT adult | Peas (without pods) | 1 | Lentils |
| 39 | LT child | Peas (without pods) | 1 | Lentils |
| 39 | FI adult | Peas (without pods) | 1 | Lentils |
| 39 | FI child | Peas (without pods) | 1 | Lentils |

No of diets exceeding ADI:

| TMDI (range) in % of ADI | minimum – maximum |
|--------------------------|--------------------|
| 37                       | 4                  |

### Chronic risk assessment – refined calculations

Conclusions:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.

A long-term intake of residues of Cycloxydim is unlikely to present a public health concern.
## Modification of existing MRL for cycloxydim in strawberries

The acute risk assessment is based on the ARfD.

For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002); for lettuce, a variability factor of 5 was used.

In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100% of the ARfD.

### Results

| Commodity                  | No of critical MRLs (IESTI 1) | No of critical MRLs (IESTI 2) |
|---------------------------|-------------------------------|-------------------------------|
| Strawberries              | 2                             | 2                             |
| Processed commodities     |                               |                               |

### Conclusion

For Cycloxydim, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

No exceedance of the ARfD/ADI was identified for any commodity.

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* The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

** pTMRL: provisional temporary MRL.

*** pTMRL: provisional temporary MRL for unprocessed commodity.

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Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100% of the ARfD.

### Modifications

- **IESTI 1**
  - For lettuce, the calculation was performed with a variability factor of 3.

- **IESTI 2**
  - For lettuce, the calculation was performed with a variability factor of 3.
### Appendix D – Input values for the exposure calculations

#### D.1. Consumer risk assessment

| Commodity                                                                 | Chronic risk assessment |          | Acute risk assessment |          |
|---------------------------------------------------------------------------|-------------------------|----------|-----------------------|----------|
|                                                                           | Input value (mg/kg)     | Comment  | Input value (mg/kg)   | Comment  |
| Strawberries                                                              | 0.94                    | STMR     |                       | 2.2      | HR       |
| Beetroot, parsnips, horseradishes, Jerusalem artichokes                   | 0.24                    | STMR (EFSA, 2015) |                      |          |
| Potatoes                                                                  | 0.735                   | STMR (FAO, 2013) |                      |          |
| Carrots                                                                   | 0.44                    | STMR (FAO, 2013) |                      |          |
| Celeriac                                                                  | 0.44                    | STMR (EFSA, 2015) |                      |          |
| Salsify                                                                   | 0.43                    | STMR (EFSA, 2015) |                      |          |
| Onions                                                                    | 0.31                    | STMR (FAO, 2013) |                      |          |
| Tomatoes                                                                  | 0.445                   | STMR (FAO, 2013) |                      |          |
| Peppers                                                                   | 1.55                    | STMR (FAO, 2013) |                      |          |
| Aubergines                                                                | 0.48                    | STMR (EFSA, 2015) |                      |          |
| Brussels sprouts                                                          | 1.5                     | STMR (EFSA, 2015) |                      |          |
| Head cabbage                                                              | 1.23                    | STMR (EFSA, 2015) |                      |          |
| Chinese cabbage, kale                                                     | 0.75                    | STMR (EFSA, 2015) |                      |          |
| Lettuce                                                                   | 0.335                   | STMR (FAO, 2013) |                      |          |
| Escaroles                                                                 | 0.26                    | STMR (EFSA, 2015) |                      |          |
| Purslane, beet leaves                                                     | 0.12                    | STMR (EFSA, 2015) |                      |          |
| Beans (with pods)                                                         | 0.35                    | STMR (FAO, 2013) |                      |          |
| Peas                                                                      | 2.7                     | STMR (FAO, 2013) |                      |          |
| Leeks                                                                     | 0.36                    | STMR (FAO, 2013) |                      |          |
| Beans (dry)                                                               | 4.4                     | STMR (FAO, 2013) |                      |          |
| Peas (dry)                                                                | 5.6                     | STMR (FAO, 2013) |                      |          |
| Rapeseed                                                                  | 2.77                    | STMR (EFSA, 2015) |                      |          |
| Linseed                                                                   | 1.9                     | STMR (FAO, 2013) |                      |          |
| Sunflower seed                                                            | 0.375                   | STMR (FAO, 2013) |                      |          |
| Soya beans                                                                | 13                      | STMR (FAO, 2013) |                      |          |
| Herbal infusions, roots                                                   | 1.88                    | STMR (EFSA, 2015) |                      |          |
| Mammalian fats (except milk fat)                                          | 0.021                   | STMR (FAO, 2013) |                      |          |
| Mammalian meat                                                           | 0.021                   | STMR (FAO, 2013) |                      |          |
| Liver, kidney, edible offal (mammalian)                                  | 0.098                   | STMR (FAO, 2013) |                      |          |
| Other commodities of plant and animal origin                              | MRL                     | MRLs listed in Reg. (EU) 2016/486(a) |          |          |

(a): Commission Regulation (EU) 2016/486 of 29 March 2016 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for cyazofamid, cycloxydim, difluoroacetic acid, fenoxycarb, flumetralin, fluopicolide, flupyradifurone, flupyradoclor, kresoxim-methyl, mandoestrobim, mepanipyrim, metalaxyl-M, pendimethalin and tefluthrin in or on certain products. OJ L 90, 6.4.2016, p. 1–66.
## Appendix E – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|---------------------------------|-------------------------------------------------|--------------------------------|
| Cycloxydim                      | (SRS)-2-[(EZ)-1-(ethoxyimino)butyl]-3-hydroxy-5-[3(RS)-thian-3-yl]cyclohex-2-en-1-one |
| BH 517H E/Z isomer              | CCC/C(C1=C(O)CC(C2CCSC2)CC1=O)=N/OCC GGWHBJGBERXSLL-JXAWBT AJSA-N |
|                                 | 2-(1-(ethoxyimino)butyl)-3-hydroxy-5-(1-oxidotetrahydro-2H-thiopyran-3-yl)cyclohex-2-en-1-one |
| BH 517-TSO E/Z isomer           | O=C1C(/C(CCC)=N\OCC)=C(O)CC(C(CCC2)CS2=O)C1 SVKHAVSUBSUF BQ-JXAWBT AJSA-N |
| BH 517-TSO2 E/Z isomer          | 5-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl)-2-(1-(ethoxyimino)butyl)-3-hydroxycyclohex-2-en-1-one |
|                                 | O=C1C(/C(CCC)=N\OCC)=C(O)CC(C(CCC2)CS2(=O)=O)C1 LOLAMFUBYOY BMU-JXAWBT AJSA-N |
| BH 517-T1SO                     | 3-hydroxy-2-(1-iminobutyl)-5-(1-oxidotetrahydro-2H-thiopyran-3-yl)cyclohex-2-en-1-one |
|                                 | O=C1C(C(CCC)=N)=C(O)CC(C(CCC2)CS2=O)C1 KLBKPSHYURKCMK-UHFFFAOYSA-N |
| BH 517-T1SO2                    | 5-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl)-3-hydroxy-2-(1-iminobutyl)cyclohex-2-en-1-one |
|                                 | O=C1C(C(CCC)=N)=C(O)CC(C(CCC2)CS2(=O)=O)C1 ISTHBMF BYUKVPJ-UHFFFAOYSA-N |
| BH-517-T2SO                     | 6-(1-oxidotetrahydro-2H-thiopyran-3-yl)-2-propyl-6,7-dihydrobenzo[d]oxazol-4(5H)-one |
|                                 | O=C1CC(C(CCC2)CS2=O)CC3=C1N=C(CCC)O3 JITTWE SKOFSQ CI-UHFFFAOYSA-N |
| BH 517-T2SO2                    | 6-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl)-2-propyl-6,7-dihydrobenzo[d]oxazol-4(5H)-one |
|                                 | O=C1CC(C(CCC2)CS2(=O)=O)CC3=C1N=C(CCC)O3 SSLMIMBQ RXNQPD-UHFFFAOYSA-N |
| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|-------------------------------|---------------------------------|---------------------------------|
| BH 517-TGSO                  | 3-(1-oxidotetrahydro-2H-thiopyran-3-yl) pentanedioic acid O=C(O)CC(C(CCC1)CS1=O)CC(O)=O DVZHDN8XUJHHIV-UHFFFAOYSA-N | ![Structural formula image] |
| BH 517-TGSO2 (also oxidation product of cycloxydim) MW=264.3 | 3-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl) pentanedioic acid O=C(O)CC(C(CCC1)CS1(=O)=O)CC(O)=O ZQTHHTAJXROHTN-UHFFFAOYSA-N | ![Structural formula image] |
| BH 517-5-OH-TGSO2 or BH 517-0H-TGSO2 (also oxidation product of BH 517-5-OH-TSO2) MW=280.3 | 3-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl)-3-hydroxypentanedioic acid O=C(O)CC(C(CCC1)CS1(=O)=O)(O)CC(O)=O PVMXEMADFFDQHF-UHFFFAOYSA-N | ![Structural formula image] |
| BH 517-5-OH-TSO               | 2-(1-(ethoxyimino)butyl)-3,5-dihydroxy-5-(1-oxidotetrahydrothiopyran-3-yl)cyclohex-2-en-1-one O=C1(C/C(CCC)=N\OCC)=C(O)CC(C(CCC2)CS2=O)(O)C1 FBBQDUMANSBOGQ-AQTBWJFISA-N | ![Structural formula image] |
| BH 517-5-OH-TSO2              | 5-(1,1-dioxidotetrahydro-2H-thiopyran-3-yl)-2-(1-(ethoxyimino)butyl)-3,5-dihydroxycyclohex-2-en-1-one O=C1(C/C(CCC)=N\OCC)=C(O)CC(O)(C(CCC2)CS2(=O)=O)C1 XJZOLYXZPUWXGQ-AQTBWJFISA-N | ![Structural formula image] |
| BH 517-T2S                   | 2-propyl-6-(tetrahydro-2H-thiopyran-3-yl)-6,7-dihydrobenzo[d]oxazol-4(5H)-one O=C1CC(C2CSCC2)CC3=C1N=C(CCC)O3 KNQGJXMVSRCKV-UHFFFAOYSA-N | ![Structural formula image] |

<sup>(a): The metabolite name in bold is the name used in the conclusion.</sup>
<sup>(b): ChemBioDraw Ultra v. 13.0.2.3021.</sup>
<sup>(c): ChemBioDraw Ultra v. 13.0.2.3021.</sup>