

## 5.8 CYCLOXYDIM (179)

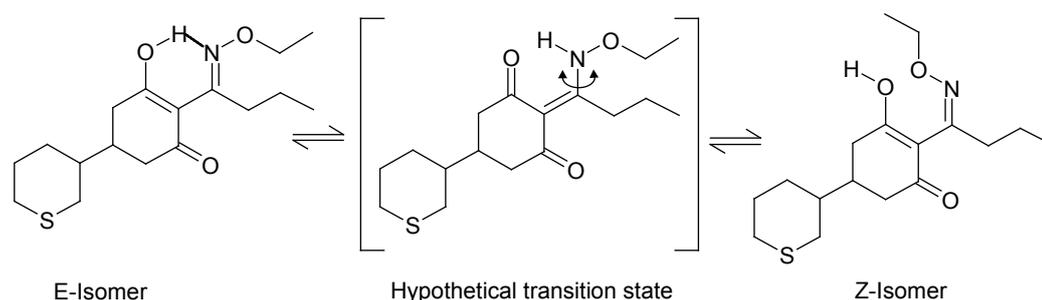
### RESIDUE AND ANALYTICAL ASPECTS

Cycloxydim is a post-emergence cyclohexene oxime herbicide that inhibits the acetylcoenzyme A carboxylase (ACCase) in chloroplasts of sensitive weeds. Cycloxydim was firstly evaluated by JMPR in 1992 (T, R). In 2009, an ADI of 0–0.07 mg/kg bw and an ARfD of 2 mg/kg bw for women of childbearing age were established; an ARfD was unnecessary for the general population. Cycloxydim was scheduled at the 43<sup>rd</sup> session of the CCPR (2011) for the periodic re-evaluation of residues by the 2012 JMPR.

Data on physical and chemical properties, metabolism in plants and livestock animals, environmental fate and analytical methods, animal feeding studies and processing studies were submitted. Residue supervised trials were submitted on pome fruits, stone fruits, grapes, strawberries, potatoes, carrots, celeriac, onions, tomatoes, peppers, cauliflower, Brussels sprouts, head cabbage, curly kale, lettuce, spinach, green beans and peas, leek, sugar beet roots, sugar beet tops, dry beans and peas, oilseed rape, sunflower, soya bean, rice and maize.

#### Metabolism studies

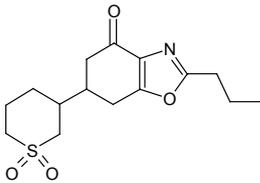
Cycloxydim is a racemic mixture. In the [<sup>14</sup>C]labelled cycloxydim stored in toluene, the compound is almost exclusively present as E-isomer, but E/Z isomerisation in the ethoxyimino group may occur in plants and in solution depending on solvent polarity, temperature and pH. In all metabolism studies, residues were reported as the sum of the two isomers.



The positions of the radiolabel compounds used in the metabolism studies and the structures of the main metabolites found in animals and plants are shown next.

Name	Structure	Name	Structure
<sup>14</sup> C-Cycloxydim		Cycloxydim-5-OH-TS	

Name	Structure	Name	Structure
<sup>14</sup> C-Cycloxydim-TSO		<sup>14</sup> C-Cycloxydim-5-OH-TSO	
Cycloxydim-TSO2		Cycloxydim-5-OH-TSO2	
Cycloxydim-T1S		Cycloxydim-5-OH-T1SO	
Cycloxydim-T1SO		Cycloxydim-6-OH-T2SO	
Cycloxydim-T1SO2		Cycloxydim-6-OH-T2SO2	
Cycloxydim-T2S		Cycloxydim-TGSO	
Cycloxydim-T2SO		Cycloxydim-TGSO2	

Name	Structure	Name	Structure
Cycloxydim-T2SO2			

### Animal metabolism

#### Rats

Metabolism studies conducted in rats were evaluated by the JMPR 2009. The studies were conducted after oral administration of the vinylogous acid [ $^{14}\text{C}$ ]cycloxydim-TS and its sodium salt and after intravenous administration of the sodium salt, at a nominal dose of 10 mg/kg bw (no-effect level) or 300 mg/kg bw (toxic effect level). The major metabolite found in urine was cycloxydim-TSO, followed by cycloxydim-T1SO and cycloxydim-TSO. In addition to unchanged parent, other metabolites were cycloxydim-T1SO2, cycloxydim-T2SO, and the metabolite hydroxylated at the 5-position of the cyclohexene ring of the parent. Patterns of metabolites in the bile were similar after the administration of either the free acid or the sodium salt of cycloxydim.

#### Lactating goats

[ $^{14}\text{C}$ ]cycloxydim was administered for 7 days to goats at 15 ppm feed. About 85% of the dose was recovered at the end of the experiment, mainly in urine (72%) and faeces (12%), and 0.09% in milk. Radioactivity in milk was constant during the 7 days dosing period (mean of 0.023 mg/kg). Total radioactive residue (TRR) was 0.005–0.006 mg/kg eq. in fat and muscle, and fat to 0.062–0.076 mg/kg eq. in liver and kidney, respectively. Non-extracted residues accounted for up to 64.1%TRR in liver, most of it solubilised by pronase. The major metabolite identified in milk was cycloxydim-T1SO (16%TRR). Cycloxydim-TSO represented 15%TRR in milk, 8%TRR in liver and 12%TRR in kidney. Parent compound was only detected in liver (10.8%TRR, 0.008 mg/kg). Minor metabolites found are cycloxydim-T1S, cycloxydim-TSO2 in liver (up to 2%TRR, 0.001 mg/kg) and cycloxydim-T2SO2 in milk (up to 2%TRR, < 0.001 to < 0.001 mg/kg).

A lactating goat was dosed with [ $^{14}\text{C}$ ]cycloxydim-TSO at 100 ppm feed for five days. At sacrifice, 89.1% of the administered dose was recovered, mostly in urine (78%) and faeces (10%). TRR in milk accounted for 0.11% of the dose (0.09–0.12 mg/kg). Liver and kidney had the highest residues, 0.46, 0.52 and, 0.52 mg/kg eq., respectively. Concentrations in fat and muscle were 0.04 mg/kg, and were not further identified. Cycloxydim-TSO and cycloxydim-T1SO were the major components in milk (about 23%TRR, 0.06 mg/kg and the only residues identified in liver (22%TRR, 0.10 mg/kg; and 10%TRR, 0.05 mg/kg, respectively). Cycloxydim-T2SO cycloxydim-T1SO2 (5%TRR, 0.01 mg/kg) and cycloxydim-TSO2 (2.7%TRR, < 0.01 mg/kg) were also found in milk. Residues in kidney were not characterized.

The [ $^{14}\text{C}$ ]cycloxydim-5-OH-TSO was administered to goats at a dose level of 12 ppm feed on nine consecutive days. In average, 97% of the administered dose was recovered in the experiment, of which 75% was in urine and 15.7% in faeces. TRR was about 0.02 mg/kg eq. in milk, 0.024 in fat and 0.025 in muscle, 0.203 in liver and 0.26 mg/kg eq. in kidney. Non-extracted residues accounted for up to 10.2% TRR in muscle. Cycloxydim-5-OH-TSO was the main residue in milk, muscle, kidney and fat (31 to 38%TRR; 0.007 to 0.10 mg/kg). In liver, the main residue was cycloxydim-5-OH-TS (17.4%TRR, 0.03 mg/kg), followed by cycloxydim-5-OH-TSO (11%TRR, 0.02 mg/kg). Cycloxydim-5-OH-TS was also a significant residue in kidney (25%TRR, 0.06 mg/kg) and fat (11%TRR, 0.003 mg/kg). Cycloxydim-6-OH-T2SO residues reached 13%TRR in muscle and cycloxydim-5-OH-T1SO represented < 10%TRR in all matrices.

### *Laying hens*

The metabolism and distribution of [ $^{14}\text{C}$ ]cycloxydim was investigated in laying hens following oral administration at 12 ppm feed for 10 days. About 80% of the administered dose was recovered at the end of the experiment, mostly in the excreta (78.0%), 0.33% in eggs, 0.11 % in muscle, 0.07 % in liver and 0.02% in fat. TRR in eggs ranged from 0.05 mg/kg eq. at day 1 to 0.14 mg/kg at day 10 (mean of 0.12 mg/kg eq.), starting to plateau at day 8. In tissues, TRR was 0.051–0.053 mg/kg eq. in fat and muscle and 0.28 mg/kg eq. in liver. Unextracted residues in muscle accounted for 4.5% TRR. Residues in eggs were mostly cycloxydim-TSO (0.04 mg/kg eq., 30.9%TRR), followed by cycloxydim-TSO<sub>2</sub> (0.008 mg/kg eq., 6.4%TRR) and the parent compound (0.004 mg/kg eq., 3.4%TRR). In muscle, only cycloxydim-TSO<sub>2</sub> was detected (0.001 mg/kg eq., 0.9%TRR) and in fat only cycloxydim-TSO (0.008 mg/kg, 18%TRR). In liver, the main residue detected was also cycloxydim-TSO (0.02 mg/kg eq., 7.4%TRR), followed by cycloxydim (0.005 mg/kg eq., 1.7%TRR) and cycloxydim-TSO<sub>2</sub> (0.002 mg/kg eq., 0.6%TRR).

The [ $^{14}\text{C}$ ]cycloxydim-TSO was administered to laying hens at a dose level of 50 ppm feed for 7 days. Treated animals were sacrificed 6 (group 2), 24 (group 3) and 48 hours (group 4) after the last dose. About 94% of the administered dose was recovered in group 4, mostly (92.3%) in the excreta, and 0.08% in eggs. In this group, TRR in eggs increased rapidly to an apparent plateau of 0.08–0.10 mg/kg after day 2. TRR from group 2 ranged from 0.10 mg/kg eq. in muscle to 0.99 mg/kg eq. in kidney, and were < 0.1 mg/kg in all tissues from group 4. Residues were only identified in eggs and liver. In eggs, cycloxydim-TSO (0.12 mg/kg, 41.4%TRR) was the major residue, followed by cycloxydim-TSO<sub>2</sub> (0.03 mg/kg, 8.8 %TRR) and cycloxydim-T<sub>2</sub>SO (0.02 mg/kg, 5.5%TRR). In liver, cycloxydim-TSO was the major residue (0.19 mg/kg, 33%TRR), followed by cycloxydim-T<sub>2</sub>SO (0.14 mg/kg, 24%TRR) and cycloxydim-T<sub>1</sub>SO (0.10 mg/kg, 17%TRR).

The [ $^{14}\text{C}$ ]cycloxydim-5-OH-TSO was administered to hens at a dose of 12 ppm feed for 11 days. The radioactivity was rapidly excreted within 24 hours after the last dose, with 93% of the applied dose recovered, mainly on excreta (89.7%). In eggs, mean residues were 0.066 mg/kg eq. (0.21% of the applied dose). In tissues, the highest radioactivity was found in liver (0.11 mg/kg eq.), followed by muscle (0.028 mg/kg eq.), and fat (0.02 mg/kg eq.). Non-extracted residues ranged from 24.1%TRR in fat to 38% TRR in muscle, with over 80% being released by protease. Cycloxydim-5-OH-TSO accounted for 15% TRR in eggs (0.01 mg/kg) to 29%TRR in fat (0.005 mg/kg). Cycloxydim-5-OH-TS accounted for about 19–22%TRR in muscle, fat and liver (0.004–0.021 mg/kg) and 50.7%TRR in eggs (0.034 mg/kg).

In summary, studies conducted with cycloxydim or its metabolites cycloxydim-TSO and cycloxydim-5-OH-TSO showed that the primary metabolic pathway of cycloxydim in animals involves two main routes: 1) oxidation to cycloxydim-TSO and subsequently to cycloxydim-TSO<sub>2</sub>, and 2) Beckmann re-arrangement with subsequent ring closure to form the oxazol cycloxydim-T<sub>2</sub>S, which can be oxidized further to cycloxydim-T<sub>2</sub>SO and cycloxydim-T<sub>2</sub>SO<sub>2</sub>. Cycloxydim was a minor component in eggs and tissues from dosed hens and was only detected in goat liver (11%TRR).

### ***Plant metabolism***

#### *Soya beans, cotton and sugar beet*

The metabolism of [ $^{14}\text{C}$ ]cycloxydim was studied in soya beans, cotton and sugar beet using two different treatments. To evaluate root uptake, the plants were cultivated in a nutrient solution containing 5 mg/L [ $^{14}\text{C}$ ]cycloxydim. To evaluate the uptake by the leaf, 10  $\mu\text{g}$  [ $^{14}\text{C}$ ]cycloxydim was applied to the upper leaf surface (soya bean, sugar beet) or one cotyledon (cotton). Samples were taken 3 and 7 days (soya bean and cotton) or 4 and 8 days (sugar beets) after the application, respectively. [ $^{14}\text{C}$ ] cycloxydim was taken up by the roots and transported acropetally to the cotyledons, stem and the remaining leaves. The highest radioactivity was detected in the primary leaves and roots (25–26  $\mu\text{g}$  [ $^{14}\text{C}$ ]cycloxydim/[ $^{14}\text{C}$ ]equiv at 7 DAT in soya beans). After leaf application, about 30% of the total radioactivity is translocated to the untreated soya bean plant parts at 7 days DAT, 8.3% to untreated cotton parts and 11.8% to untreated sugar beet parts.

In another study conducted with sugar beet at the 3-leaves stage, the seedlings were treated with [<sup>14</sup>C]cycloxydim at 0.2 kg ai/ha. Immediately after application, TRR was 8.48 mg/kg eq. in the tops. At harvest (119 DAT), TRR was 0.13 mg/kg eq. in the tops and 0.015 mg/kg eq. in roots. At 22 DAT, cycloxydim-TSO<sub>2</sub> and cycloxydim-T<sub>2</sub>SO were found in the tops at 0.18 mg/kg eq. (13.9% TRR) and 0.14 mg/kg eq. (11% TRR), respectively. At 46 DAT, various metabolites were found in the tops at low levels (0.0026 to 0.023 mg/kg eq., up to 4%TRR). No hydroxylated metabolites were detected in any sample.

In a third study on sugar beet, [<sup>14</sup>C]cycloxydim was applied at 0.65 kg ai/ha 2 months after sowing and samples taken 1 day after treatment and at crop maturity (94 DAT). At 1 DAT, TRR were 23 and 4 mg/kg eq. in leaves and roots, respectively, mostly extracted in methanol and dichloromethane. At harvest, residues were 2.2 and 0.16 mg/kg eq. in tops and roots, respectively. Cycloxydim was not detected in any of the top and root samples taken. At 1 DAT, residues mainly of cycloxydim-TSO, with 7.6 mg/kg (31.6%) in the tops and 2.4 mg/kg (60.1%) in roots. Cycloxydim-TSO<sub>2</sub> accounted for 16–18%TRR. At harvest, both metabolites were still present (< 10%TRR), but cycloxydim-T<sub>1</sub>SO was the predominant metabolite (0.42–0.02 mg/kg, 19–14%TRR in tops and roots, respectively). Only cycloxydim-T<sub>2</sub>S was present in amounts greater than 10%TRR (13.7%). No hydroxylated metabolite was observed.

[<sup>14</sup>C]cycloxydim was applied to soya beans at 0.2 kg ai/ha two to eight weeks after sowing (three trials, group 1) or at 1 kg ai/ha two months after sowing (one trial, group 2). TRR were 20, 2.3 and 0.46 mg/kg eq. at 45, 71 and 82 DAT in seeds from the group 1 and 12.5, 0.76 and 0.31 mg/kg eq. in straw and stalk. TRR in straw and seed from group 2 were 91 and 38.4 mg/kg eq., respectively. In most plant samples, more than 85% of the TRR were extracted with aqueous methanol and at later sampling intervals, considerable amounts of radioactivity were detected in the aqueous phase. The parent molecule was detected only at the day of application in all trials. The major metabolites found in seed samples were cycloxydim-TSO (0.078 to 0.42 mg/kg, 11.9 to 18.3%TRR), cycloxydim-T<sub>2</sub>SO (0.11 to 3.7 mg/kg, 4.8 to 18%TRR), cycloxydim-5-OH-TSO (0.2 to 1.3 mg/kg, 6.4 to 8.7% TRR) and cycloxydim-5-OH-TSO<sub>2</sub> (0.06 to 0.90 mg/kg, 4.5 to 12%TRR). In straw the hydroxylated metabolites were detected at low levels (up to 3.4%TRR).

### *Maize*

In two studies conducted in tolerant maize, [<sup>14</sup>C]cycloxydim was applied at 0.4 kg ai/ha (normal rate) at BBCH growth stage 22–23 or at 0.8 kg ai/ha during flowering (BBCH 61-67). In the normal use rate, TRR at harvest (96 DAT) were 0.123 mg/kg eq. in grain, 0.06 mg/kg eq. in cobs, 0.118 mg/kg eq. in husks and 0.17 mg/kg in straw; residues in forage at 72 DAT were 31 mg/kg eq. In the exaggerated rate samples, the TRRs ranged from 4.9 mg/kg eq. in grain to 13 mg/kg in straw eq.. Cycloxydim was not detected in any sample from any trial. In the normal rate trials, metabolite levels accounted for up to 1%TRR in grain, up to 8.7%TRR in straw (0.015 mg/kg cycloxydim-TGS + cycloxydim-TGSO<sub>2</sub>) and up to 11%TRR in forage (3.6 mg/kg cycloxydim-T<sub>1</sub>SO). In grain from the exaggerated rate trial, cycloxydim-TSO (0.53 mg/kg, 10.6%TRR), cycloxydim-T<sub>1</sub>SO + cycloxydim-T<sub>2</sub>SO<sub>2</sub> and cycloxydim-T<sub>2</sub>SO<sub>2</sub> + cycloxydim-T<sub>1</sub>SO<sub>2</sub> (0.71 mg/kg, 14%TRR each) were the major metabolites. Only cycloxydim-T<sub>2</sub>SO accounted for higher than 10%TRR in straw, husks and cobs. In all normal use rate samples except forage, the most prominent peak was very polar and eluted with the void volume from the HPLC column. The metabolites formed were further degraded and radioactivity incorporated into the carbohydrate pool.

In summary, cycloxydim is metabolized in plants mainly by four steps: 1) oxidation at the sulphur of the thiopyrane ring to the sulfoxide and to the sulphone, 2) cleavage of the oxime ether group (loss of the alkyl side chain), 3) hydroxylation at the 5-position of the cyclohexenone ring system and 4) oxidative cleavage of the cyclohexenone ring resulting in substituted glutaric acid derivatives. Cycloxydim was not present in any of the samples from treated crops at harvest, with the main metabolites being cycloxydim-TSO, cycloxydim-T<sub>2</sub>SO, cycloxydim-T<sub>1</sub>SO (sugar beet root) and cycloxydim-5-OH-TSO (soya bean).

### *Environmental fate in soil*

The aerobic degradation and metabolism of [<sup>14</sup>C]cycloxydim was studied in a loamy sand soil treated with 10 mg/kg dry soil, equivalent to a maximum single application rate of about 7.5 kg ai/ha, and to a multiple dose of 0.6 kg ai/ha. The soil was incubated at 22 ± 2 °C for 90 day. About 14% TRR was detected as cycloxydim at day 0, decreasing to 0.9%TRR after 14 days. Cycloxydim-TSO/cycloxydim-T1SO/cycloxydim-T2SO represented 16% TRR at 56 DAT and cycloxydim-T1S/cycloxydim-T2S/cycloxydim-TSO<sub>2</sub> represented 2.7% TRR at 28 DAT. After three months, bound residues accounted for about 40% TRR and CO<sub>2</sub> to 38% TRR. In another study conducted under the same conditions with loamy sand and a loam soils, cycloxydim accounted for over 90% TRR at day 0, decreasing to 4.6 and 0%TRR at day 21, respectively. Cycloxydim-TSO was the major metabolite found in soils (up to 39.5%TRR at 21 DAT and to 11% TRR at 90 DAT). In another study conducted with seven batches of sandy loam and loam sandy soils treated at 0.8 mg/kg, the soils were incubated for 119 days in the dark at 20 °C and 40% maximum water holding capacity. The degradation of cycloxydim was very fast in the soils (DT<sub>50</sub> < 9 hours), with up to 18% of the applied radioactivity (TAR) found at 0 DAT. Cycloxydim-TSO (5–6%TAR), cycloxydim-TSO<sub>2</sub> (1.5–2.8%TAR) and cycloxydim-T2SO (about 1%TAR) were the major metabolites at 60 DAT, with DT<sub>50</sub> of 9.3–1.6 days, 8.8–13 days and 19–291 days, respectively.

The photolytic degradation of cycloxydim was studied on loamy sand soil treated with 10 mg/kg dry and incubated at 30 ± 5 °C for 8 hours. Bound residues were similar with and without irradiation (maximum about 8–15% TAR). Polar degradation products did not accumulate in the course of the study. Cycloxydim residues dropped to 2% TAR at 8 hours. Cycloxydim-TSO/cycloxydim-T2SO accounted to 77–81% TAR after 3 to 8 hours of incubation.

Confined rotational studies were conducted with [<sup>14</sup>C]cycloxydim applied to soils at 0.65 kg ai/ha. The treated soils were aged for 30 days (radish and lettuce), 80 days (wheat), 120 days and 365 days. Residues in soil were 4.84 mg/kg eq. at day 0 and 0.034 to 0.136 mg/kg eq. after aging and harvesting in all cases. At 30 DAT, TRRs in lettuce (67 days after planting, DAP) and radish root and top (86 DAP) ranged from 0.032 to 0.051 mg/kg eq. At 120 and 365 DAT they ranged from 0.003 to 0.011 mg/kg. At 80, 120 and 365 DAT (118 to 169 DAP) residues ranged from 0.014 to 0.098 mg/kg eq. in wheat grain, from 0.07 to 0.14 mg/kg in straw and from 0.05 to 0.14 mg/kg in chaff. In wheat forage (57 to 70 DAP), they ranged from 0.008 to 0.031 mg/kg. At 30 DAT, cycloxydim-TSO and cycloxydim-TSO<sub>2</sub> were the major metabolites in lettuce (0.008 mg/kg, 16%TRR), radish root (0.002 mg/kg, 6.3% TRR) and top (0.006 mg/kg, 12% TRR). At 120 DAT, only cycloxydim-TSO<sub>2</sub> could be detected as a single compound (in radish, 10%TRR, 0.001 mg/kg). At 80 DAT, cycloxydim-TGSO<sub>2</sub> was the major metabolite in wheat forage (0.008 mg/kg, 26% TRR), and cycloxydim-T2SO (0.03 mg/kg, 20% TRR) and cycloxydim-T1SO (0.02 mg/kg, 16% TRR) in straw. No single residues > 10%TRR were found in wheat commodities at 120 and 365 DAT.

In summary, cycloxydim is extensively and rapidly degraded in soil (DT<sub>50</sub> < 9 hours), mainly to cycloxydim-TSO, cycloxydim-T1SO and cycloxydim-T2SO. Cycloxydim-TSO and cycloxydim-TSO<sub>2</sub> were found in lettuce and radish planted on aged treated soil. Cycloxydim-TGSO<sub>2</sub> (cycloxydim-1-dicarboxylic acid) was the main residue in succeeding wheat forage, and cycloxydim-T1SO and cycloxydim-T2SO in wheat straw (80 DAT). No single residues were detected in wheat grain planted in aged treated soil.

### *Methods of analysis*

Two common moiety analytical methods were developed, allowing the determination of cycloxydim, cycloxydim-5-OH-TSO<sub>2</sub> and all metabolites that can be oxidized to cycloxydim-TGSO<sub>2</sub> or cycloxydim-5-OH-TGSO<sub>2</sub> with H<sub>2</sub>O<sub>2</sub> under alkaline conditions in various plant matrices. In the LC-MS/MS method, the residues are extracted with isopropanol/water and hydrogen peroxide to form the corresponding pentane acids, the acids removed by precipitation with Ca(OH)<sub>2</sub>, the excess of oxidizing agent eliminated using a C<sub>18</sub>-column and, after a NH<sub>2</sub>-column clean-up, cycloxydim-TGSO<sub>2</sub> and cycloxydim-5-OH-TGSO<sub>2</sub> are analysed. In the GC method, the acids are converted into the dimethyl esters cycloxydim-TDME and cycloxydim-OH-TDME, cleaned up in silica gel and

analysed by GC/FPD or GC/MS. [<sup>14</sup>C]cycloxydim studies showed that extraction with isopropanol/water released from 66 to 94%TRR. Both GC and LC methods were satisfactorily validated at 0.05 mg/kg (LOQ) or higher levels (up to 5 mg/kg), using cycloxydim and cycloxydim-OH-SO<sub>2</sub> as representative analytes for the non-hydroxylated and hydroxylated compounds, respectively, or with different metabolites.

Cycloxydim-TSO can be selectively analysed in plant matrices after extraction with methanol/water buffer, saturation with NaCl-solution and partitioned with dichloromethane. The aqueous phase is acidified, residues extracted with isoctane/dichloromethane, the extract washed with saturated NaCl-solution, re-extracted with NaCl-solution, the aqueous phase purified by C<sub>18</sub>SPE and residues determined by HPLC/UV. LOQ was 0.05 mg/kg.

Common moiety methods were also validated in matrices of animal origin, with an LOQ of 0.05 mg/kg for tissues and eggs and 0.01 mg/kg for milk (GC method) or 0.01 mg/kg (tissues and eggs) and 0.003 mg/kg (milk) in the LC methods. Efficiency of the acetonitrile/hexane extraction was comparable with the results from hen metabolism studies (methanol extraction) for eggs and muscle, but not for liver, where acetonitrile/hexane only extracts about 50–70% of the radioactivity. The efficiency of the acetonitrile/hexane extraction of liver, kidney and milk was also comparable with the results obtained in the goat metabolism studies.

### ***Stability of residues in stored analytical samples***

The stability of cycloxydim, cycloxydim-TSO + cycloxydim-T<sub>2</sub>SO<sub>2</sub> and/or cycloxydim-5-OH-TSO<sub>2</sub> residues was investigated in various plant matrices fortified at 0.4 to 0.5 mg/kg levels stored at -20 °C over a period of up to 2 years. Samples were analysed immediately after spiking and after different storing intervals using the common moiety methods. The results showed that the residues were stable (70–110% remaining) for at least 2 years of storage in most cases.

Liver and milk samples from animal metabolism studies with [<sup>14</sup>C]cycloxydim or [<sup>14</sup>C]cycloxydim-5-OH-TSO were re-extracted with methanol or acetonitrile/hexane (4:3) in order to investigate their stability in animal matrices stored for a period of 78–89 month at -20 °C. The results showed that cycloxydim levels decreased over time while its metabolites increased (cycloxydim-TISO and cycloxydim-5-OH-T<sub>2</sub>SO). This degradation is not relevant when the common moiety method is used to analyse the samples in the trials.

### ***Residue definition***

Metabolism studies conducted in hens and goats with cycloxydim showed that the parent compound was only detected in liver (0.008 mg/kg, 10.8%TRR). The main metabolites found were cycloxydim-TSO, cycloxydim-TSO<sub>2</sub> (hens and goats) and cycloxydim-TISO (up to 14.8%TRR in milk). Residues were present in fat and muscle at about the same level.

Metabolism studies conducted in soya bean, cotton, sugar beet and maize with cycloxydim have showed that the parent compound was not present in any of the samples at harvest, with the main metabolites being cycloxydim-TSO, cycloxydim-T<sub>2</sub>SO, cycloxydim-TSO<sub>2</sub>, cycloxydim-TISO and cycloxydim-5-OH-TSO.

In all the supervised trials and animal feeding studies submitted to the Meeting, residues were measured using one of the common moiety methods, where residues present in the samples are oxidized to cycloxydim-TGSO<sub>2</sub> (including cycloxydim-TSO, cycloxydim-T<sub>2</sub>SO, cycloxydim-TSO<sub>2</sub>, cycloxydim-TISO) and/or cycloxydim-5-OH-TGSO<sub>2</sub> (including cycloxydim-5-OH-TSO) and analysed by LC-MS/MS or further methylated to cycloxydim-TMDE and/or cycloxydim-5-OH-TMDE for analysis by GC/FPD or GC/MS.

The Meeting agreed that the common moiety analytical methods analyse all the relevant residues formed when cycloxydim is applied on the field or when residues present in feed are ingested by farm animals.

The residue definition for animal and plant commodities for enforcement and risk assessment purposes is: *Cycloxydim, metabolites and degradation products which can be oxidized to 3-(3-thianyl) glutaric acid S-dioxide and 3-hydroxy-3-(3-thianyl) glutaric acid S-dioxide, expressed as cycloxydim.*

The residue is not fat-soluble

### ***Results of supervised residue trials on crops***

In some countries, cycloxydim label does not specify the PHI, indicating that the product should be applied when the weeds are actively growing. When a GAP with no specified PHI was used to support the trials, the highest residue found in the trials at any DAT, except the 0 day, was selected for the estimation.

The OECD MRL calculator was used to assist in the estimation of maximum residue levels from the selected residue data set obtained from the supervised residue trials. The Meeting reviewed the trial conditions and other relevant factors related to each dataset to arrive at a best estimate of the maximum residue level using expert judgment. When the OECD calculator suggested a different value, an explanation on the discrepancy was included in the text.

#### *Pome fruits and stone fruits*

Cycloxydim is registered to be used by direct spraying to control weeds in apple and pear orchards in Portugal using one application at 0.4 kg ai/ha and 28 days PHI. Two trials were conducted with apples and two with pears in Italy and Spain, matching the GAP of Portugal, gave residues of cycloxydim < 0.09 mg/kg (4).

Cycloxydim is registered to be used by direct spraying to control weeds in Italy in apricot and peach orchards up to 0.6 kg ai/ha with a 30 day PHI. In three trials in peaches and two in apricots conducted in Italy, at GAP, residues were < 0.09 mg/kg (5).

The Meeting concluded that on the basis of the data from these nine trials that the application of cycloxydim to the orchard floor, matching GAP, does not result in residues in the fruit.

The Meeting estimated a maximum residue level of 0.09\* mg/kg, a HR of 0.09 mg/kg and a STMR of 0.09 mg/kg for cycloxydim in pome fruits and stone fruits

#### *Grapes*

The critical application rate of cycloxydim used for directed spraying to control weeds in grapes is a single application at 0.4 kg ai/ha in Spain and 0.6 kg ai/ha in Switzerland, with no specified PHI.

Eight trials were conducted in northern/central France and Germany, matching the GAP of Switzerland, gave residues of (n=8) < 0.09 (4), 0.13 (2) and 0.18 (2) mg/kg.

In eight trials conducted in Italy, Greece and Spain according to Spanish GAP, residues were < 0.09 mg/kg (8).

Based on the residue data from trials conducted in northern Europe, the Meeting estimated a maximum residue level of 0.3 mg/kg, a HR of 0.18 mg/kg and a STMR of 0.11 mg/kg for cycloxydim in grape.

The Meeting withdrew its previous recommendation of 0.5 mg/kg for cycloxydim in grape.

#### *Strawberry*

Cycloxydim is registered for use in strawberries in Switzerland at 1 × 0.6 kg ai/ha with a 42 day PHI and in Slovakia at 1 × 0.4 kg ai/ha and no PHI specified. The product is also registered in Romania at 1 × 0.4 kg ai/ha with no PHI specified.

Seven trials conducted according to Slovakian GAP in France (north), the Netherlands, Germany and the UK, gave total cycloxydim residues of 0.19, 0.22, 0.29, 0.33, 0.34 0.47 and

0.61 mg/kg. One trial conducted in Sweden according to the GAP of Switzerland gave residues of 0.63 mg/kg.

Eight trials were conducted in southern France, Greece, Italy and Spain matching Romanian GAP, gave residues of 0.29, 0.33, 0.35, 0.49, 0.57, 0.74, 1.2 1.4 and 1.4 mg/kg

Based on the residue data from trials conducted in southern Europe, the Meeting estimated a maximum residue level of 3 mg/kg, a HR of 1.4 mg/kg and a STMR of 0.53 mg/kg for cycloxydim in strawberries.

The Meeting withdrew its previous recommendation of 0.5 mg/kg for cycloxydim in strawberries.

#### *Onion, Bulb*

Cycloxydim is registered in the Netherlands at up to 2 × 0.6 kg ai/ha with a 21 day PHI. In Belgium, the GAP is for 1 × 0.6 kg ai/ha and a 28 day PHI. In Italy, the GAP is for 1 × 0.6 kg ai/ha and a 60 day PHI. In Spain, it is 1 × 0.4 kg ai/ha with no PHI specified.

In four trials conducted in the UK matching the GAP of the Netherlands, residues were < 0.09 (4).

In seven trials conducted in France, the Netherlands, Sweden and the UK, complying with Belgian GAP, residues were: < 0.09 (3), 0.21, 0.25, 0.31 and 0.39 mg/kg.

In four trials conducted in Greece, Spain and Italy matching Italian GAP, residues were < 0.09 (2), 0.19 and 0.24 mg/kg.

In four trials conducted in France (south), Italy, Greece and Spain according to Spanish GAP residues were: 0.17, 0.25, 0.32 0.98, and 1.3 mg/kg

Based on the residue trials conducted according to GAP in Spain, and with the results from the other trials conducted in Europe used as supporting data, the Meeting estimated a maximum residue level of 3 mg/kg, a HR 1.3 mg/kg and a STMR of 0.285 mg/kg for cycloxydim in bulb onions.

#### *Leek*

Cycloxydim is registered for use in leeks in Portugal with a GAP of 1 × 0.4 kg ai/ha and a 42 day PHI. In Ireland, the rate is the same but no PHI is specified. In Switzerland, GAP consists of 1 × 0.6 kg ai/ha and a 56 day PHI

In six trials conducted in Belgium, Denmark, Germany and the UK matching Irish GAP, residues were 0.13, 0.28, 0.33, 0.39, 0.62 and 2.3 mg/kg.

In four trials conducted in the Netherlands according to the GAP of Switzerland, residues were 0.11, 0.12, 0.21 and 0.24 mg/kg.

In three trials conducted in southern France, Italy and Spain according to Portuguese GAP, residues were < 0.09 (2) and 0.09 mg/kg.

Based on the residue trials conducted according to the GAP in Ireland, the Meeting estimated a maximum residue level of 4 mg/kg, a HR of 2.3 mg/kg and a STMR of 0.36 mg/kg for cycloxydim in leek.

#### *Brassica vegetables*

Cycloxydim is registered in Brassica vegetables in Switzerland at 1 × 0.6 kg ai/ha and a 28 day PHI, and in Spain at 1 × 0.4 kg ai/ha with no specified PHI.

Twelve trials were conducted in Brussels sprouts in Europe at 0.5 kg ai/ha. Residues from seven trials conducted in Belgium, France (north), Germany, the Netherlands and the UK according to the GAP in Switzerland were: 1.0, 1.1, 1.8 (2), 2.0, 2.9 and 3.6 mg/kg.

Four trials conducted in France (south), Italy, Spain and Greece according to Spanish GAP gave residues of 1.9, 2.6, 3.5 and 6.0 mg/kg.

Residues in Brussels sprouts from trials matching comparable GAP in northern and southern Europe were considered similar and could be combined, were (n=12): 1.0 (2), 1.1, 1.8 (2), 1.9, 2.0, 2.6, 2.9, 3.5, 3.6 and 6.0 mg/kg.

Fourteen trials were conducted in cabbages at 0.5–0.6 kg ai/ha. In nine trials conducted in France (north), Germany, Sweden, Belgium and the UK according to the GAP of Switzerland, residues were: < 0.09, 0.40, 0.50 (2), 0.63, 0.74, 1.0, 1.3 and 3.0 mg/kg. In five trials conducted in Spain, France (south), Greece and Italy according to Spanish GAP (sample taken at 28 days after application), residues were: 0.88, 1.0, 1.2, 1.4 and 1.7 mg/kg.

Twelve trials were conducted in Europe in cauliflower at 0.5–0.6 kg ai/ha. In eight trials conducted in Belgium, France (north), Sweden and the UK according to the GAP of Switzerland, residues were: 0.27, 0.59, 1.5 (2), 1.7, 1.9, 2.1 and 2.3 mg/kg. Four trials conducted in southern Europe did not match the GAP.

Based on the residue data for Brussels sprouts the Meeting estimated a maximum residue level of 9 mg/kg, a HR of 6 mg/kg and a STMR of 5 mg/kg for cycloxydim in Brassica (Cole or Cabbage) Vegetables, Head Cabbage and Flowerhead Brassicas

The Meeting withdrew its previous recommendations.

#### *Peppers*

Cycloxydim is registered in peppers (chili and sweet) in Italy at  $1 \times 0.60$  kg ai/ha and a 20 day PHI. In eight trials conducted peppers in southern Europe according to this GAP, residues were: 0.68, 0.78, 1.2, 1.5, 1.6, 3.0, 3.1, and 5.3 mg/kg.

The Meeting estimated a maximum residue level of 9 mg/kg, a HR of 5.3 mg/kg and a STMR of 1.55 mg/kg for cycloxydim in peppers.

The Meeting also estimated a maximum residue level of 90 mg/kg, a HR-P of 53 mg/kg and a STMR-P of 15.5 mg/kg for cycloxydim in dried chili peppers, by applying a factor of 10 to the MRL, HR and STMR values estimated for peppers.

#### *Tomatoes*

Cycloxydim is registered in tomatoes at  $1 \times 0.4$  kg ai/ha and a 35 day PHI in Greece, and at 0.6 kg ai/ha and a 56 day PHI in Switzerland.

In eight trials conducted in southern Europe according to Greek GAP, residues were: 0.12, 0.17, 0.25, 0.26, 0.31, 0.39, 0.43 and 0.55 mg/kg.

In eight trials conducted in northern Europe according to the GAP of Switzerland, residues were: 0.21, 0.39 (2), 0.44, 0.45, 0.46, 0.50 and 0.84 mg/kg.

Based on the residue trial population in North of Europe, the Meeting estimated a maximum residue level of 1.5 mg/kg, a HR of 0.84 mg/kg and a STMR of 0.445 mg/kg for cycloxydim in tomatoes.

#### *Chinese cabbage*

Cycloxydim is registered for brassica vegetables in Spain at  $1 \times 0.4$  kg ai/ha with no specified PHI.

In two trials conducted in Greece and Italy according to this GAP, residues were < 0.09 and 0.23 mg/kg

The Meeting agreed that there were insufficient data complying with GAP with which to estimate a maximum residue level for cycloxydim in Chinese cabbage.

*Kale*

Cycloxydim is registered for brassica vegetables in Switzerland at  $1 \times 0.6$  and a 28 day PHI and in Spain at  $1 \times 0.4$  kg ai/ha with no specified PHI.

In four trials conducted in kale, curly in France (north), Germany and the Netherlands according to the GAP of Switzerland, residues were: 0.77, 0.90 and 1.8 mg/kg.

In four trials conducted in France (south), Greece, Italy and Spain according to Spanish GAP, residues were:  $< 0.09$ , 0.23, 0.98 and 1.1 mg/kg.

Based on the residue data from trials conducted in south of Europe, the Meeting estimated a maximum residue level of 3 mg/kg, a HR of 1.1 mg/kg and a STMR of 0.65 mg/kg for cycloxydim in kale.

*Lettuce*

Cycloxydim is registered in lettuce (leaf and head) in Austria at  $1 \times 0.5$  kg ai/ha and a 14 day PHI, in France at 0.4 kg ai/ha and a 21 day PHI and in Slovenia at 0.4 kg ai/ha with a 14 day PHI. Twenty two trials were conducted in lettuce in Europe at 0.5 kg ai/ha, matching GAP rate in northern and southern Europe.

Six trials were conducted in northern Europe according to Austrian GAP, giving residues of 0.18, 0.28, 0.48, 0.65, 0.69 and 0.71 mg/kg.

Six trials were conducted in northern Europe according to French GAP, giving residues of 0.11, 0.12, 0.21, 0.28 and 0.34 (2) mg/kg.

In ten trials conducted in southern Europe according to Slovenian GAP, residues were: 0.09, 0.11, 0.24, 0.31 (2), 0.36, 0.38, 0.41 (2) and 1.0 mg/kg

Based on the residue trial population in southern Europe, the Meeting estimated a maximum residue level of 1.5 mg/kg, a HR of 1 mg/kg and a STMR of 0.335 mg/kg for cycloxydim in lettuce, head and lettuce, leaf.

The Meeting withdrew its previous recommendation of 0.2 mg/kg for cycloxydim in lettuce, head and lettuce, leaf.

*Spinach*

Cycloxydim is registered in spinach at  $1 \times 0.4$  kg ai/ha in Slovenia and in France, with PHIs of 28 days and 42 days, respectively. Eight trials were conducted in Europe at 0.5 kg ai/ha.

In four trials conducted in north of Europe according to French GAP, residues were:  $< 0.09$  (3) and 0.10 mg/kg

In four trials conducted in south of Europe according to Slovenian GAP, residues were:  $< 0.09$ , 0.19, 0.20 and 2.4 mg/kg.

The Meeting agreed that there were insufficient trials according to GAP to estimate a maximum residue level of cycloxydim in spinach.

*Green beans with pods*

Cycloxydim is registered in green beans at  $1 \times 0.6$  kg ai/ha in Belgium with a 28 day PHI. In Spain, the rate is 0.4 kg ai/ha with no PHI specified.

In ten trials conducted in northern Europe according to Belgian GAP, residues were:  $< 0.09$ , 0.21, 0.22, 0.26, 0.30, 0.40, 0.64, 0.73, 1.2 and 1.3 mg/kg

In eleven trials conducted in southern Europe according to Spanish GAP, residues were:  $< 0.05$ , 0.20 (2), 0.24, 0.29, 0.35, 0.41, 0.52, 0.56, 4.4 and 11 mg/kg.

Based on the residue trial population from southern Europe (statistically higher), the Meeting estimated a maximum residue level of 15 mg/kg, a HR of 11 mg/kg and a STMR of 0.35 mg/kg for cycloxydim in beans except broad bean & soya bean (green pods & immature seeds).

The Meeting withdrew its previous recommendation of 1 mg/kg for cycloxydim in common bean (pods and/or immature seeds).

#### *Peas, Shelled (succulent seeds)*

Cycloxydim is registered in green peas at 1 × 0.5 kg ai/ha in Germany with a 35 day PHI. In Spain, the rate is up to 0.4 kg ai/ha and no PHI is specified.

In seven trials conducted in northern Europe according to German GAP, residues in peas (seeds) were: 0.80, 1.2, 1.8, 2.5, 3.2, 4.4 and 4.7 mg/kg.

In eight trials conducted in south of Europe according to Spanish GAP rate (PHI from 28 to 49 days) were: 0.45, 0.84, 2.1, 2.3, 3.1, 5.3, 5.9 and 8.5 mg/kg.

Based on the residue trials in southern Europe, the Meeting estimated a maximum residue level of 15 mg/kg, and a STMR of 2.7 mg/kg for cycloxydim in peas, shelled (succulent seeds). The Meeting withdrew its previous recommendation of 2 mg/kg for cycloxydim in peas, shelled (succulent seeds) and of 1 mg/kg in peas (pods and succulent = immature seeds).

#### *Dry beans*

Cycloxydim is registered in dry beans at 1 × 0.45 kg ai/ha in France, with no PHI specified. Twenty one trials were conducted in Europe matching this GAP.

In eight trials conducted in northern Europe, residues were: 0.51, 1.5, 2.8, 4.4 (2), 7.9, 9.8 and 15 mg/kg.

In thirteen trials conducted in southern Europe, residues were: 0.20, 0.31, 0.57, 0.70, 1.1, 2.0, 2.4, 3.0, 3.5, 3.6, 4.0, 4.5 and 6.1 mg/kg

Based on the trials conducted in northern Europe the Meeting estimated a maximum residue level of 30 mg/kg, and a STMR of 4.4 mg/kg for cycloxydim in beans, dry.

The Meeting withdrew its previous recommendation of 2 mg/kg for cycloxydim in beans (dry).

#### *Dry peas*

Cycloxydim is registered in peas at 1 × 0.60 kg ai/ha in Sweden with no PHI specified. In Italy, the rate is the same with a 60 day PHI.

In four trials conducted in the Netherlands and the UK matching the GAP rate in Sweden, residues at 55 days PHI were: 1.2, 3.4, 5.9 and 12 mg/kg.

In ten trials conducted in south of Europe according to Italian GAP, residues were: 0.30, 0.69, 0.84, 1.6 (2), 3.2 (2), 3.6, 5.5 and 5.9 mg/kg.

The Meeting estimated a maximum residue level of 30 mg/kg, and a STMR of 5.6 mg/kg for cycloxydim in peas, dry.

#### *Soya beans*

Cycloxydim is registered in soya beans at 1 × 0.40 kg ai/ha in France with a 56 day PHI. In Spain, the rate is the same, with no PHI specified,

In thirteen trials conducted in Europe at 0.5 kg ai/ha and PHI of 49–63, matching GAP in France and Spain, residues were: 0.23, 0.83, 1.2, 2.8, 3.4, 9.2, 13, 14, 26, 30 (2), 33 and 40 mg/kg.

The Meeting estimated a maximum residue level of 80 mg/kg, and a STMR of 13 mg/kg for cycloxydim in soya bean, dry.

The Meeting withdrew its previous recommendation of 2 mg/kg for cycloxydim in soya beans.

#### *Carrots*

Cycloxydim is registered in carrots in Belgium at a single application up to 0.60 kg ai/ha and in Portugal at 0.40 kg ai/ha, with a PHI of 28 days. Eleven trials were conducted in Europe at 0.50 kg ai/ha, matching both the GAP rates of Belgium and Portugal.

Residues, at the 28 day PHI, from northern European trials according to Belgian GAP were: 0.32, 0.42, 0.44 and 0.64 mg/kg.

Trials from southern Europe, according to Portuguese GAP at the 28 day PHI, gave residues of: 0.18, 0.29, 0.33, 0.44, 0.47, 1.1 and 3.0 mg/kg.

Based on the residue trials from southern Europe, the Meeting estimated a maximum residue level of 5 mg/kg, a HR of 3 mg/kg and a STMR of 0.44 mg/kg for cycloxydim in carrots.

The Meeting withdrew its previous recommendation of 0.5 mg/kg for cycloxydim in carrots.

#### *Celeriac*

Cycloxydim is registered in celeriac in France at 1 × 0.60 kg ai/ha and a 48 day PHI.

In eight trials conducted in Europe according to this GAP, residues were: 0.10, 0.12, 0.13 (3), 0.14, 0.19 and 0.64 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, a HR of 0.64 mg/kg and a STMR of 0.13 mg/kg for cycloxydim in celeriac.

#### *Potatoes*

Cycloxydim is registered in potatoes at 1 × 0.60 kg ai/ha in Belgium and the Netherlands with a 56 day PHI. In Italy, the rate is the same with a 100 day PHI. In ten trials conducted in northern Europe according to Belgian GAP, residues were: 0.31, 0.41, 0.55, 0.65, 0.72, 0.75, 0.79, 1.0, 1.2 and 1.6 mg/kg.

Seven trials conducted in southern Europe, according to Italian GAP, residues were: < 0.09 (2), 0.10, 0.21, 0.27, 0.44 and 0.46 mg/kg.

Based on the residue trials in north of Europe, the Meeting estimated a maximum residue level of 3 mg/kg, a HR of 1.6 mg/kg and a STMR of 0.735 mg/kg for cycloxydim in potatoes.

The Meeting withdrew its previous recommendation of 2 mg/kg for cycloxydim in potatoes.

#### *Turnips*

From six trials on turnips conducted in Norway at a rate of 0.6 kg ai/ha residues in turnip roots 77 to 103 days post application were: < 0.09 to 0.13 mg/kg. The GAP rate in Europe is up to 0.4 kg ai/ha.

As no trials were conducted according to GAP, the Meeting did not estimate a maximum residue level for cycloxydim in turnips.

#### *Sugar beet*

Cycloxydim is registered in sugar beet at 1 × 0.50 and 0.60 kg ai/ha in Germany and the Netherlands, respectively, no PHI specified. In Italy, the rate is 0.60 kg ai/ha and 100 days PHI. GAP for swede in THE UK is 0.45 kg ai/ha with 56 days PHI and for beetroot in Switzerland is 0.60 kg ai/ha with 56 days PHI.

In ten trials conducted in north of Europe according to German GAP, residues were < 0.09 (9) and 0.10 mg/kg.

In eight trials conducted in south of Europe according to Italian GAP, residues were < 0.09 (8) mg/kg.

Based on the residue trials in north of Europe, the Meeting estimated a maximum residue level of 0.2 mg/kg, a HR of 0.1 mg/kg and a STMR of 0.09 mg/kg for cycloxydim in sugar beet.

The Meeting agreed to extrapolate these estimations to beetroot and swede.

The Meeting confirms its previous recommendation of 0.2 mg/kg for cycloxydim in sugar beet.

#### *Maize*

Cycloxydim is registered in Germany for use in maize at  $1 \times 0.40$  kg ai/ha (no PHI specified) and France (90 days PHI).

In six trials conducted in northern Europe, matching German GAP, residues were: < 0.09 (5) and 0.12 mg/kg.

In eight trials conducted in southern Europe, according to French GAP, residues were: < 0.09 (8) mg/kg.

Based on trials conducted in northern Europe, the Meeting estimated a maximum residue level of 0.2 mg/kg, and a STMR of 0.09 mg/kg for cycloxydim in maize grain.

#### *Rice*

Cycloxydim is registered in rice in Italy at  $1 \times 0.40$  two days before sowing, with no PHI specified. In 11 trials conducted in the country according to GAP, residues found in grain, 133 to 162 days after treatment, were: < 0.09 (11) mg/kg.

The Meeting estimated a maximum residue level of 0.09\* mg/kg, and a STMR of 0.09 mg/kg for cycloxydim in rice.

#### *Rape seed*

Cycloxydim is registered in rape seed at  $1 \times 0.60$  kg ai/ha in Italy, with a PHI of 100 days. In Germany the rate is 0.50 kg ai/ha with no PHI specified.

In nine trials conducted in northern Europe, according to German GAP, residues at PHIs from 85 to 100 days PHI were: 0.77, 1.0, 1.5, 1.6, 1.8, 1.9, 2.2, 2.5 and 5.3 mg/kg

In six trials conducted in southern Europe, according to Italian GAP residues were: 0.54, 1.6, 1.8, 2.8, 3.1 and 4.0 mg/kg

The fifteen trials conducted according to the same GAP in the south and north of Europe belonged to the same residue population and were combined: 0.54, 0.77, 1.0, 1.5, 1.6 (2), 1.8, 1.9, 2.2, 2.5, 2.8 (2), 3.1, 4.0 and 5.3 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg, and a STMR of 1.9 mg/kg for cycloxydim in rape seed.

The GAP for linseed in Sweden is 0.6 kg ai/ha with no PHI specified. The Meeting agreed to extrapolate the rape seed estimates to linseed.

The Meeting withdrew its previous recommendation of 2 mg/kg for cycloxydim in rape seed.

#### *Sunflower*

Cycloxydim is registered in sunflower at  $1 \times 0.60$  kg ai/ha in Italy, with a PHI of 80 days. In Germany the rate is 0.50 kg ai/ha with a 100 day PHI.

In four trials conducted in northern Europe according to German GAP, residues were: < 0.09, 0.37, 0.38 and 2.8 mg/kg.

In 15 trials conducted in southern Europe, according to Italian GAP, residues were: < 0.09 (4), 0.09, 0.12, 0.14, 0.25, 0.28, 0.37, 0.38, 0.39, 0.50, 0.94 and 1.8 mg/kg.

Based on the data coming from northern Europe, and with the support of the other trials conducted in Europe, the Meeting estimated a maximum residue level of 6 mg/kg, and a STMR of 0.375 mg/kg for cycloxydim in sunflower seed.

### ***Feed commodities***

Maximum residue levels will not be estimated for forage commodities as it is understood that the international trade of such commodities is unlikely. Highest residue and/or STMR will be estimated for commodities listed in the OECD feeding table for animal dietary burden calculation purposes.

#### *Bean vines*

Residues of cycloxydim in bean vine (whole plant or rest of the plant) from trials conducted in northern Europe, according to GAP (0.4–0.45 kg ai/ha, no PHI specified), were (n=7): 0.3, 0.84, 0.9, 0.99, 1.2, 1.4 and 1.5 mg/kg.

Residues of cycloxydim in bean vine from trials conducted in southern Europe, according to GAP, were (n=9): 0.34, 0.43, 0.67, 0.71, 0.77, 1.2 (2), 1.3 and 2.0 mg/kg.

Based on the southern European trials, which gave the highest residues, the Meeting estimated a highest residue of 2 mg/kg and a STMR of 0.77 mg/kg for cycloxydim in bean vines.

#### *Pea vines*

Residues of cycloxydim in pea vine (whole plant or without the seed, or rest of the plant) from trials conducted in northern Europe, according to GAP (0.6 kg ai/ha, no PHI specified) were (n=8): 0.8, 0.93, 2.4, 2.5, 2.6, 3.5, 3.6 and 3.9 mg/kg.

Residues of cycloxydim in pea vine from trials conducted in southern Europe, according to GAP (0.6 kg ai/ha, 60 day PHI or 0.4 kg ai/ha no PHI specified), were (n=17): 0.14, 0.16, 0.21, 0.24, 0.27, 0.45, 1.1, 1.8 (2), 2.1, 2.2, 2.3, 5.5, 5.9, 6.1, 8.4 and 9.0 mg/kg.

Based on the southern European trials, which gave the highest residues, the Meeting estimated a highest residue of 9 mg/kg and a STMR of 1.48 mg/kg for cycloxydim in pea vines.

The Meeting also recommends a maximum residue level of 60 mg/kg for pea vines (dry) (25% DM).

#### *Sugar beet leaves or tops*

In ten trials conducted in northern Europe, according to GAP (0.5 kg ai/ha, no PHI specified), residues in the leaves (tops) were: < 0.09 (6), 0.09, 0.16, 0.33 and 0.50 mg/kg.

In six trials conducted in southern Europe according to GAP (0.6 kg ai/ha, 100 day PHI), residues were: < 0.09 (6) mg/kg.

Based on the northern European trials, the Meeting estimated a highest residue of 0.50 mg/kg and a STMR of 0.09 mg/kg for cycloxydim in sugar beet leaves or tops.

#### *Maize fodder*

In ten trials conducted with cycloxydim in northern Europe according to GAP (0.4 kg ai/ha, no PHI specified), residues in fodder were: < 0.09 (7), 0.11, 0.3 and 0.41 mg/kg.

In four trials conducted in south of Europe according to GAP (0.4 kg a.i./ha, 90 days PHI), residues were 0.10, 0.11, 0.29 and 1.1 mg/kg

Based on the trials conducted in southern Europe and with the support of the trials conducted in northern Europe the Meeting estimated a highest residue of 1.1 mg/kg and a STMR of 0.247 mg/kg for cycloxydim in maize fodder.

The Meeting also estimated a maximum residue level of 2 mg/kg in maize fodder, dry (85% DM).

#### *Rice straw and fodder*

In eight trials conducted with cycloxydim in Italy, according to GAP, residues in rice straw were: < 0.09 (8) mg/kg.

The Meeting estimated a maximum residue level of 0.09\* mg/kg, a HR of 0.09 mg/kg and a STMR of 0.09 mg/kg for cycloxydim rice straw (DM=90%).

#### *Rape forage*

In three trials conducted in Norway according to GAP, residues in rape seed forage were 0.24, 0.25 and 0.26 mg/kg.

The Meeting agreed that three trials according to GAP was sufficient to estimate a highest residue for cycloxydim in rape forage.

#### ***Fate of residues in processing***

The [<sup>14</sup>C]-cycloxydim was dissolved in aqueous buffer solution at pH 4 and heated for 20 minutes at 90 °C to simulate pasteurization, at pH 5 and refluxed at 100 °C for 60 minutes to simulate baking, brewing and boiling, and at pH 6 at about 120 °C in an autoclave for 20 minutes to simulate pasteurization. Cycloxydim degraded mainly to cycloxydim-T2S, which accounted for 93.5, 86.8 and 75% of the total applied radioactivity (TAR), respectively. T2SO accounted for up to 11% TAR (at pH 6).

A variety of processing studies were conducted with crops treated with cycloxydim. Processing factors (PF) in commodities with relevance for dietary exposure assessment and for animal dietary burden calculation are shown in the Table below. The estimated PFs were multiplied by the estimated HR and STMR of the raw commodity to estimate the HR-P and STMR-P for the processed commodity.

Processing factor (PF) and estimations for processed commodities

Commodity	Best estimate PF (n)*	STMR-P, mg/kg	HR- P, mg/kg
<i>Strawberry, STMR= 0.53 mg/kg, HR=1.4 mg/kg</i>			
Strawberry jam	0.55 (4)	0.291	
Strawberry canned	0.90 (4)	0.447	1.26
<i>Onion, STMR=0.285 mg/kg, HR= 1.3 mg/kg</i>			
Onion, peeled	1.1 (2)	0.31	1.43
<i>Cabbage, STMR=1.95 mg/k, HR= 9.0 mg/kg</i>			
Cabbage, cooked	0.56 (4)	1.09	5.04
Pasteurized sauerkraut	0.78 (4)	1.17	
<i>Tomato, STMR=0.445mg/kg , HR= 0.89 mg/kg</i>			
Tomato, canned	0.57 (4)	0.254	0.51
Tomato juice	1.1 (4)	0.49	
Ketchup	1.8 (4)	0.801	
Tomato pure, pasteurized	3.7 (4)	1.65	
<i>Pea, STMR=5.6 mg/kg</i>			
Pea, cooked	0.7 (4)	3.92	
Pea, canned	0.2 (4)	1.12	
<i>Carrot, STMR= 0.44 mg/k, HR= 3.0 mg/kg</i>			
Carrot, cooked	0.77 (4)	0.339	2.31
Carrot, juice	0.50 (4)	0.22	
Carrot, canned	0.36 (4)	0.158	1.08

Commodity	Best estimate PF (n)*	STMR-P, mg/kg	HR- P, mg/kg
<i>Potato, STMR= 0.735 mg/kg, HR= 1.6 mg/kg</i>			
Potato, peeled	1.3 (4)	0.960	2.08
Potato, boiled	1.5 (4)	1.10	2.4
Potato, steamed	1 (4)	0.735	1.6
French fries	1.3 (4)	0.956	2.08
<i>Rape seed, STMR= 1.9 mg/kg</i>			
Rape oil, refined	< 0.05 (4)	0.095	
Rape oil meal	1.5 (6)	2.85	
<i>Sunflower, STMR=0.05 mg/kg</i>			
Sunflower oil	0.1 (2)	0.00	

\* number of processing studies

### Residues in animal commodities

#### Farm animal dietary burden

The Meeting estimated the dietary burden of cycloxydim in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops), the STMR, STMR-Ps or highest residue levels estimated at the present Meeting (see Table below). Dietary burden calculations are provided in Annex 6.

#### Livestock dietary burden for cycloxydim, ppm of dry matter diet

	US-Canada		EU		Australia		Japan	
	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Beef cattle	3.54	2.09	22.4	7.26	26.8 <sup>a</sup>	8.5 <sup>c</sup>	2.28	2.28
Dairy cattle	8.1	2.96	22.6 <sup>b</sup>	7.55 <sup>d</sup>	20.4	7.0	1.55	1.55
Poultry - broiler	3.47	3.47	6.06	3.92	5.1	5.1	0.07	0.07
Poultry - layer	3.47	3.47	10.89 <sup>e</sup>	4.32	5.1 <sup>f</sup>	5.1	0.08	0.08

<sup>a</sup> Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimated for mammalian tissues

<sup>b</sup> Highest maximum dairy cattle dietary burden suitable for maximum residue level estimated for mammalian milk

<sup>c</sup> Highest mean beef or dairy cattle dietary burden suitable for STMR estimated for mammalian tissues.

<sup>d</sup> Highest mean dairy cattle dietary burden suitable for STMR estimated for milk.

<sup>e</sup> Highest maximum poultry dietary burden suitable for maximum residue level estimated for poultry tissues and eggs.

<sup>f</sup> Highest mean poultry dietary burden suitable for STMR estimated for poultry tissues and eggs.

### Animal feeding studies

#### Cattle

A mixture of cycloxydim and cycloxydim-5-OH-TSO (2:1) was administered orally to cattle for 28 days at 5.1, 15.2 and 50.2 ppm feed levels. Residues (sum of non-hydroxylated and hydroxylated metabolites; expressed as parent equivalents) in milk was only detected at the highest dose, with a mean of 0.044 mg/kg. Mean residues in skim milk and cream (from day 21) were similar (0.044 and 0.033 mg/kg, respectively).

In muscle, residues were not detected at the lowest dose. Mean and highest residues were 15.2 ppm of 0.023 and 0.026 mg/kg, respectively. Mean and highest residues at 50.2 ppm were 0.073 and 0.088 mg/kg, respectively

In liver, mean residues were 0.043, 0.128 and 0.336 mg/kg were at feeding levels of 5.1, 15.2 and 50.2 ppm, respectively, with the highest residues of 0.045, 0.151 and 0.381 mg/kg, respectively. Residue 2 days after the dose withdrawal was 0.079 mg/kg.

In kidney, mean residues were 0.068, 0.202 and 0.593 mg/kg at feeding levels of 5.1, 15.2 and 50.2 ppm, respectively, with the highest residues of 0.073, 0.239 and 0.727 mg/kg, respectively. The residue 2 days after dose withdrawal was 0.057 mg/kg.

In fat, mean residues were < 0.019, 0.025 and 0.119 mg/kg at feeding levels of 5.1, 15.2 and 50.2 ppm, respectively, with the highest residues of < 0.019, 0.030 and 0.138 mg/kg, respectively. The residue 2 days after dose withdrawal was 0.020 mg/kg.

In another study conducted at the same dose levels, residues in milk (total, skin and cream), muscle and fat were only detected at the highest dose: mean of 0.020 mg/kg in milk and skim milk and 0.016 mg/kg in cream; mean and highest in muscle of 0.06 and 0.07 mg/kg, respectively and in fat of 0.10 and 0.12 mg/kg.

In liver, mean residues were 0.03, 0.12 and 0.29 mg/kg at 5, 15 and 50 mg/kg dose levels, respectively, with the highest residues of 0.04, 0.15 and 0.31 mg/kg, respectively. The residue 2 days after dose withdrawal was 0.06 mg/kg.

In kidney, mean residues were 0.05, 0.14 and 0.44 mg/kg at 5, 15 and 50 mg/kg dose levels, respectively, with the highest residues of 0.06, 0.18 and 0.51 mg/kg, respectively. The residue 2 days after dose withdrawal was 0.05 mg/kg.

### Poultry

A mixture of cycloxydim and cycloxydim-OH-TSO (1:1) was administered orally to groups of hens for 28 days at doses of 2.29, 6.71 and 23.2 ppm in the feed. Mean and highest residues in eggs detected at 6.71 ppm dose were 0.022 and 0.058 mg/kg, respectively (n=9). At the highest dose, mean and highest values were 0.065 and 0.102 mg/kg, respectively (n=9). Residues were < 0.02 mg/kg during the depuration phase (between 29 and 33 days). Residues were not detected above the LOQ in muscle and fat in any dose group. In liver, residues were detected only at the highest dose group (mean of 0.022 mg/kg and highest of 0.03 mg/kg).

In another study, cycloxydim and cycloxydim-OH-TSO (1:1) was administered to laying hens at a target dose level of 2.5, 7.5 and 25 ppm. Residues were not detected in muscle, liver and fat at any dose level. In eggs, residues were detected at the 7.5 ppm (mean of < 0.03 mg/kg, highest of 0.041 mg/kg) and at the 25 mg/kg dose (mean of 0.046 mg/kg, highest of 0.069 mg/kg). Residues during the depuration phase (3–7 days) were < 0.03 mg/kg.

### Animal commodity maximum residue levels

The residues expected in animal commodities based on the calculated animal burden and the feeding studies are shown in Table 3. The levels which the estimations were based are in bold.

Residues in kidney and liver at the expected dietary burden are outlined below.

	Feed level, ppm, for		Residue, mg/kg					Eggs
	Milk residues	Tissues and eggs residues	Milk	Muscle	Liver	Kidney	Fat	
<b>Highest residue level, cattle</b>								
Feeding study	50	15 50	0.032	0.026 0.088	0.151 0.381	0.239 0.727	0.030 0.138	
Burden and residue	22.6	26.8	0.014	0.047	0.228	0.40	0.066	
<b>STMR, cattle</b>								
Feeding study	50	5 15	0.032	< 0.019 0.026	0.036 0.124	0.059 0.171	< 0.019 0.027	
Burden and residue	7.55	8.5	0.0054	0.021	0.067	0.0984	0.022	
<b>Highest residue level, hens</b>								
Feeding study		6.7/7.5 23.2		< 0.02	0.03		< 0.02/< 0.03	0.058/0.041

	Feed level, ppm, for		Residue, mg/kg					Eggs
	Milk residues	Tissues and eggs residues	Milk	Muscle	Liver	Kidney	Fat	
Burden and residue		10.8		< 0.03	0.014		< 0.03	0.092/0.023
STMR, hens								
Feeding study		6.7/7.5 23.5		< 0.02	0.022		< 0.03	0.022/0.03
Burden and residue		5.1		0	0.0054		0	0.02/0.017

Based on the results obtained for cattle, the Meeting estimated for cycloxydim a maximum residue level of 0.02 mg/kg and a STMR of 0.005 mg/kg in milks; a maximum residue level of 0.06 mg/kg, a HR of 0.047 mg/kg and a STMR of 0.021 mg/kg in meat (from mammalian other than marine mammals); a maximum residue of 0.1 mg/kg, a HR of 0.066 mg/kg and a STMR of 0.021 mg/kg for mammalian fats (except milk fats); and a maximum residue level of 0.5 mg/kg, a HR of 0.403 mg/kg and a STMR of 0.098 mg/kg in edible offal (mammalian).

Based on the results obtained for hens, the Meeting estimated for cycloxydim a maximum residue level of 0.15 mg/kg, a HR of 0.092 mg/kg, and a STMR of 0.018 mg/kg in eggs; a maximum residue level of 0.03\* mg/kg, a HR of 0.03 mg/kg and a STMR of 0 mg/kg in poultry meat and poultry fats; and a maximum residue level of 0.02 mg/kg, a HR of 0.014 mg/kg and a STMR of 0.005 mg/kg for cycloxydim in poultry edible offal

## DIETARY RISK ASSESSMENT

### *Long-term intake*

The ADI for cycloxydim is 0–0.07 mg/kg bw. The International Estimated Daily Intakes (IEDI) for cycloxydim was estimated for the 13 GEMS/Food cluster diets using the STMR or STMR-P values estimated by the current JMPR. The results are shown in Annex 3. The IEDI ranged from 7–50% of the maximum ADI. The Meeting concluded that the long-term intake of residues of cycloxydim from uses that have been considered by the JMPR is unlikely to present a public health concern.

### *Short-term intake*

An ARfD for cycloxydim for women of childbearing age is 2 mg/kg bw; ARfD was unnecessary for the general population. The International Estimated Short-Term Intake (IESTI) for cycloxydim was calculated for the plant commodities for which STMRs, HRs and maximum residue levels were estimated by the current Meeting and for which consumption data were available. The results are shown in Annex 4. The IESTI represented a maximum of 10% of the ARfD for peppers, chili dried. The Meeting concluded that the short-term intake of cycloxydim residues from uses considered by the current Meeting was unlikely to present a public health concern.