## 5.24 SULFOXAFLOR (252)

### TOXICOLOGY

Sulfoxaflor is the International Organization for Standardization (ISO)–approved name for [methyl(oxo){1-[6-(trifluoromethyl)-3-pyridyl]ethyl}-$\lambda^6$-sulfanylidene]cyanamide (International Union of Pure and Applied Chemistry) (Chemical Abstracts Service No. 946578-00-3), a novel insecticide from the sulfoximine class. Sulfoxaflor contains two chiral centres (the sulfur atom and the carbon atom attached to position 3 of the pyridine ring) and is a mixture of the four possible stereoisomers. Both (*E*)- and (*Z*)-isomers (involving the S=N double bond and the cyano group) exist, but they rapidly interconvert at ambient temperatures. Sulfoxaflor is effective against a wide range of sap-feeding insects and exerts its insecticidal activity as an agonist at the insect nicotinic acetylcholine receptor (nAChR), which plays a central role in the mediation of fast excitatory synaptic transmission in the insect central nervous system. Sulfoxaflor has not been evaluated previously by the Joint FAO/WHO Meeting on Pesticide Residues and was reviewed at the present Meeting at the request of the Codex Committee on Pesticide Residues.

All pivotal studies were certified as complying with good laboratory practice or an approved quality assurance programme.

#### *Biochemical aspects*

In rats given sulfoxaflor labelled with $^{14}C$ at the pyridine ring orally by gavage, absorption was rapid and accounted for at least 93% of the total recovered radioactivity after a single dose of 5 mg/kg body weight (bw) or 100 mg/kg bw; the maximum plasma concentrations of radiolabelled material were reached after 0.5–1.6 hours and after 1.3–2.3 hours, respectively. Radiolabel was widely distributed throughout the body. Elimination of the radiolabel was mainly via the urine (≥ 92%). After intravenous administration, faecal excretion accounted for up to 9% of total excretion. Elimination of the radiolabel from plasma was bi-exponential, with most of the elimination occurring during the alpha phase, with a half-life of 4–6 hours, whereas the half-life of the beta phase was 39–45 hours. Residues in tissues 168 hours after a single oral or intravenous dose as well as after repeated oral dosing accounted for less than 1.3% of the administered dose, with liver, kidney and erythrocytes containing the highest concentrations of residues.

Sulfoxaflor was metabolized to only a very limited extent. The metabolism included oxidative cleavage of the parent molecule, leading to metabolite X11721061, which was subsequently conjugated with glucuronic acid. This was the only metabolite identified in urine, accounting for 3–4% of the administered dose.

#### *Toxicological data*

The median lethal dose ($LD_{50}$) in rats treated orally with sulfoxaflor was 1000 mg/kg bw. The dermal $LD_{50}$ in rats was greater than 5000 mg/kg bw, and the inhalation median lethal concentration ($LC_{50}$) in rats was greater than 2.09 mg/L. Sulfoxaflor was not a skin irritant in rabbits, was not irritating to the eye of rabbits and was not a skin sensitizer in the local lymph node assay in mice.

At least in part as a result of its unpleasant smell, sulfoxaflor is of limited oral palatability, so that repeated-dose studies by dietary as well as gavage administration were dose limited by effects on feed intake and consequent body weight reductions.

Following repeated administration of sulfoxaflor to mice and rats, the liver was the main target organ, and males were affected more than females. The effects noted at lower doses (increased liver weights, hepatocellular hypertrophy) were consistent with the induction of hepatic cytochrome P450, whereas effects observed at higher doses included hepatocellular degeneration or necrosis and

related clinical chemistry findings (e.g., increased serum levels of liver enzymes, cholesterol or triglycerides). In mice, the adrenals were an additional target, with hypertrophy and/or vacuolization of the zona fasciculata. In dogs, gavage administration gave the highest achievable doses, but the only effects were decreases in feed consumption and body weight gain and increased incidences of soft or watery faeces.

In a 28-day study in mice, the no-observed-adverse-effect level (NOAEL) was 300 ppm (equal to 43.9 mg/kg bw per day), based on effects in the liver (increased serum alanine aminotransferase, vacuolization/fatty change of hepatocytes) at 1500 ppm (equal to 230 mg/kg bw per day). In a 90-day study in mice, the NOAEL was 100 ppm (equal to 12.8 mg/kg bw per day), based on effects in the liver (vacuolization/fatty change of hepatocytes) and the adrenals (hypertrophy and/or vacuolization of the zona fasciculata) observed in males at 750 ppm (equal to 98 mg/kg bw per day) and in females at 1500 ppm (equal to 247 mg/kg bw per day).

In a 28-day study in rats, the NOAEL was 300 ppm (equal to 24.8 mg/kg bw per day), based on marginal liver toxicity (increased serum cholesterol and total protein levels) in males at 1000 ppm (equal to 79.4 mg/kg bw per day). In a 90-day study in rats, the NOAEL was 100 ppm (equal to 6.36 mg/kg bw per day), based on effects in the liver (increased serum cholesterol level, vacuolization/fatty change of hepatocytes) in males at 750 ppm (equal to 47.6 mg/kg bw per day). After a 28-day recovery phase, very slight histopathological changes in the liver (hypertrophy and fatty change of hepatocytes) were seen in males at 1500 ppm (equal to 94.9 mg/kg bw per day).

In a 90-day oral gavage study in dogs, the NOAEL was 6 mg/kg bw per day, based on decreased feed consumption and decreased body weights during the first week of exposure at 10 mg/kg bw per day. After reduction of this dose to 6 mg/kg bw per day on study day 5, no treatment-related adverse effects were observed. In a 1-year oral gavage study in dogs, the NOAEL was 6 mg/kg bw per day, the highest dose tested. The increased incidences of soft/watery faeces in two males at this dose were not considered adverse, as these changes were not accompanied by any other toxicological effect. Also, the slight decreases in feed consumption and body weight in two females during the first 2 weeks of dosing at 6 mg/kg bw per day were not considered adverse, as there were no changes during the remainder of the study. The overall NOAEL for the 90-day and 1-year studies was 6 mg/kg bw per day.

Long-term studies of toxicity and carcinogenicity were conducted in mice and rats. In an 18-month study of carcinogenicity in mice, the NOAEL for carcinogenicity was 100 ppm (equal to 10.4 mg/kg bw per day), based on an increased incidence of hepatocellular adenomas and/or carcinomas in males at 750 ppm (equal to 79.6 mg/kg bw per day). The NOAEL for non-neoplastic changes was 100 ppm (equal to 10.4 mg/kg bw per day), based on liver toxicity (vacuolization/fatty change of hepatocytes) in males at 750 ppm (equal to 79.6 mg/kg bw per day).

In a series of mechanistic studies in mice, including C57BL/6J “knockout” mice for pregnane X receptor (PXR) and constitutive androstane receptor (CAR) and C57BL/6J mice “humanized” for PXR and CAR, it was demonstrated that sulfoxaflor was a relatively potent phenobarbital-like inducer of hepatic P450 enzymes via activation of CAR and possibly, to some extent, PXR. This was apparent at the messenger ribonucleic acid, protein and enzyme activity level. Activation of the mouse CAR (and possibly PXR) resulted in increased hepatocyte hypertrophy and proliferation. The human CAR (and possibly PXR) supported modest P450 induction and hepatic hypertrophy by sulfoxaflor, but did not support any effect on hepatocyte proliferation.

In a 24-month study of toxicity and carcinogenicity in Fischer 344 rats, the NOAEL for carcinogenicity was 100 ppm (equal to 4.24 mg/kg bw per day), based on an increased incidence of hepatocellular adenomas in males at 500 ppm (equal to 21.3 mg/kg bw per day). Also at 500 ppm, there was an increased incidence of bilateral Leydig (interstitial) cell adenomas of the testes, whereas there was no effect on the incidence of combined unilateral/bilateral Leydig cell adenomas. The size and weight of the testes and the size of Leydig cell adenomas were increased at 100 and 500 ppm and were associated with the secondary changes in the testes and epididymides listed below. The NOAEL

for non-neoplastic effects was 25 ppm (equal to 1.04 mg/kg bw per day), based on changes in the testes (increased testes weights, increased incidence of severe bilateral atrophy of seminiferous tubules) and epididymides (decreased epididymal weights, increased incidence of severe bilateral decreased spermatic elements of the epididymides) in males at 100 ppm (equal to 4.24 mg/kg bw per day). In females, the NOAEL for non-neoplastic effects was 100 ppm (equal to 5.13 mg/kg bw per day), based on hepatocellular degeneration at 750 ppm (equal to 39.0 mg/kg bw per day).

In a mechanistic study on liver tumorigenesis in rats, 3-day or 7-day exposure to sulfoxaflor at dietary concentrations up to 1500 ppm (equal to 83–102 mg/kg bw per day) resulted in increased liver weights, increased cell proliferation in the centrilobular and midzonal regions of the hepatic lobules, marked induction of Cyp2b1 gene expression and hepatic activities of pentoxyresorufin-O-deethylase (PROD) and benzyloxyresorufin-O-deethylase (BROD), and moderate induction of Cyp2b2 and Cyp3a3 expression levels. The pattern of changes was phenobarbital-like, as evidenced by the CAR- and PXR-related molecular, enzymatic and proliferative responses.

The Meeting concluded that for the liver tumours in both mice and rats, there was sufficient evidence to support the proposed phenobarbital-like mode of action (MOA). In particular, sulfoxaflor exhibited clearly higher activity towards rodent CAR than towards human CAR. The marked qualitative and quantitative species differences in the key events in the MOA for neoplasia in response to CAR activation allowed for the conclusion that the sulfoxaflor-induced liver tumours in rats and mice are not relevant to humans.

In a mechanistic study conducted to examine the potential MOA for the Leydig cell effects seen in the rat carcinogenicity study, 8-week exposure of male Fischer 344 rats to sulfoxaflor at dietary concentrations up to 500 ppm (equal to 28 mg/kg bw per day) resulted in decreased serum prolactin and increased serum luteinizing hormone (LH) and testosterone levels and in decreased testis LH receptor (LHR) and prolactin receptor gene expression at week 4, but not at week 2 or week 8. Treatment had no effect on the percentage of Leydig cells with intracellular staining of LHR, biliary excretion of [$^{14}$C]testosterone, serum 17β-estradiol level or any measured gene in the steroidogenic pathway. Because Fischer 344 rats are particularly susceptible to effects on Leydig cells, analogous treatment of male Sprague-Dawley rats was performed, resulting in increased serum LH and testosterone levels at week 2 and a decrease in serum prolactin level at week 4.

In a mechanistic study using intracerebral microdialysis in rats, sulfoxaflor infusion (0.4 and 2 mmol/L) evoked dose-related increases in the extracellular level of dopamine in the mediobasal hypothalamus, with a maximal rise of 39%, 40 minutes after the onset of infusion at 2 mmol/L.

In a further mechanistic study on Leydig cell effects, sulfoxaflor did not bind to the estrogen receptor (ER) alpha and had weak binding affinity to the androgen receptor (AR), whereas it did not show any agonism or antagonism in the ER and ARe transactivation assays. In addition, there was no evidence for aromatase inhibition by sulfoxaflor.

Although the proposed MOA—that sulfoxaflor can act as a dopamine agonist in the central nervous system and may inhibit prolactin release in the pituitary (an MOA for the induction of Leydig cell tumours that is considered to be not relevant to humans)—has not been completely demonstrated, the Meeting concluded that the increased incidences of bilateral Leydig cell adenomas in male rats are of low relevance to humans, as there are large qualitative and quantitative differences between rats and humans regarding Leydig cell responses to hormonal stimuli. In addition, these effects occurred only at high doses, did not occur in mice and would be anticipated to exhibit a threshold. As a consequence, the secondary changes in the testes and epididymides would not be relevant to the dietary risk assessment of sulfoxaflor.

Sulfoxaflor was tested for genotoxicity in vitro and in vivo in an adequate range of assays. It was not found to be genotoxic in mammalian or microbial test systems.

The Meeting concluded that sulfoxaflor was unlikely to be genotoxic.

On the basis of the absence of genotoxicity, the human non-relevance of the liver tumours in both mice and rats and the fact that the Leydig cell responses observed in rats are unlikely to be relevant to humans, the Meeting concluded that sulfoxaflor is unlikely to pose a carcinogenic risk to humans at dietary exposure levels.

In a reproduction/developmental toxicity screening study in rats, the NOAEL for both parental toxicity and effects on offspring was 100 ppm (equal to 8.26 mg/kg bw per day), based on decreased body weight gains in females during the first week of gestation and reduced pup survival at 500 ppm (equal to 40.7 mg/kg bw per day).

In a two-generation reproductive toxicity study in rats, the NOAEL for effects on fertility was 400 ppm (equal to 24.6 mg/kg bw per day), the highest dose tested. The NOAEL for parental toxicity was 100 ppm (equal to 6.07 mg/kg bw per day), based on liver toxicity (increase in vacuolization/fatty change of centrilobular hepatocytes) in F0 males at 400 ppm (equal to 24.6 mg/kg bw per day). The NOAEL for offspring toxicity was 100 ppm (equal to 6.07 mg/kg bw per day), based on reduced pup survival and delayed preputial separation (puberty onset) in F2 males at 400 ppm (equal to 24.6 mg/kg bw per day).

In a cross-fostering study conducted to assess whether the observed effects of sulfoxaflor on neonatal survival in rats resulted from in utero and/or lactational exposure, all offspring from dams exposed to sulfoxaflor (1000 ppm, equal to 60–81 mg/kg bw per day) prior to birth died by postnatal day 4, irrespective of whether they were cross-fostered to control or treated foster dams. There was no effect on survival for pups exposed only after birth. Thus, the effect of sulfoxaflor on pup survival was due to in utero, not lactational, exposure.

In a developmental toxicity study in rats, the NOAEL for maternal toxicity was 150 ppm (equal to 11.5 mg/kg bw per day), based on decreased body weight and body weight gain and decreased feed consumption at 1000 ppm (equal to 70.2 mg/kg bw per day). The NOAEL for developmental toxicity was 150 ppm (equal to 11.5 mg/kg bw per day), based on increases in several fetal abnormalities (forelimb flexure, hindlimb rotation, bent clavicle, fused sternebrae, convoluted ureter and hydroureter) at 1000 ppm (equal to 70.2 mg/kg bw per day).

A series of special studies conducted to determine the critical window of developmental susceptibility of rat fetuses demonstrated that late gestational exposure (i.e. from gestation day 20 to gestation day 21 or 22) of dams to sulfoxaflor (1000 ppm, equal to 36–39 mg/kg bw per day) resulted in reduced neonatal survival and limb abnormalities seen in pups at postnatal days 1–3, whereas no limb abnormalities were observed at postnatal day 4 in the same litters. Offspring from dams exposed (at 1000 ppm, equal to 43–77 mg/kg bw per day) up to gestation day 19 did not show any limb abnormalities or reduced neonatal survival.

Histopathological evaluation of fetal lung samples from the prenatal developmental toxicity study in rats did not reveal any morphological abnormalities that could have contributed to the sulfoxaflor-induced neonatal mortality in rat pups.

In mechanistic studies conducted to test the hypothesis that the limb abnormalities and bent clavicles in rat fetuses are mediated by the pharmacological agonist action of sulfoxaflor at the fetal neuromuscular junction nAChR, radioligand binding and electrophysiological examination revealed that sulfoxaflor is an agonist of the rat fetal muscle nAChR (which contains the rat γ subunit), whereas it has no agonist activity on the equivalent human fetal nAChR (containing the human γ subunit) or on the rat or human adult muscle nAChR (containing the rat or human ε subunit). In rodents, replacement of the γ subunit by the ε subunit commences late during the first postnatal week and is largely complete by the end of the second postnatal week, whereas in humans, the switch from γ to ε subunit expression occurs predominantly during the late fetal period. These results were considered to support the hypothesis that sulfoxaflor induces fetal abnormalities and neonatal death in rats via its pharmacological action on the fetal muscle nAChR. This receptor develops functional expression between gestation days 16 and 17 in the rat, resulting in synchronized fetal limb movements and diaphragmatic responsiveness important for the transition to extrauterine respiration.

Two developmental toxicity range-finding studies in rabbits demonstrated that administration of sulfoxaflor in the diet afforded a greater applied maximally tolerated dose (1000 ppm, equal to 36.6 mg/kg bw per day) relative to gavage (15 mg/kg bw per day caused excessive maternal toxicity). Thus, dietary administration of sulfoxaflor was chosen for the main developmental toxicity study.

In a developmental toxicity study in rabbits, the NOAEL for maternal toxicity was 150 ppm (equal to 6.6 mg/kg bw per day), based on decreased faeces and decreases in body weight gain and feed consumption at 750 ppm (equal to 31.9 mg/kg bw per day). The NOAEL for prenatal developmental toxicity was 750 ppm (equal to 31.9 mg/kg bw per day), the highest dose tested.

In a special study conducted to assess the effects of sulfoxaflor on neonatal survival in rabbits, dams were exposed to sulfoxaflor (750 ppm, equal to 29 mg/kg bw per day) from gestation day 7 through the initiation of parturition and allowed to deliver and rear their offspring to lactation day 4. Dams showed decreased body weight gains and feed consumption, whereas no treatment-related effects on the mean number of offspring born, offspring survival or the general physical condition of the offspring were observed.

The Meeting concluded that for the limb abnormalities and bent clavicles observed in rats, there is sufficient evidence that these effects were induced by pharmacological action of sulfoxaflor at the rat fetal muscle nAChR, whereas sulfoxaflor has no agonist activity on the equivalent human fetal nAChR or on the rat or human adult muscle nAChR. This allowed for the conclusion that these effects are not relevant to humans. Regarding the reduced neonatal survival observed in rats, the Meeting noted that the human relevance for this effect cannot be excluded, as the underlying MOA is unclear.

In an acute neurotoxicity study in rats, the NOAEL for neurotoxicity was 25 mg/kg bw, based on decreased motor activity at 75 mg/kg bw. There was no evidence for neuropathological effects up to the highest dose tested (750 mg/kg bw).

In a developmental neurotoxicity study in rats, the NOAEL for maternal and reproductive toxicity was 400 ppm (equal to 28.8 mg/kg bw per day), the highest dose tested. The NOAEL for developmental neurotoxicity was 400 ppm (equal to 28.8 mg/kg bw per day), as there were no signs of developmental neurotoxicity at any exposure level. The NOAEL for neonatal toxicity was 100 ppm (equal to 7.4 mg/kg bw per day), based on the reduction in postnatal survival and pup body weights at 400 ppm (equal to 28.8 mg/kg bw per day).

***Toxicological data on metabolites***

X11719474, the major soil and plant metabolite of sulfoxaflor, was of low acute oral toxicity in rats ($LD_{50}$ > 5000 mg/kg bw) and showed no genotoxic potential in vitro in mammalian or microbial test systems. In a 90-day oral toxicity study in rats, the NOAEL was 1000 ppm (equal to 65.3 mg/kg bw per day), based on effects in the liver (vacuolization/fatty change) at 5000 ppm (equal to 327 mg/kg bw per day). In a reproduction toxicity screening study in rats, the NOAEL for reproductive and offspring performance was 5000 ppm (equal to 396 mg/kg bw per day), the highest dose tested. In a prenatal developmental toxicity study in rats, the NOAEL for developmental toxicity was 5000 ppm (equal to 368 mg/kg bw per day), the highest dose tested.

X11721061, a plant and animal (rat) metabolite of sulfoxaflor, was of low acute oral toxicity in rats ($LD_{50}$ > 2000 mg/kg bw) and showed no genotoxic potential in vitro in mammalian or microbial test systems. In a 28-day oral toxicity study in rats, the NOAEL was 3000 ppm (equal to 236 mg/kg bw per day), based on reduced feed consumption at 8000 ppm (equal to 622 mg/kg bw per day).

X11596066, a metabolite of sulfoxaflor identified in hens and goats, was of low acute oral toxicity in rats ($LD_{50}$ > 2000 mg/kg bw) and showed no genotoxic potential in vitro (Ames test).

X11579457, a soil metabolite of sulfoxaflor, was of low acute oral toxicity in rats ($LD_{50}$ > 2000 mg/kg bw) and showed no genotoxic potential in vitro in mammalian or microbial test systems.

X11519540, a soil and animal (hen) metabolite of sulfoxaflor, was of moderate acute oral toxicity in rats ($LD_{50}$ > 565 mg/kg bw) and showed no genotoxic potential in vitro in mammalian or microbial test systems. In a 28-day oral toxicity study in rats, the NOAEL was less than 100 ppm (equal to 7.7 mg/kg bw per day) in males, based on effects in liver (increased serum cholesterol), thyroid (follicular cell hypertrophy) and adrenals (increased vacuolization of the cortex).

All metabolites were less toxic than the parent compound, except for X11519540, which had higher acute and higher short-term toxicity than the parent.

There were no reports of adverse health effects in manufacturing plant personnel. Also, there were no reports of poisonings with sulfoxaflor.

The Meeting concluded that the existing database on sulfoxaflor was adequate to characterize the potential hazards to fetuses, infants and children.

## Toxicological evaluation

The Meeting established an acceptable daily intake (ADI) for sulfoxaflor of 0–0.05 mg/kg bw, based on a NOAEL of 5.13 mg/kg bw per day for hepatocellular degeneration in female rats in a 2-year toxicity and carcinogenicity study and application of a safety factor of 100. The ADI is supported by the NOAEL of 6.07 mg/kg bw per day for systemic toxicity (increased vacuolization/fatty change of centrilobular hepatocytes in $F_0$ males) and offspring toxicity (reduced neonatal survival) at 24.6 mg/kg bw per day in a two-generation rat study, the NOAEL of 6.36 mg/kg bw per day, based on effects in the liver (increased serum cholesterol, vacuolization/fatty change of hepatocytes) in a 13-week study in rats, and the overall NOAEL of 6 mg/kg bw per day in the 90-day and 1-year dog studies.

The Meeting established an acute reference dose (ARfD) for sulfoxaflor of 0.3 mg/kg bw, based on the NOAEL of 25 mg/kg bw for decreased motor activity at 75 mg/kg bw in an acute neurotoxicity study in rats. A 100-fold safety factor was applied.

A toxicological monograph was prepared.

### *Levels relevant to risk assessment*

| Species | Study | Effect | NOAEL | LOAEL |
|---|---|---|---|---|
| Mouse | Thirteen-week study of toxicity | Toxicity | 100 ppm, equal to 12.8 mg/kg bw per day | 750 ppm, equal to 98 mg/kg bw per day |
| | Eighteen-month study of toxicity and carcinogenicity | Toxicity | 100 ppm, equal to 10.4 mg/kg bw per day | 750 ppm, equal to 79.6 mg/kg bw per day |
| | | Carcinogenicity | 100 ppm, equal to 10.4 mg/kg bw per day | 750 ppm, equal to 79.6 mg/kg bw per day |
| Rat | Thirteen-week study of toxicity | Toxicity | 100 ppm, equal to 6.36 mg/kg bw per day | 750 ppm, equal to 47.6 mg/kg bw per day |
| | Two-year study of toxicity and carcinogenicity | Toxicity | 100 ppm, equal to 5.13 mg/kg bw per day | 750 ppm, equal to 39.0 mg/kg bw per day |
| | | Carcinogenicity | 100 ppm, equal to 4.24 mg/kg bw per day[a] | 500 ppm, equal to 21.3 mg/kg bw per day |
| | Two-generation study of reproductive toxicity | Reproductive toxicity | 400 ppm, equal to 24.6 mg/kg bw per day[b] | — |
| | | Parental toxicity | 100 ppm, equal to 6.07 mg/kg bw per day | 400 ppm, equal to 24.6 mg/kg bw per day |

| Species | Study | Effect | NOAEL | LOAEL |
|---|---|---|---|---|
| | | Offspring toxicity | 100 ppm, equal to 6.07 mg/kg bw per day | 400 ppm, equal to 24.6 mg/kg bw per day |
| | Developmental toxicity study | Maternal toxicity | 150 ppm, equal to 11.5 mg/kg bw per day | 1000 ppm, equal to 70.2 mg/kg bw per day |
| | | Embryo and fetal toxicity | 150 ppm, equal to 11.5 mg/kg bw per day | 1000 ppm, equal to 70.2 mg/kg bw per day |
| | Acute neurotoxicity study[b] | Neurotoxicity | 25 mg/kg bw | 75 mg/kg bw |
| | Developmental neurotoxicity study | Developmental neurotoxicity | 400 ppm, equal to 28.8 mg/kg bw per day[b] | — |
| Rabbit | Developmental toxicity study | Maternal toxicity | 150 ppm, equal to 6.6 mg/kg bw per day | 750 ppm, equal to 31.9 mg/kg bw per day |
| | | Embryo and fetal toxicity | 750 ppm, equal to 31.9 mg/kg bw per day[b] | — |
| Dog | Thirteen-week and 1-year studies of toxicity[c,d] | Toxicity | 6 mg/kg bw per day | 10 mg/kg bw per day |

[a] Not considered relevant for human risk assessment.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two studies combined.

*Estimate of acceptable daily intake for humans*

0–0.05 mg/kg bw

*Estimate of acute reference dose*

0.3 mg/kg bw

*Information that would be useful for the continued evaluation of the compound*

Results from epidemiological, occupational health and other such observational studies of human exposure

***Critical end-points for setting guidance values for exposure to sulfoxaflor***

| *Absorption, distribution, excretion and metabolism in mammals* | |
|---|---|
| Rate and extent of oral absorption | Rapid; ≥ 93% |
| Distribution | Extensive; highest concentrations in liver, kidney and erythrocytes |
| Rate and extent of excretion | ≥ 93% within 168 h (≥ 92% in urine; 5–9% in faeces) |
| Potential for accumulation | None |
| Metabolism in animals | Very limited, oxidative cleavage of the molecule, followed by conjugation with glucuronic acid; one metabolite identified in urine (conjugate of X11721061, 3–4% of administered dose) |
| Toxicologically significant compounds | Sulfoxaflor, X11519540 (soil metabolite) |

| (animals, plants and the environment) | |
|---|---|
| *Acute toxicity* | |
| Rat, $LD_{50}$, oral | 1000 mg/kg bw |
| Rat, $LD_{50}$, dermal | > 5000 mg/kg bw |
| Rat, $LC_{50}$, inhalation | > 2.09 mg/L (4 h, nose-only exposure) |
| Rabbit, dermal irritation | Not irritating |
| Rabbit, eye irritation | Not irritating |
| Mouse, dermal sensitization (local lymph node assay) | Not sensitizing |
| *Short-term studies of toxicity* | |
| Target/critical effect | Liver (liver cell vacuolization/fatty change) in mice and rats; adrenals (cortical hypertrophy and vacuolation) in mice; decreased feed consumption and body weight gain in dogs |
| Lowest relevant oral NOAEL | 6.36 mg/kg bw per day (90-day study in rats) |
| Lowest relevant dermal NOAEL | 500 mg/kg bw per day (28-day study in rats) |
| Lowest relevant inhalation NOAEC | No data |
| *Long-term toxicity and carcinogenicity* | |
| Target/critical effect | Liver (liver cell vacuolization/fatty change) in mice and in female rats |
| Lowest relevant NOAEL | 5.13 mg/kg bw per day (2-year study in rats) |
| Carcinogenicity | Unlikely to pose a carcinogenic risk to humans at levels of dietary exposure |
| *Genotoxicity* | |
| | Not genotoxic |
| *Reproductive toxicity* | |
| Reproductive target/critical effect | No effects on fertility at highest dose tested; reduced pup survival and delayed preputial separation at parentally toxic dose |
| Lowest relevant reproductive NOAEL | 6.07 mg/kg bw per day for offspring toxicity (two-generation study in rats) |
| Developmental target/critical effect | Fetal abnormalities (forelimb flexure, hindlimb rotation, bent clavicle, fused sternebrae, convoluted ureter) at maternally toxic dose |
| Lowest relevant developmental NOAEL | 11.5 mg/kg bw per day (rat) |
| *Neurotoxicity* | |
| Acute neurotoxicity | Decrease in motor activity; NOAEL: 25 mg/kg bw |
| Developmental neurotoxicity | No evidence of developmental neurotoxicity at highest dose tested |
| *Other toxicological studies* | |
| Mechanistic studies | Studies on liver tumorigenesis (rats, mice) demonstrate non-relevance to humans |
| | Studies on Leydig cell effects in rats suggested evidence for an MOA unlikely to be relevant to humans |

| | |
|---|---|
| | Studies demonstrated that limb and clavicle abnormalities are due to rat-specific agonist activity on the fetal muscle nAChR not relevant to humans |
| Studies on metabolites | X11719474: lower toxicity than parent compound, not genotoxic in vitro, no developmental toxicity |
| | X11721061, X11596066 and X11579457: lower toxicity than parent compound, not genotoxic in vitro |
| | X11519540: higher toxicity than parent compound, not genotoxic in vitro |
| *Medical data* | |
| | Limited data; no adverse health effects reported in manufacturing plant personnel |

***Summary***

| | Value | Study | Safety factor |
|---|---|---|---|
| ADI | 0–0.05 mg/kg bw | Two-year study in rat (supported by two-generation study in rats, 90-day study in rats and 1-year study in dogs) | 100 |
| ARfD | 0.3 mg/kg bw | Acute neurotoxicity study in rat | 100 |

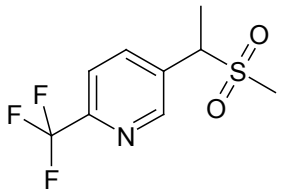
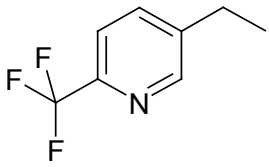
## RESIDUE AND ANALYTICAL ASPECTS

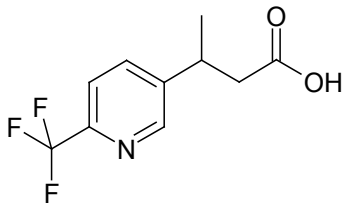
Residue, analytical, and toxicological aspects of sulfoxaflor were considered for the first time by the present meeting. The Forty-second Session of the CCPR initiated a pilot project using sulfoxaflor in which JMPR would conduct an independent, parallel review along with a joint review team from Australia, Canada, and the USA, and recommend maximum residue levels before national governments or other regional registration authorities.

Sulfoxaflor (ISO common name), a member of the novel sulfoximine class of insecticides, has broad spectrum activity against sucking and chewing insects in cereal grains (wheat and barley), soya bean, oilseed rape, cotton seed, pome fruits, stone fruits, citrus fruits, tree nuts, grapes, dried grapes, strawberries, leafy vegetables, fruiting vegetables, cucurbits, brassica vegetables, and bulb vegetables. It is currently proposed only for foliar applications.

The IUPAC name for sulfoxaflor is [methyl(oxo){1-[6-(trifluoromethyl)-3-pyridine]ethyl}-$\lambda^6$-sulfanylidene]cyanamide and the CAS name is *N*-[methyloxido[1-[6-(trifluoromethyl)-3-pyridinyl]ethyl]-$\lambda^4$-sulfanylidene]cyanamide.

Sulfoxaflor labelled in the pyridine ring was used in the metabolism and environmental fate studies. The chemical structures of sulfoxaflor and its metabolites/degradates are shown below.

| | | |
|---|---|---|
| Sulfoxaflor (Parent)<br>: [1-(6-trifluoromethylpyridin-3-yl)ethyl](methyl)-oxido-$\lambda^4$-sulfanylidenecyanamide | X11719474 (Urea)<br>1-[methyl(oxido){1-[6-(trifluoromethyl)pyridin-3-yl]ethyl}- $\lambda^6$-sulfanylidene]urea | X11721061 (Alcohol)<br>1-[6-(trifluoromethyl)pyridin-3-yl]ethanol |
|  |  | |
| X11519540 (Sulfonyl)<br>5-[1-(methanesulfonyl)ethyl]-2-(trifluoromethyl)pyridine | X11596066 (Ethyl)<br>5-ethyl-2-(trifluoromethyl)pyridine | X11579457 (Des-cyano)<br>5-[1-(S-methylsulfonimidoyl)ethyl]-2-(trifluoromethyl)pyridine |



X11821639 (Acid)

3-[6-(trifluoromethyl) pyridin-3-yl]butanoic acid

***Animal metabolism***

Information was available on metabolism of sulfoxaflor in laboratory animals, lactating goats and laying hens.

When rats were orally dosed with labelled sulfoxaflor, approximately 93% of the dose was eliminated in the urine and faeces as parent sulfoxaflor. The main metabolite in urine was a glucuronide conjugate of sulfoxaflor metabolite X11721061, accounting for approximately 2–4% of the dose. Several other unidentified minor components, each less than 1% of the administered dose, were present in the urine and faecal samples. Metabolism in laboratory animals was summarized and evaluated by the WHO panel of the JMPR in 2011.

When lactating goats were orally dosed with labelled sulfoxaflor at 12.2 ppm in the diet, approximately 4% of the dose appeared in the milk and 3% in the tissues.

Residue levels in milk reached a plateau during days 3–4 of the dosing phase, at about 0.2 mg/kg eq. $^{14}C$ levels were highest in liver and kidney, and lowest in fat tissues. Parent sulfoxaflor was the predominant residue in all tissues, comprising over 89% TRR in milk, muscle, fat, and kidney; and approximately 60% TRR in liver. Metabolite X11519540 (sulfonyl metabolite) was found

at low levels (≤ 0.009 mg/kg eq) in several matrices; while X11596066 (ethyl metabolite) was reported only in liver samples, at 18% TRR (0.095 mg/kg eq).

Metabolite X11719474 was usually found at more than 10% TRR in plants, and consequently is considered a major plant metabolite. When lactating goats were orally dosed with labelled sulfoxaflor metabolite X11719474 at 11.4 ppm in the diet, approximately 1% of the dose appeared in the milk and 1% in the tissues.

Residue levels in milk reached a plateau during days 3–4 of the dosing phase, at about 0.2 mg/kg eq. Similar $^{14}C$ levels were found in liver, kidney, milk, and muscle; while lower levels were reported in fat tissues. This study demonstrated that X11719474 is not metabolized in goats: no metabolites were identified, and the radioactivity found in all tissues was from X11719474.

When laying hens were dosed with labelled sulfoxaflor at 10.9 ppm in the feed, most of the dose was excreted in the droppings. Approximately 0.5% of the dose was recovered in the combined eggs, fat, and tissues. Residue levels in eggs reached a plateau during days 6–7 of the dosing phase, at about 0.06 mg/kg eq. $^{14}C$ levels were highest in liver and lowest in fat tissues. Parent sulfoxaflor was the predominant residue in all tissues, comprising over 83% TRR in eggs, muscle, fat, and skin with fat; and approximately 68% TRR in liver. Metabolite X11519540 was found at low levels (≤ 0.005 mg/kg eq) in several matrices, while X11596066 was reported only in liver samples, at 14% TRR (0.020 mg/kg eq).

When laying hens were orally dosed with labelled sulfoxaflor metabolite X11719474 at 11.8 ppm in the feed, approximately 0.5% of the applied dose was recovered in the combined eggs, fat, and tissues. Similar $^{14}C$ levels were noted in liver, muscle, and egg; lower levels were found in fat tissues. Approximately 92% of the dose was recovered from the excreta, and 0.3% in the cage rinse. Residue levels in eggs reached a plateau by day 4 of the dosing phase, with no compounds other than X11719474 being identified. This study demonstrated that X11719474 is not metabolized in hens: no metabolites were identified and the radioactivity found in all tissues was from X11719474.

*Animal metabolism summary*

Metabolism studies in the laying hen and lactating goat demonstrated limited metabolism of sulfoxaflor and no metabolism of X11719474. In most hen and goat matrices, sulfoxaflor comprised approximately 80% or more of the total radioactivity when $^{14}C$-sulfoxaflor was fed. Metabolites X11721061 [≤ 0.017 mg/kg eq] and X11519540 [≤ 0.009 mg/kg eq] were found at < 10% TRR in several matrices. However, more extensive metabolism occurred in liver, with metabolite X11596066 comprising up to 18% TRR (0.095 mg/kg eq). Overall, the metabolism found in livestock was qualitatively similar to that observed in laboratory animals.

***Plant metabolism***

Information was available on the metabolism of sulfoxaflor in tomato, lettuce, succulent peas and rice. Separate studies were reported for foliar and soil applications to all four crops.

In a foliar treatment experiment, [$^{14}C$-pyridine]sulfoxaflor was applied to immature tomato plants in four separate applications at 213, 202, 129, and 74 g ai/ha (1.5 × proposed GAP rate). Immature plants (after the 2nd treatment), ripe tomatoes (1, 7, and 14 DAT), and vines (14 DAT) were analysed. Parent sulfoxaflor was the most abundant residue in ripe tomatoes (0.012 mg/kg), but metabolites X11719474 (0.009 mg/kg eq) and X11721061 (in conjugated form) (0.004 mg/kg eq) were also found. In addition, low levels of free X11721061 were observed (2–3% TRR; 0.020–0.030 mg/kg eq) in the immature plants and mature vines, and a metabolite tentatively identified as X11821639 was observed at levels up to 1.2% of the TRR (0.016 mg/kg eq) in the immature plants and mature vines.

In a soil treatment experiment with tomatoes, [$^{14}C$- pyridine]sulfoxaflor was applied to the soil around immature tomato plants in two separate treatments at 249 and 211 g ai/ha. Metabolite

X11719474 was the primary identified component of the residue in all tomato matrices, especially in mature fruit (59–73% TRR; 0.016–0.019 mg/kg eq), while parent sulfoxaflor was present at considerably lower levels (11–17% TRR; 0.003–0.005 mg/kg eq). All other metabolites comprised less than 10% TRR in tomato matrices.

In a foliar treatment lettuce experiment, [$^{14}$C-pyridine]sulfoxaflor was applied to immature lettuce plants in three separate applications at 195, 199, and 205 g ai/ha (1.5 × proposed GAP rate). Immature plants were collected 14 days after the first and second applications. Mature lettuce was harvested at a 7-day PHI. While higher residue levels were found in the mature lettuce (4.4 mg/kg eq vs. 0.18 mg/kg eq), the residue distribution was essentially the same. Following three foliar applications of sulfoxaflor, major lettuce metabolites include sulfoxaflor (17% TRR; 0.031–0.73 mg/kg), and metabolite X11719474 (27–31% TRR; 0.49–1.36 mg/kg eq). The glucose conjugate of X11721061 (3–5% TRR; 0.009–0.12 mg/kg eq) and the glucose plus malonyl conjugate of X11721061 (6% TRR; 0.011–0.24 mg/kg eq) were found at lower levels. Low levels of free X11721061, X11579457, and X11519540 (each < 1% TRR) were also reported.

In a soil treatment lettuce experiment, [$^{14}$C- pyridine]sulfoxaflor was applied to the soil around immature lettuce plants in two separate treatments at 238 and 216 g ai/ha. Immature lettuce was collected 14 days after the first application. Mature lettuce was collected 14 days after the second application. While higher residue levels were found in the mature lettuce (1.4 mg/kg eq vs. 0.14 mg/kg eq), the residue distribution was essentially the same. X11719474 was the only major metabolite in lettuce, comprising 49–60% of the TRR (0.081-0.69 mg/kg eq). Glucose and glucose plus malonyl conjugates of X11721061 were found at ≤ 4% TRR. Sulfoxaflor, X11721061, X11579457, and X11519540 were each present at ≤ 1% TRR.

In a foliar treatment succulent pea experiment, [$^{14}$C-pyridine]sulfoxaflor was applied to immature pea plants in three separate applications at 197, 201, and 203 g ai/ha. Immature plants were collected 14 days after the first and second applications. Mature pods and vines were harvested at a 14-day PHI. Following three foliar applications of sulfoxaflor, significant residues of parent sulfoxaflor (59–71% TRR; 0.62–3.9 mg/kg), and X11719474 (12–13% TRR; 0.14–0.63 mg/kg eq) were found in mature pea pods and vines. The glucose conjugate of X11721061 (7–10% TRR; 0.11–0.37 mg/kg eq) and the glucose plus malonyl conjugate of X11721061 (1–3% TRR; 0.030–0.067 mg/kg eq) were found at lower levels, and free X11711061 was only found at 1% TRR in mature pea matrices. The immature pea plants demonstrated lower overall residue levels, together with relatively more of the glucose conjugate of X11721061 than found in the mature pea plants.

In a soil treatment succulent pea experiment, [$^{14}$C- pyridine]sulfoxaflor was applied to the soil around immature pea plants in two separate treatments at 212 and 222 g ai/ha. Immature pea plants were collected 14 days after the first application. Mature pods and vines were collected 14 days after the second soil application. For soil application of sulfoxaflor, the primary residue in mature pods and vines was metabolite X11719474 (88–90% TRR; 0.037–0.13 mg/kg eq). Parent sulfoxaflor (ND–5% TRR; < 0.001–0.002 mg/kg) and the glucose conjugate of X11721061 (2–8% TRR; 0.001–0.011 mg/kg eq) were minor metabolites in the mature pea plants.

In a rice experiment a foliar treatment of [$^{14}$C-pyridine]sulfoxaflor was applied to immature rice plants in three separate applications at 227, 205, and 145 g ai/ha. Immature plants were collected 14 days after the first application. Grain and straw were separated, and mature grain was separated into white rice and hulls. Following three foliar applications of sulfoxaflor, parent sulfoxaflor was the major residue in mature rice matrices (33–44% TRR; 0.086–2.5 mg/kg). Metabolite X11719474 was found at lower levels (7–10% TRR; 0.021–0.55 mg/kg eq), as was the glucose conjugate of X11721061 (5–11% TRR; 0.027–0.30 mg/kg eq). Free X11721061 (2–4% TRR; 0.005–0.23 mg/kg eq) was also found in the mature rice matrices. The immature rice plants contained mostly parent sulfoxaflor (74% TRR; 2.1 mg/kg) and correspondingly lower levels of metabolites. The glucose plus malonyl conjugate of X11721061 was only detected in mature rice straw (3% TRR; 0.16 mg/kg eq).

In a soil treatment rice experiment, one application of [$^{14}$C- pyridine]sulfoxaflor was made at transplant at 474 g ai/ha. Rice plants at the 3–4 leaf stage were planted immediately following soil application. Immature rice plants were collected 14 days after the first application. Following this, the plants were flooded. Immature rice plants were collected 14 and 28 days after the soil application. Mature rice was collected 138 days after the soil application. Grain and straw were separated, and mature grain was separated into white rice and hulls. After one soil application of sulfoxaflor, the major residue in the mature rice matrices was metabolite X11719474 (31–40% TRR; 0.018–0.56 mg/kg eq). No other metabolites were reported in white rice grain, and relatively low levels of metabolite X11721061 (5–6% TRR; 0.026–0.11 mg/kg eq) and its glucose conjugate (5–6% TRR; 0.024–0.098 mg/kg eq) occurred in mature rice hulls and straw. Similar residue distributions were reported in immature rice plants, although higher overall residue levels were obtained. Additionally, low levels of the metabolite X11821639 (≤ 1% TRR; ≤ 0.13 mg/kg eq) was reported in immature rice plants.

*Plant metabolism summary*

Metabolism studies were conducted in tomato, lettuce, succulent pea, and rice. For each metabolism study, foliar and soil application were studied separately, although currently only foliar uses are proposed. Metabolism of sulfoxaflor was similar in all four crops: oxidation of the cyano-carbon bond to form X11719474 and loss of the sulfur side chain to form X11721061. X11721061 is then conjugated with glucose, which may then be conjugated with malonic acid. Metabolism continues through natural incorporation of the radiolabelled carbon into natural plant constituents, such as lignin and starch. A very minor pathway (< 1%) included degradation of the X11719474 urea side chain to form X1159540 and X11479457, which are further reduced to give X11721061.

The primary difference noted between the foliar and soil metabolism studies was that parent sulfoxaflor, X11719474, and X11721061 conjugates commonly were found at > 10% TRR following foliar applications, while X11719474 was the only residue consistently exceeding 10% TRR following soil applications. The plant metabolism studies demonstrate that sulfoxaflor residues translocate throughout the crop matrices; thus, sulfoxaflor may be considered systemic.

## ***Environmental fate***

*Aerobic Soil Metabolism*

Sulfoxaflor biodegrades rapidly in laboratory soil studies, with a reported half-life of 0.3 to 0.6 days, to form X11719474. Degradation of sulfoxaflor was also very rapid under field conditions, with sulfoxaflor half-lives ranging from < 1 to 8 days observed in field dissipation studies conducted at five sites in North America.

When sulfoxaflor was applied to soil in the laboratory, the $DT_{50}$ of resulting X11719474 ranged from 85 to 370 days. Field studies yielded half-lives of 30–277 days for X11719474.

*Photolysis*

No major photodegradation products of sulfoxaflor were detected in studies conducted with sterile buffered water. One minor photoproduct, X11721061, reaching a maximum concentration of 2.5% AR at 14 DAT was identified. Photodegradation of sulfoxaflor in sterile buffer and natural surface waters was slow, with estimated half–lives in excess of one year in both media. Likewise, photolytic degradation of sulfoxaflor on soil surfaces is not a significant route of degradation.

### *Rotational crops*

*Confined rotational crop study*

When lettuce, radish and wheat were grown in a rotational crop situation 30, 120 and 365 days after treatment of bare ground with labelled sulfoxaflor at 0.6 kg ai/ha, significant TRR levels were found: 0.74 mg/kg eq and below for mature lettuce; 1.2 mg/kg eq and below for mature radish tops; 0.16 mg/kg eq and below for mature radish roots and 0.081 mg/kg eq and below for wheat grain. Higher TRR levels were found in wheat hay and straw: 0.71–3.8 mg/kg eq.

X11719474 was the most abundant metabolite in terms of either % of TRR or mg/kg observed in all crops at all three plant-back intervals (PBIs). X11719474 ranged from 35.3% of the TRR (1.3 mg/kg eq) in 120 DAT wheat straw to 87.8% of the TRR (0.077 mg/kg eq) in 120 DAT mature radish roots. The results of the confined rotational crop study indicate that X11719474 may be taken up by plant roots. Therefore, a limited field rotational crop study was conducted to assess the potential for accumulation in successive crops at various PBIs.

*Limited field rotational crop study*

Limited field rotational crop studies confirmed the general findings from the confined rotational crop study. Four foliar broadcast applications at 100 g ai/ha were applied to a primary crop of spinach, carrot, or leaf lettuce. The primary crops were harvested at a 3-day PHI. Rotational crops of radish, mustard green, sorghum, and grass were planted at PBIs of 30, 90, 120, and 365 days. Consistent with the confined rotational crop study, X11719474 was the primary residue. No parent sulfoxaflor residues were found in any plant matrix at any PBI, except for one sample [120 day radish tops], where residues were attributed to contamination. Metabolites X11721061, X11519540, and X11579457 were found in several matrices, but at significantly lower levels than X11719474.

The edible plant parts having measurable X11719474 residues in the field rotational crop study were radish root and mustard green leaves. In both cases, residues declined with PBI: from 0.031 to < 0.01mg/kg eq (31 to 124 days after planting for radish), and from 0.28 to 0.017 mg/kg eq (31 to 361 days after planting for mustard greens). These results indicate that for rotational crops planted after sulfoxaflor treatments, residues of X11719474 may be higher than indicated by the supervised residue trials. In particular, for root and tuber vegetables, residues of X11719474 may be approximately 0.03 mg/kg eq higher, and for leafy vegetables, residues of X11719474 may be approximately 0.3 mg/kg eq higher.

### *Analytical methods*

HPLC methods with positive-ion electrospray (ESI) tandem mass spectrometry (LC/MS/MS) were developed for data collection and enforcement of sulfoxaflor residues and the two metabolites X11719474 and X11721061. Method 091116 was developed for plant commodities, and Method 091188 was developed for animal commodities. Successful validation of both methods was demonstrated for both methods. Additionally, successful radio-validation was also reported for both methods. The lowest LOQ was 0.01 mg/kg for each of sulfoxaflor, X11719474, and X11721061 in all matrices. The limit of detection (LOD) was 0.003 mg/kg for all three analytes in all matrices.

The generally good agreement between the results from the metabolism study and the proposed enforcement methods (Method 091116 for plants and 091188 for animals) demonstrated successful radio-validation of the analytical method and provides assurance that the enforcement methods are capable of extracting bio-incurred residues of interest from plant and animal commodities.

The FDA Multi-Residue Method Test guidelines in the Pesticide Analytical Manual (PAM) (Third Edition, January 1994) is not applicable for the analysis of sulfoxaflor, due to low recoveries.

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

Results were available to evaluate the stability of sulfoxaflor and its major metabolites in oranges, peach, wheat grain, and soya bean seed stored under frozen conditions up to 680 days. Through 680 days of frozen storage, no stability problems in any crop matrix were identified.

Additional freezer storage stability studies were performed in conjunction with the poultry and bovine feeding studies to determine residue stability in frozen livestock matrices. The maximum storage interval for the poultry study was 9 weeks, while that for the bovine study was 6–8 weeks. Sulfoxaflor, X11719474, and X11721061 were stable in frozen livestock matrices over the tested intervals.

The periods of demonstrated stability cover the frozen storage intervals in the residue studies.

***Definition of the residue***

In animal commodities, parent sulfoxaflor was a major component of the residue in goat muscle, fat, milk and kidney, comprising 89% or more of the TRR. In goat liver, sulfoxaflor constituted approximately 60% of the residue with metabolite X11596066 at about 18% TRR (0.095 mg/kg eq). Low levels of metabolites X11721061 (0.017 mg/kg eq in liver) and X11519540 (≤ 0.009 mg/kg eq) were found in several matrices. For goats dosed with the major plant metabolite X11719474, no metabolism of X11719474 was observed.

In laying hens, the results were similar to that found in the goat study, with parent sulfoxaflor the major component in egg, muscle, skin, and fat. In hen liver, sulfoxaflor constituted approximately 68% of the residue with metabolite X11596066 at about 14% TRR (0.020 mg/kg eq). A low level (< 8% TRR) of metabolite X11519540 was found in several matrices (≤ 0.005 mg/kg eq). For hens dosed with the major plant metabolite X11719474, no metabolism of X11719474 was observed.

As sulfoxaflor was the major residue in all livestock commodities, the Meeting decided that, for animal commodities, parent sulfoxaflor is the appropriate residue of concern for MRL enforcement and dietary risk assessment. Although metabolite X11519540 is approximately two times more toxic than parent sulfoxaflor and is present in livestock commodities, however, it is present in such low levels (< 0.01 mg/kg) that it is not appropriate to include this metabolite in the residue definition.

Available studies indicate that parent sulfoxaflor is the best marker compound for plants, and is appropriate for MRL enforcement.

Metabolites X11719474 and X11721061 are commonly present in plant matrices at levels above 10% TRR. Also, limited field rotational crop studies indicate that levels of X11719474 may be up to 0.3 mg/kg higher in rotational crops than indicated by the crop field trial studies. However, the WHO Panel has confirmed that metabolites X11719474 and X11721061 are approximately seven times less toxic than parent sulfoxaflor. Taking into account this information, the Meeting decided that for plant commodities parent sulfoxaflor is the appropriate residue of concern for dietary risk assessment.

The Meeting recommended the following residue definition for sulfoxaflor.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities: *sulfoxaflor.*

*The residue is not fat soluble.*

***Results of supervised trials on crops***

The Meeting received supervised field trials data for sulfoxaflor uses on cereal grains (wheat and barley), soya bean, oilseed rape, cottonseed, pome fruits, stone fruits, citrus fruits, tree nuts, grapes,

dried grapes, strawberries, leafy vegetables, fruiting vegetables, cucurbits, brassica vegetables, and bulb vegetables.

The OECD calculator was used as a tool in the estimation of the maximum residue level from the selected residue data set obtained from trials conducted according to proposed GAP. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at a best estimate of the maximum residue level using expert judgement. Then, the OECD calculator was employed. If the statistical calculation spreadsheet suggested a different value from that recommended by the JMPR, a brief explanation of the deviation was provided.

*Citrus fruits*

Supervised trials data for citrus were available from Australia, Brazil, and the USA.

Proposed GAP for citrus fruit is for two foliar treatments at a rate of 0.2 kg ai/ha, a re-treatment interval (RTI) of 7 days, and harvest of fruit 1 day after the second application (1-day PHI).

*Grapefruit*

In eight trials on grapefruit in the USA matching proposed GAP, Residues of sulfoxaflor measured in whole grapefruit, in ranked order, were: < 0.01, 0.01, 0.012, 0.013, 0.016, 0.024, 0.11, and 0.13 mg/kg.

*Lemon*

In six trials on lemons in the USA matching proposed GAP, Residues of sulfoxaflor, in ranked order, measured in whole lemons were: < 0.010 (2), 0.040, 0.083, 0.11, and 0.29 mg/kg.

*Oranges*

A total of 26 trials on oranges were available from Australia (10), Brazil (4), and the USA (12).

Residues of sulfoxaflor measured in whole oranges from Australia, in ranked order, were: 0.090, 0.15 (2), 0.16, 0.28, 0.33, 0.34, 0.41, 0.43, and 0.44 mg/kg.

Residues of sulfoxaflor measured in whole oranges from Brazil, in ranked order, were: 0.096, 0.099, 0.12, and 0.28 mg/kg.

Residues of sulfoxaflor measured in whole oranges from the USA, in ranked order, were: 0.038, 0.050, 0.062, 0.074, 0.085, 0.093, 0.11, 0.12 (3), 0.16, and 0.23 mg/kg.

*Summary – Citrus fruits*

Residue data from trials complying with the proposed GAP were available for grapefruit, lemons, and oranges. The Meeting noted that sulfoxaflor residues were highest in orange trials from Australia and decided to estimate a citrus group maximum residue level based on this data set.

The Meeting estimated a maximum residue level of 0.9 mg/kg for residues of sulfoxaflor in citrus fruits. The Meeting estimated STMR and HR values of 0.31 and 0.44 mg/kg, respectively, for sulfoxaflor residues in citrus fruits.

*Pome fruits*

Supervised trials data were available for apple and pear from Australia/New Zealand, Northern and Southern Europe, and the USA.

Proposed GAP for pome fruit is for two foliar applications of sulfoxaflor at 0.2 kg ai/ha with a 7-day RTI and a 7-day PHI.

*Apple*

A total of 22 trials on apples were available from Australia and New Zealand (6), Northern Europe (2), Southern Europe (2), and USA (12).

Residues of sulfoxaflor measured in apples from Australia/New Zealand, in ranked order, were: 0.020, 0.065, 0.070, 0.10, 0.14, and 0.19 mg/kg.

Sulfoxaflor residue concentrations in apples from Northern Europe were: 0.078 and 0.18 mg/kg.

Sulfoxaflor residue concentrations in apples from Southern Europe were: 0.074 and 0.27 mg/kg.

Residues of sulfoxaflor measured in apples from the USA, in ranked order, were: < 0.010, 0.039, 0.040, 0.043, 0.056, 0.063, 0.064, 0.066, 0.068, 0.072, 0.10, and 0.12 mg/kg.

*Pears*

A total of 14 trials on pears were available from Australia (2), Northern Europe (3), Southern Europe (3) and the USA (6).

Sulfoxaflor residue concentrations in pears from Australia were: 0.11 and 0.22 mg/kg.

Residues of sulfoxaflor measured in pears from Northern Europe, in ranked order, were: 0.052, 0.058, and 0.10 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in pears from Southern Europe were: 0.099 and 0.18 (2) mg/kg.

Residues of sulfoxaflor, in ranked order, measured in pears from USA were: 0.078, 0.13, 0.16, 0.18, 0.23, and 0.26 mg/kg.

*Summary – Pome fruits*

Residue data from trials complying with the proposed GAP were available for apples and pears. The Meeting decided to estimate pome fruit group maximum residue level based on combining the apple and pear data sets from the USA.

In 18 apple and pear trials from the USA matching the pome fruit GAP, Residues of sulfoxaflor, in ranked order, measured were: < 0.010, 0.039, 0.040, 0.043, 0.056, 0.063, 0.064, 0.066 0.068, 0.072, 0.078, 0.10, 0.12, 0.13, 0.16, 0.18, 0.23, and 0.26 mg/kg.

The Meeting estimated a maximum residue level of 0.4 mg/kg for sulfoxaflor in pome fruits. The Meeting estimated STMR and HR values of 0.07 and 0.26 mg/kg, respectively, for sulfoxaflor residues in pome fruits.

*Stone fruits*

Supervised trial data were available for apricot, cherries, nectarine, peach, and plums.

Proposed GAP for stone fruits is for two foliar applications of sulfoxaflor at 0.2 kg ai/ha with a 7-day RTI and a 7-day PHI.

*Cherries*

A total of 14 trials on cherries were available from Australia (2), Northern Europe (3), Southern Europe (3), and USA (6).

Residues of sulfoxaflor, in ranked order, measured in cherries from Australia were: 0.35 and 0.38 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cherries from Northern Europe were: 0.77, 0.90, and 1.49 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cherries from Southern Europe were: 0.54, 0.80, and 0.98 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cherries from USA were: 0.55, 0.59, 0.76, 1.05, 1.22, and 1.24 mg/kg.

*Nectarines*

Five nectarine trials were available from Australia and New Zealand.

In five nectarine trials matching the proposed stone fruit GAP, sulfoxaflor residues found in in nectarine pitted fruit were: 0.10, 0.11, 0.12, 0.14, and 0.18 mg/kg

*Apricot*

Two apricot trials from Australia/New Zealand, matching the proposed stone fruit GAP, had sulfoxaflor residues of 0.15 and 0.42 mg/kg.

*Peach*

A total of 20 trials on peach, matching the proposed stone fruit GAP, were available from Australia (8), Northern Europe (3), Southern Europe (3), and USA (6).

Residues of sulfoxaflor, in ranked order, measured in peach from Australia and New Zealand were: 0.012, 0.11 (2), 0.12, 0.14, 0.15, 0.24, and 0.27 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in peach from Northern Europe were: 0.20, 0.36, and 0.54 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in peach from Southern Europe were: 0.21, 0.27, and 0.83 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in peach from USA were: 0.032, 0.054, 0.12, 0.14, 0.17, and 0.90 mg/kg.

*Plums*

A total of seven trials on plums were available from Australia (1) and USA (6).

The sulfoxaflor residue concentration in plums from Australia was 0.020 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in plums from USA were: 0.030, 0.054, 0.066, 0.090, 0.11, and 0.36 mg/kg.

*Summary – Stone fruits*

Residue data from trials complying with the proposed GAP and with a sufficient number of trials were available for cherries, peaches and plums. The Meeting noted that sulfoxaflor residues were highest in the cherry trials from the USA and decided to estimate stone fruit crop group maximum residue level on this data set.

The Meeting estimated a maximum residue level of 3 mg/kg for sulfoxaflor on stone fruit. The Meeting estimated STMR and HR values of 0.91 and 1.2 mg/kg, respectively, for sulfoxaflor residues in stone fruit.

*Grapes*

The proposed GAP for grapes is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha with a 7-day RTI and a 7-day PHI.

A total of 33 trials on grapes, complying with the proposed GAP, were available from Australia and New Zealand (12), Northern Europe (6), Southern Europe (6), and USA (9).

Residues of sulfoxaflor, in ranked order, measured in grapes from Australia/New Zealand were: 0.013, 0.034, 0.095, 0.10, 0.11, 0.13, 0.14, 0.20, 0.35, 0.45, 0.56, and 1.59 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in grapes from Northern Europe were: 0.12, 0.15 (2), 0.23, 0.29, and 0.46 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in grapes from Southern Europe were: 0.061, 0.080, 0.23, 0.36, 0.96, and 1.02 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in grapes from the USA were: 0.042, 0.049, 0.091, 0.10 (3), 0.12, 0.14, and 0.33 mg/kg.

Based on the Australia/New Zealand trials, the Meeting estimated a maximum residue level of 2 mg/kg for sulfoxaflor in grape. The Meeting estimated STMR and HR values of 0.14 and 1.6 mg/kg, respectively, for sulfoxaflor residues in grape.

*Strawberries*

The proposed GAP for strawberries is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha with a 7-day RTI and a 1-day PHI.

A total of 13 trials on field-grown strawberries, complying with the proposed GAP, were available from Australia and New Zealand (4) and USA (9).

Residues of sulfoxaflor, in ranked order, measured in strawberries from Australia/New Zealand were: 0.030, 0.13, 0.21, and 0.49 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in strawberries from USA were: 0.065, 0.14 (2), 0.18, 0.19 (2), 0.20, and 0.21 (2) mg/kg.

Based on the USA trials, the Meeting estimated a maximum residue level of 0.5 mg/kg for sulfoxaflor in strawberry. The Meeting estimated STMR and HR values of 0.19 and 0.21 mg/kg, respectively, for sulfoxaflor residues in strawberry.

*Bulb vegetables*

Supervised trials data were available for bulb and spring onions from USA.

The proposed GAP for onions is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha with a 7-day RTI and a 7-day PHI.

*Bulb Onion*

In six bulb onion trials matching the proposed foliar GAP conditions, sulfoxaflor residues in bulb onion did not exceed the LOQ (< 0.01 mg/kg) in any sample.

The Meeting estimated a maximum residue level of 0.01* mg/kg for sulfoxaflor in bulb onion. The Meeting also estimated STMR and HR values of 0.01 mg/kg, for sulfoxaflor residues in bulb onion.

The Meeting decided to extrapolate the estimated maximum residue level, STMR, and HR values for bulb onions to garlic.

*Spring Onion*

In six spring onion trials in USA matching the proposed GAP conditions, residues of sulfoxaflor, in ranked order, measured in spring onion were: < 0.01, 0.048, 0.09, 0.13 (2), and 0.39 mg/kg.

The Meeting estimated a maximum residue level of 0.7 mg/kg for sulfoxaflor in spring onion. The Meeting estimated STMR and HR values of 0.11 and 0.39 mg/kg, respectively, for sulfoxaflor residues in spring onion.

*Brassica vegetables*

Supervised trials data, matching the proposed GAP, were available for broccoli, head cabbage, and cauliflower.

Proposed GAP for head and stem *Brassica* vegetables is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha, with a 7-day RTI and a 3-day PHI.

*Broccoli*

A total of 15 trials on broccoli were available from Australia (2), Northern Europe (5), Southern Europe (2), and USA (6).

Sulfoxaflor residue concentrations in broccoli from Australia were: 0.07 (2) mg/kg.

Residues of sulfoxaflor, in ranked order, measured in broccoli from Northern Europe were: 0.057, 0.073, 0.074, 0.32, and 1.58 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in broccoli from Southern Europe were: 0.036 and 0.16 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in broccoli from USA were: < 0.01, 0.029, 0.050, 0.060, 0.12, and 0.39 mg/kg.

Based on the Northern European trials, the Meeting estimated a maximum residue level of 3 mg/kg for sulfoxaflor in broccoli. The Meeting estimated STMR and HR values of 0.074 and 1.6 mg/kg, respectively, for sulfoxaflor residues in broccoli.

*Head cabbage*

A total of 14 trials on head cabbage were available from Australia (2), Northern Europe (3), Southern Europe (3), and USA (6).

Residues of sulfoxaflor, in ranked order, measured in head cabbage from Australia were: 0.01 and 0.15 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in head cabbage from Northern Europe were: 0.034, 0.081, and 0.38 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in head cabbage from Southern Europe were: 0.016, 0.019, and 0.066 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in head cabbage from USA were: < 0.01, 0.040, 0.097, 0.10 (2), and 0.19 mg/kg.

Although the highest residues in head cabbage were found in the trials from Northern Europe, an insufficient number of trials were available to recommend a maximum residue level from this data set. Based on the six USA trials, the Meeting estimated a maximum residue level of 0.4 mg/kg for sulfoxaflor in head cabbage. The Meeting estimated STMR and HR values of 0.099 and 0.19 mg/kg, respectively, for sulfoxaflor residues in head cabbage.

*Cauliflower*

A total of ten trials on cauliflower were available from Australia (2) and Northern Europe (6), and Southern Europe (2).

Sulfoxaflor residue concentrations in cauliflower from Australia were: < 0.01 and 0.050 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cauliflower from Northern Europe were: < 0.01 (2), 0.011, 0.014 (2), and 0.021 mg/kg.

Sulfoxaflor residue concentrations in cauliflower from Southern Europe were: 0.022 and 0.029 mg/kg.

Based on the Northern European trials, the Meeting estimated a maximum residue level of 0.04 mg/kg for sulfoxaflor in cauliflower. The Meeting estimated STMR and HR values of 0.013 and 0.021 mg/kg, respectively, for sulfoxaflor residues in cauliflower.

*Fruiting vegetables - Cucurbit*

Supervised trials data were available for cucumbers and melons. All trials were conducted outdoors.

The proposed GAP for cucurbit vegetables is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha, with a 7-day RTI and a 1-day PHI.

*Cucumber*

A total of 18 trials on cucumber were available from Northern Europe (6), Southern Europe (6), and USA (6).

Residues of sulfoxaflor, in ranked order, found in cucumber from Northern Europe were: 0.023, 0.029, 0.034, 0.088, 0.10, and 0.15 mg/kg. .

Residues of sulfoxaflor, in ranked order, found in cucumber from Southern Europe were: 0.031, 0.052, 0.055, 0.073, 0.083, and 0.11 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cucumber from USA were: < 0.01, 0.014, 0.018, 0.025, 0.041, and 0.071 mg/kg.

*Summer Squash*

A total of five trials on summer squash were available from Australia (2) and USA (3).

Sulfoxaflor residue concentrations in summer squash from Australia were: 0.025 and 0.10 mg/kg.

Sulfoxaflor residue concentrations in summer squash from USA were: < 0.01 (3) mg/kg.

*Cantaloupe*

A total of 16 trials on cantaloupe were available from Brazil (4), Southern Europe (6) and the USA (6).

Residues of sulfoxaflor, in ranked order, found in cantaloupe from Brazil were: 0.012, 0.020, 0.027, and 0.055 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cantaloupe from Southern Europe were: 0.015, 0.040, 0.045, 0.048, 0.10, and 0.13 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cantaloupe from the USA were: < 0.01, 0.018, 0.025, 0.032, 0.038, and 0.27 mg/kg.

*Winter Squash*

Three winter squash trials were available from the USA, with the following residue levels: < 0.01, 0.011, and 0.018 mg/kg.

*Summary – Fruiting vegetables, Cucurbits*

The Meeting noted that sulfoxaflor residues were higher in cantaloupe than in cucumber, and decided to estimate a maximum residue level for the cucurbit vegetables group based on the USA cantaloupe data set.

The Meeting estimated a maximum residue level of 0.5 mg/kg for sulfoxaflor for fruiting vegetables, cucurbits. The Meeting estimated STMR and HR values of 0.029 and 0.27 mg/kg, respectively, for sulfoxaflor residues in fruiting vegetables, cucurbits.

*Fruiting vegetables other than cucurbits*

Supervised trials data were available for pepper and tomato.

Proposed GAP for fruiting vegetables other than cucurbits is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha, a 7-day RTI, and a 1-day PHI.

*Peppers*

A total of 20 trials on field-grown peppers were available from Australia (6), Southern Europe (6), and USA (8).

Residues of sulfoxaflor, in ranked order, found in peppers from Australia were: < 0.010, 0.010, 0.08 (2), 0.40, and 0.45 mg/kg.

Residues of sulfoxaflor, in ranked order, found in peppers from Southern Europe were: 0.093 (2), 0.12, 0.18, 0.23, and 0.26 mg/kg.

Residues of sulfoxaflor, in ranked order, found in peppers from the USA were: 0.01, 0.015, 0.020, 0.055, 0.085, 0.086, 0.20, and 0.21 mg/kg.

The Meeting noted that the peppers data from Australia showed the highest sulfoxaflor residue levels and decided to estimate the peppers residue levels based on this data set.

*Tomato*

A total of 44 trials on tomato were available from Australia (6), Brazil (4), Northern Europe (11), Southern Europe (11) and USA (12).

Residues of sulfoxaflor, in ranked order, found in tomatoes from Australia were: 0.014, 0.015 (2), 0.025, 0.030, and 0.050 mg/kg.

Residues of sulfoxaflor, in ranked order, found in tomatoes from Brazil were: 0.015, 0.035, 0.074, and 0.096 mg/kg.

Residues of sulfoxaflor, in ranked order, found in tomatoes from Northern Europe were: 0.022, 0.024, 0.042, 0.047, 0.052, 0.054, 0.057, 0.076, 0.085, 0.095, and 0.37 mg/kg.

Residues of sulfoxaflor, in ranked order, found in tomatoes from Southern Europe were: 0.026, 0.030, 0.035, 0.054, 0.063, 0.11, 0.15, 0.31, 0.41, 0.53, and 0.60 mg/kg. Four tomato trials in Southern Europe were conducted indoors. However, residue levels in the indoor trials were not appreciably different from those in the outdoor trials.

Residues of sulfoxaflor, in ranked order, found in tomatoes from the USA were: < 0.01 (2), 0.010, 0.026, 0.030, 0.047, 0.061, 0.077, 0.082, 0.085, 0.094, and 0.15 mg/kg.

The Meeting noted that the tomato data from Southern Europe showed the highest sulfoxaflor residue levels and decided to estimate the tomato residue levels based on this data set.

*Summary – Fruiting vegetables other than cucurbits*

The Meeting noted that sulfoxaflor residues were higher in tomatoes than in peppers. The Meeting decided to estimate a group maximum residue level for the fruiting vegetables other than cucurbits, (except sweet corn and mushroom) based on the tomato data set.

The Meeting estimated a maximum residue level of 1.5 mg/kg for sulfoxaflor in fruiting vegetables other than cucurbits (except sweet corn and mushrooms). The Meeting estimated STMR and HR values of 0.11 and 0.60 mg/kg, respectively, for sulfoxaflor residues in fruiting vegetables other than cucurbits (except sweet corn and mushrooms).

The JMPR Manual (Section 6.9.2) indicates that a generic factor of 10 may be used for conversion of residues from fresh peppers to dried chili peppers in the estimation of maximum residue levels.

The Meeting agreed to apply the default factor of 10 for dried chili peppers to the STMR and HR values for sulfoxaflor in sweet peppers and estimated a maximum residue level, an STMR and an HR for sulfoxaflor in dried chili peppers of 15, 1.1 and 6.0 mg/kg, respectively.

*Leafy vegetables*

Supervised trial data were available for lettuce, mustard greens, radish tops, and spinach.

The proposed GAP for leafy vegetables is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha, a 7-day RTI, and a 3-day PHI.

*Head Lettuce*

A total of 14 trials on field-grown head lettuce, complying with the proposed GAP, were available from Australia (4), Northern Europe (3), Southern Europe (3), and USA (4).

Residues of sulfoxaflor, in ranked order, found in head lettuce from Australia were: < 0.010, 0.035 (2), and 0.065 mg/kg.

Residues of sulfoxaflor, in ranked order, found in head lettuce from Northern Europe were: 0.015, 0.24, and 0.32 mg/kg.

Residues of sulfoxaflor, in ranked order, found in head lettuce from Southern Europe were: 0.17 and 0.49 (2) mg/kg.

Residues of sulfoxaflor, in ranked order, found in head lettuce from the USA were: < 0.01, 0.010, 0.014, and 0.18 mg/kg.

The Meeting noted that the data from Europe had the highest residue levels, and decided to combine the data from Northern and Southern Europe in mutual support. Thus, in six trials from Europe, residues of sulfoxaflor, in ranked order, found in head lettuce were: 0.015, 0.17, 0.24, 0.32, and 0.49 (2) mg/kg.

*Leaf Lettuce*

A total of 18 trials on field-grown leaf lettuce were available from Australia (4), Northern Europe (3), Southern Europe (3), and the USA (8). Three of the leaf lettuce trials matching the proposed foliar GAP were 'side-by-side' trials providing bridging data for the use of SC and WDG formulations at one location [Guadalupe, California trial]. Sulfoxaflor residues in lettuce leaves were 0.36, 1.10, and 0.49 mg/kg for SC; and 0.40, 0.81, and 0.58 mg/kg for WDG. The results suggest equivalence, so only one of the bridging trials (that bearing the highest residue) was included in the dataset for STMR

and maximum residue level estimation. Thus, only six of the USA trials were considered independent and used in the following analysis.

Residues of sulfoxaflor, in ranked order, found in leaf lettuce from Australia were: 0.055, 0.17, 0.23, and 0.93 mg/kg.

Residues of sulfoxaflor, in ranked order, found in leaf lettuce from Northern Europe were: 0.32, 0.42, and 0.75 mg/kg.

Residues of sulfoxaflor, in ranked order, found in leaf lettuce from Southern Europe were: 0.18, 0.42, and 1.36 mg/kg.

Residues of sulfoxaflor, in ranked order, found in leaf lettuce from the USA were: 0.41, 0.79, 1.07, 1.10, 1.59, and 2.74 mg/kg.

*Mustard Greens*

In eight mustard green trials from the USA matching the proposed GAP conditions for leafy vegetables, residues of sulfoxaflor, in ranked order, found in mustard greens were: 0.29, 0.50, 0.60, 0.67, 0.77, 0.82, and 0.90 (2) mg/kg.

*Radish Tops*

In six radish top trials from the USA matching the proposed GAP conditions for leafy vegetables, residues of sulfoxaflor, in ranked order, found were: 0.21, 0.25, 0.27, 0.42, 0.44, and 0.48 mg/kg.

*Spinach*

A total of seven trials on spinach were available from Australia (1) and USA (6).

The sulfoxaflor residue concentration in spinach from one Australian trial was 0.37 mg/kg.

Residues of sulfoxaflor, in ranked order, found in spinach from USA were: 0.041, 0.40, 1.04, 1.43, 1.87, and 2.86 mg/kg.

*Summary – leafy vegetables*

Residue data from trials complying with the proposed GAP were available for leaf lettuce, head lettuce, mustard greens, radish tops, and spinach. The Meeting noted that sulfoxaflor residues were highest in spinach and decided to estimate leafy vegetables group maximum residue levels based on this data set.

The Meeting estimated a maximum residue level of 6 mg/kg for sulfoxaflor on leafy vegetables. The STMR and HR values were 1.2 and 2.9 mg/kg, respectively.

*Legume vegetables*

Supervised trials data were available for common beans and succulent soya beans.

The proposed GAP for beans is for four foliar applications of sulfoxaflor with at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI.

*Common bean (pods and/or immature seeds)*

A total of six trials on common bean were available from Northern Europe (3) and Southern Europe (3).

Residues of sulfoxaflor, in ranked order, found in common bean from Northern Europe were: 0.072, 0.076, and 0.31 mg/kg.

Residues of sulfoxaflor, in ranked order, found in common bean seed from Southern Europe were: 0.029, 0.12, and 1.94 mg/kg.

The Meeting concluded that no maximum residue level could be estimated for common bean due to an insufficient number of trials.

*Soya bean (immature seeds)*

A total of 18 trials on soya bean were available from Brazil (4) and USA (14).

Residues of sulfoxaflor, in ranked order, found in soya bean seed from Brazil were: < 0.010 (2), 0.030, and 0.039 mg/kg.

Residues of sulfoxaflor, in ranked order, found in soya bean seed from USA were: < 0.010 (6), 0.010, 0.012, 0.013, 0.017, 0.030, 0.034 (2), and 0.20 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg for sulfoxaflor on soya bean (immature seeds). The STMR value was 0.011 mg/kg.

*Beans, dry*

Proposed GAP for beans allows the use of sulfoxaflor with four foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI.

A total of six trials on dry beans were available from Brazil (4) and Northern Europe (1), and Southern Europe (1).

Residues of sulfoxaflor, in ranked order, found in dry beans from Brazil were: 0.049, 0.074, 0.080, and 0.082 mg/kg.

The sulfoxaflor residue concentration in dry beans from Northern Europe was 0.10 mg/kg.

The sulfoxaflor residue concentration in dry beans from Southern Europe was 0.022 mg/kg.

The Meeting concluded that no maximum residue level could be estimated for dry beans as there were an insufficient number of trials.

*Root and tuber vegetables*

Supervised trials data were available for carrot, potato, radish and sugar beet.

The proposed GAP for root and tuber vegetables is for four foliar applications of sulfoxaflor at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI.

*Carrot*

A total of 11 trials on carrot were available from Northern Europe (4), Southern Europe (3), and USA (4).

Residues of sulfoxaflor, in ranked order, found in carrot root from Northern Europe were: < 0.010 (2), 0.010, and 0.017 mg/kg.

Residues of sulfoxaflor, in ranked order, found in carrot root from Southern Europe were: 0.014, 0.030, and 0.031 mg/kg.

Residues of sulfoxaflor, in ranked order, found in carrot root from the USA were: < 0.010 (2), 0.010, and 0.013 mg/kg.

Four trials are considered insufficient to allow a maximum residue level estimate for carrot. Therefore, the Meeting could not make a maximum residue level estimate for carrot due to an inadequate number of trials.

*Potatoes*

In 18 potato trials [Canada (1), Northern Europe (4), Southern Europe (4), and USA (9)] matching the proposed GAP conditions, sulfoxaflor residues in potatoes did not exceed the LOQ (< 0.01 mg/kg) in any tuber sample.

*Radish*

In six radish trials from the USA, matching the proposed GAP conditions, residues of sulfoxaflor, in ranked order, in radish roots were: < 0.010 (3), 0.01, 0.012, and 0.014 mg/kg.

*Sugar Beet*

A total of 13 trials on sugar beet were available from Northern Europe (4), Southern Europe (4), and the USA (5).

Residues of sulfoxaflor, in ranked order, found in sugar beet roots from Northern Europe were: < 0.010 (3), and 0.012 mg/kg.

Residues of sulfoxaflor, in ranked order, found in sugar beet roots from Southern Europe were: < 0.010 (3), and 0.023 mg/kg.

None of the USA trials reported residues above the LOQ of 0.01 mg/kg in sugar beet roots.

Noting the similar residue distributions for the Northern and Southern European trials, the Meeting decided to combine these data sets in mutual support. Thus, the rank-order sulfoxaflor residues in sugar beet roots from Northern and Southern Europe were: < 0.010(6), 0.012, and 0.023 mg/kg.

*Summary – Root and tuber vegetables*

Sufficient residue data from trials complying with the proposed GAP were available for radish, potato, and sugar beet. Residues were highest in sugar beet and the Meeting decided to estimate a root and tuber vegetables (except carrot) group maximum residue level based on the sugar beet data.

The Meeting estimated a maximum residue level of 0.03 mg/kg for sulfoxaflor on root and tuber vegetables (except carrot). The Meeting estimated STMR and HR values of 0.010 and 0.023 mg/kg, respectively, for sulfoxaflor residues in root and tuber vegetables (except carrot).

*Celery*

Supervised trials data were available for celery from the USA (6).

Sulfoxaflor is proposed for use on celery as a maximum of four foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 3-day PHI.

In six celery trials matching the proposed GAP conditions, residues of sulfoxaflor, in ranked order, found in celery were: 0.10, 0.16, 0.17, 0.20, 0.69, and 0.77 mg/kg.

The Meeting estimated a maximum residue level of 1.5 mg/kg for sulfoxaflor on celery. The Meeting estimated STMR and HR values of 0.19 and 0.77 mg/kg, respectively, for sulfoxaflor residues in celery.

*Barley*

The proposed GAP for barley is for two foliar applications of sulfoxaflor at 0.05 kg ai/ha, a 14-day RTI, and a 14-day PHI for grain and straw [7-day PHI for forage and hay].

A total of 25 trials on barley grain were available from Australia/New Zealand (6), Northern Europe (7), Southern Europe (6), and the USA (6).

Residues of sulfoxaflor, in ranked order, found in barley grain from Australia/New Zealand were: < 0.010, 0.025, 0.050, 0.075, 0.11, and 0.32 mg/kg.

Residues of sulfoxaflor, in ranked order, found in barley grain from Northern Europe were: < 0.010, 0.050, 0.057, 0.058, 0.060, 0.079, and 0.085 mg/kg.

Residues of sulfoxaflor, in ranked order, found in barley grain from Southern Europe were: 0.015, 0.042, 0.052, 0.053, 0.055, and 0.061 mg/kg.

Residues of sulfoxaflor, in ranked order, found in barley grain from the USA were: 0.038, 0.043, 0.044, 0.047, 0.072, and 0.088 mg/kg.

The Meeting noted that sulfoxaflor residues were highest in barley trials from Australia/New Zealand, and decided to estimate maximum residue levels on this data set. The Meeting estimated a maximum residue level of 0.6 mg/kg and a STMR value of 0.063 mg/kg for sulfoxaflor residues in barley grain.

*Wheat*

The proposed GAP for wheat allows the use of sulfoxaflor with two foliar applications at 0.05 kg ai/ha, a 14-day RTI, and a 14-day PHI for grain and straw [7-day PHI for forage and hay].

A total of 33 trials on wheat grain were available from Australia/New Zealand (6), Brazil (4), Northern Europe (6), Southern Europe (6) and USA/Canada (11).

Residues of sulfoxaflor, in ranked order, found in wheat grain from Australia/New Zealand were: < 0.010 (2), 0.015 (2), 0.035, and 0.040 mg/kg.

Residues of sulfoxaflor, in ranked order, found in wheat grain from Brazil were: < 0.010 (3) and 0.034 mg/kg.

Residues of sulfoxaflor, in ranked order, found in wheat grain from Northern Europe were: 0.018, 0.019, 0.023, 0.027, 0.032, and 0.11 mg/kg.

Residues of sulfoxaflor, in ranked order, found in wheat grain from Southern Europe were: 0.011, 0.013, 0.014, 0.020, 0.024, and 0.056 mg/kg.

Residues of sulfoxaflor, in ranked order, found in wheat grain from USA/Canada were: < 0.010 (6), 0.012, 0.015, 0.020, 0.037, and 0.063 mg/kg.

The Meeting observed that sulfoxaflor residues were highest in wheat trials from Northern Europe, and decided to estimate maximum residue levels based on this data set. The Meeting estimated a maximum residue level of 0.2 mg/kg for sulfoxaflor on wheat grain. The Meeting estimated an STMR value of 0.025 mg/kg for sulfoxaflor residues in wheat grain.

Noting that the proposed GAP includes triticale with the same use pattern as wheat and barley, the Meeting decided to extrapolate the estimated maximum residue level and STMR value for wheat to triticale.

*Tree nuts*

Sulfoxaflor is proposed for use on tree nuts as two foliar applications at 0.2 kg ai/ha, a 7-day RTI, and a 7-day PHI.

*Almond*

In six almond trials from the USA matching the proposed GAP, residues of sulfoxaflor in almond nutmeat were less than the LOQ of 0.01 mg/kg in five trials, and 0.012 mg/kg in one trial.

*Pecan*

In six pecan trials from the USA matching the proposed GAP, residues of sulfoxaflor in pecan nutmeat did not exceed the LOQ (0.01 mg/kg).

*Summary – tree nuts*

Residue data from trials complying with the proposed GAP were available for almonds and pecans. Residues were higher in almonds and the Meeting decided to estimate a tree nut group maximum residue level based on the almond data.

The Meeting estimated a maximum residue level of 0.015 mg/kg for sulfoxaflor on tree nuts. The Meeting estimated STMR and HR values of 0.01 and 0.012 mg/kg, respectively, for sulfoxaflor residues in tree nuts.

*Oilseeds*

Supervised trials data were available for cotton seed and rape seed.

*Cotton Seed*

The proposed GAP for use of sulfoxaflor in cotton consists of a maximum of four foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 14-day PHI.

A total of 22 trials on cotton seed were available from Australia (4), Brazil (4), Southern Europe (8), and the USA (6).

Residues of sulfoxaflor, in ranked order, found in cotton seed from Australia were: < 0.010, 0.015, 0.045, and 0.080 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cotton seed from Brazil were: < 0.010, 0.014, 0.039, and 0.042 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cotton seed from Southern Europe were: 0.010, 0.012, 0.013, 0.018, 0.031, 0.043, 0.070, and 0.080 mg/kg.

Residues of sulfoxaflor, in ranked order, found in cotton seed from the USA were: 0.010, 0.015, 0.017, 0.023, 0.041, and 0.18 mg/kg.

The Meeting observed that sulfoxaflor residues were highest in cotton trials from the USA, and decided to estimate maximum residue levels on this data set. The Meeting estimated a maximum residue level of 0.4 mg/kg for sulfoxaflor on cotton seed. The Meeting estimated an STMR value of 0.020 mg/kg for sulfoxaflor residues in cotton seed.

*Rape seed*

The proposed GAP for oilseed rape allows the use of sulfoxaflor with two foliar applications at 0.05 kg ai/ha, a 14-day RTI, and a 14-day PHI.

A total of 14 trials on rape seed were available from Australia (1), Northern Europe (3), Southern Europe (2), and USA/Canada (8).

The sulfoxaflor residue concentrations in rape seed from Australian trial was 0.060 mg/kg.

Residues of sulfoxaflor, in ranked order, found in rape seed from Northern Europe were: 0.027, 0.038, and 0.057 mg/kg.

The sulfoxaflor residue concentrations in rape seed from Southern Europe were: 0.12 and 0.30 mg/kg.

Residues of sulfoxaflor, in ranked order, found in rape seed from USA/Canada were: < 0.010, 0.017, 0.035, 0.042, 0.047, 0.051, 0.072, and 0.085 mg/kg.

The Meeting observed that a sufficient number of trials were only available from USA/Canada, and decided to estimate a maximum residue level based on this data set. The Meeting estimated a maximum residue level of 0.15 mg/kg for sulfoxaflor on rape seed. The Meeting estimated an STMR value of 0.045 mg/kg for sulfoxaflor residues in rape seed.

***Residues in animal feed***

*Straw, fodder and forage of cereal grains*

*Barley straw and fodder*

Supervised trials data were available for barley straw and hay.

Proposed GAP for barley allows the use of sulfoxaflor for two foliar applications at 0.050 kg ai/ha, with a 14-day RTI and a 7-day PHI for hay and a 14-day PHI for straw.

*Barley Straw*

A total of 24 trials on barley straw were available from Australia/New Zealand (6), Northern Europe (7), Southern Europe (6), and the USA (5).

Residues of sulfoxaflor found in barley straw from Australia/New Zealand, in ranked order, were: 0.03, 0.090, 0.10, 0.22, 0.24, and 1.41 mg/kg.

Residues of sulfoxaflor found in barley straw from Northern Europe, in ranked order, were: 0.014, 0.051, 0.073, 0.11, 0.13, 0.22, and 0.26 mg/kg.

Residues of sulfoxaflor found in barley straw from Southern Europe, in ranked order, were: 0.12, 0.32, 0.37, 0.52, 0.53, and 0.58 mg/kg.

Residues of sulfoxaflor measured in barley straw from USA, in ranked order, were: 0.039, 0.19, 0.20, 0.59, and 0.70 mg/kg.

The Meeting observed that the highest sulfoxaflor residues occurred in the Australia/New Zealand trials for barley straw.

*Barley Hay*

A total of 20 trials on barley hay were available from Northern Europe (6), Southern Europe (8), and USA (6).

Residues of sulfoxaflor measured in barley hay, in ranked order, from Northern Europe were: 0.041, 0.086, 0.20 (2), 0.25, and 0.64 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in barley hay from Southern Europe were: 0.030, 0.037, 0.21, 0.36, 0.38, 0.39, 0.41, and 0.43 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in barley hay from USA were: < 0.010, 0.11, 0.12, 0.31 (2) and 0.46 mg/kg.

The Meeting observed that the highest sulfoxaflor residues occurred in the Northern European trials for barley hay.

*Wheat straw, fodder, and forage*

Supervised trials data were available for wheat straw, hay and forage.

The proposed GAP for wheat allows the use of sulfoxaflor for two foliar applications at 0.050 kg ai/ha, a 14-day RTI and with PHI's for hay and forage of 7-days and a PHI for straw of 14-days.

*Wheat Straw*

A total of 34 trials on wheat straw were available from Australia/New Zealand (6), Brazil (4), Northern Europe (7), Southern Europe (6), and USA/Canada (11).

Residues of sulfoxaflor, in ranked order, measured in wheat straw from Australia/New Zealand were: 0.060, 0.29 (2), 0.41, 0.46, and 1.38 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat straw from Brazil were: 0.052, 0.084, 0.24, and 1.06 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat straw from Northern Europe were: 0.11, 0.22, 0.23, 0.32, 0.35, 0.49, and 0.51 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat straw from Southern Europe were: 0.18, 0.21, 0.32, 0.62 (2), and 0.81 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat straw from USA/Canada were: 0.043, 0.063, 0.071, 0.11 (2), 0.12, 0.17, 0.22, 0.31, 1.34, and 1.60 mg/kg.

The Meeting observed that the highest sulfoxaflor residues occurred in the USA/Canada trials for wheat straw.

*Wheat Hay*

A total of 29 trials on wheat hay were available from Brazil (4), Northern Europe (7), Southern Europe (7), and USA/Canada (11).

Residues of sulfoxaflor, in ranked order, measured in wheat hay from Brazil were: 0.26, 0.42, and 0.53(2) mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat hay from Northern Europe were: 0.074, 0.19, 0.21, 0.22, 0.34, 0.49, and 0.60 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat hay from Southern Europe were: 0.087, 0.10, 0.28, 0.31, 0.43, 0.57, and 0.85 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat hay from USA/Canada were: 0.026, 0.048, 0.082, 0.10, 0.15, 0.16, 0.19, 0.20, 0.21, 0.35, and 0.41 mg/kg.

The Meeting observed that the highest sulfoxaflor residues occurred in the Southern European trials for wheat hay.

*Summary of 'barley straw and fodder' and 'wheat straw and fodder'*

'Barley straw and fodder' and 'wheat straw and fodder', as commodities moving in trade, may not always be readily distinguishable from each other. Consequently, the Meeting considered it preferable that the two commodities have the same Codex MRL. For sulfoxaflor, residues in wheat straw were higher than in the barley straw, and higher than residues in hay samples. The Meeting agreed to use

the wheat straw data from USA/Canada for the maximum residue level estimation for both 'barley straw and fodder' and 'wheat straw and fodder'.

On a dry-weight basis (DM = 88%), sulfoxaflor residues in wheat straw were (n = 11): 0.049, 0.072, 0.081, 0.13 (2), 0.14, 0.19, 0.25, 0.35, 1.52, and 1.82 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg for sulfoxaflor on wheat and barley straw and fodder, dry. The Meeting estimated median and highest residue values of 0.14 and 1.8 mg/kg, respectively, for sulfoxaflor residues in wheat and barley straw and fodder, dry.

*Wheat Forage*

A total of 30 trials on wheat forage were available from Australia (1), Brazil (4), Northern Europe (8), Southern Europe (6), and USA/Canada (11).

The sulfoxaflor residue concentration in wheat forage from the Australian trial was 0.92 mg/kg.

Residues of sulfoxaflor measured in wheat forage from Brazil, in ranked order, were: 0.095, 0.11 (2), and 0.39 mg/kg.

Residues of sulfoxaflor measured in wheat forage from Northern Europe, in ranked order, were: 0.020, 0.15, 0.17, 0.18, 0.19, 0.23, 0.37, and 0.44 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat forage from Southern Europe were: 0.033, 0.035, 0.066, 0.070, 0.10, and 0.37 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in wheat forage from USA/Canada were: 0.011, 0.024, 0.042, 0.052, 0.065, 0.086, 0.092, 0.099, 0.11, 0.20, and 0.29 mg/kg.

The Meeting observed that the highest sulfoxaflor residues occurred in the wheat forage trials from Northern Europe, and based residue estimates for wheat forage on this data set.

For livestock dietary burden purposes, the Meeting estimated median and highest residue values for sulfoxaflor on wheat forage at 0.19 and 0.44 mg/kg, respectively. There is no need for a maximum residue level estimate as wheat forage is not considered a tradeable commodity.

*Soya bean forage and hay (fodder)*

Supervised trials data were available for soya bean forage and hay.

The proposed GAP for soya bean forage allows the use of sulfoxaflor with two foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI; while that for soya bean hay (fodder) allows the use of four applications at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI.

*Soya bean forage*

A total of 19 trials on soya bean forage were available from Brazil (4) and USA (15).

Residues of sulfoxaflor, in ranked order, measured in soya bean forage from Brazil were: 0.11, 0.22, 0.28, and 0.37 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in soya bean forage from the USA were: 0.020, 0.036, 0.11, 0.13, 0.16, 0.19, 0.21, 0.22, 0.36, 0.37, 0.40, 0.44, 0.53, 1.14, and 1.69 mg/kg.

On the basis of the soya bean forage trials from the USA, the Meeting estimated median and highest residue values of 0.22 and 1.7 mg/kg, respectively, for soya bean forage.

*Soya bean hay*

A total of 19 trials on soya bean hay were available from Brazil (4) and USA (15).

Residues of sulfoxaflor, in ranked order, measured in soya bean hay from Brazil were: 0.25, 0.72, 1.01, and 1.22 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in soya bean hay from USA were: 0.072, 0.12, 0.13, 0.25, 0.46, 0.50, 0.56, 0.67, 0.87, 0.89, 0.94, 0.97, 1.01, 1.05, and 1.24 mg/kg.

On the basis of the soya bean hay trials from the USA, the Meeting estimated a maximum residue level of 3 mg/kg for sulfoxaflor on soya bean fodder. The median and highest residue values were 0.67 and 1.2 mg/kg, respectively.

*Almond hulls*

Supervised trials data were available for almond hulls. The proposed GAP for sulfoxaflor use on almond specifies two foliar applications at 0.2 kg ai/ha, a 7-day RTI, and a 7-day PHI.

In six almond trials from the USA matching GAP, Residues of sulfoxaflor, in ranked order, measured in almond hulls were: 1.22, 1.48, 1.52, 2.15, 2.25, and 3.06 mg/kg.

The Meeting estimated a median residue value of 1.8 mg/kg for sulfoxaflor residues in almond hulls.

*Sugar beet leaves and tops*

Supervised trials data were available for sugar beet tops from Northern Europe (4), Southern Europe (4), and the USA (5).

The proposed GAP for the use of sulfoxaflor on sugar beet specifies four foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 7-day PHI.

Residues of sulfoxaflor, in ranked order, measured in sugar beet tops from Northern Europe were: 0.84, 0.86, 0.91, and 1.61 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in sugar beet tops from Southern Europe were: 0.064, 0.37, 0.53, and 0.75 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in sugar beet tops from USA were: 0.15, 0.39, 0.42, 0.55, and 1.61 mg/kg.

The Meeting observed that sulfoxaflor residues were highest in sugar beet trials from Northern Europe and the USA. However, as there were five trials from the USA and only four trials from Northern Europe, the Meeting decided to use the USA data set in its estimations. The Meeting estimated median and highest residue values of 0.42 and 1.6 mg/kg for sulfoxaflor residues in sugar beet tops or leaves.

*Cotton gin trash*

A total of 21 trials on cotton gin trash were available from Australia (4), Brazil (4), Southern Europe (7), and the USA (6).

The proposed GAP for sulfoxaflor use on cotton specifies a maximum of four foliar applications at 0.1 kg ai/ha, a 7-day RTI, and a 14-day PHI.

Residues of sulfoxaflor measured in cotton gin trash from Australia, in ranked order, were: 0.17, 0.59, 1.60, and 3.85 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cotton gin trash from Brazil were: 0.35, 0.51, 0.93, and 1.52 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cotton gin trash from Southern Europe were: 0.19, 0.23, 0.35, 0.41, 0.49, 0.89, and 1.4 mg/kg.

Residues of sulfoxaflor, in ranked order, measured in cotton gin trash from USA were: 0.042, 0.048, 0.061, 0.23, 0.58, and 4.03 mg/kg.

The Meeting observed that the USA data set had the highest cotton gin trash residue values, and decided to estimate residue levels on this data set. The Meeting estimated median and highest residue levels of 0.15 and 4.0 mg/kg, respectively, for sulfoxaflor residues in cotton gin trash.

***Fate of residues during processing***

The Meeting received information on the fate of sulfoxaflor residues during the processing of apple to juice and pomace; barley to pearled barley, barley bran, barley flour, beer and malt; cabbage to sauerkraut; carrot to carrot juice; cherry to dried cherry; cotton seed to meal, hulls, and refined oil; grapes to juice, pomace, raisin, and wine; oranges to pulp, juice and oil; plums to dried prunes; potato to wet peelings, flakes, fries, chips, and dried potato; soya bean to aspirated grain fractions, meal, hulls, and refined oil; strawberry to juice and jam; sugar beet to juice, sugar, molasses, and dried pulp; tomatoes to juice, ketchup, puree, and paste; and wheat to aspirated grain fractions, bran, middlings, shorts, flour, gluten, starch, and bread.

Also information was provided on hydrolysis studies of sulfoxaflor to assist with identification of the nature of the residue during processing.

Sulfoxaflor was stable during the hydrolysis conditions simulating food processing conditions.

Calculated processing factors are summarized in the following table. Factors are indicated with a '<' (less-than) sign when the residue in the processed commodity is below the LOQ of the analytical method. The calculation is then made on the LOQ of the analytical method and the residue concentration of the RAC (raw agricultural commodity). The best estimates of the processing factors are summarized in the middle column of the table. The fourth column provides the STMR or HR of the RAC, and the last column presents the STMR-P or HR-P values obtained by multiplying the PF with the RAC STMR or HR value, as appropriate for the particular processed commodity under consideration.

Processes included in the table are those that lead to STMR-P or HR-P values useful for dietary intake estimations or for livestock dietary burden calculations.

| Raw Agricultural Commodity (RAC) | Processed Commodity | Best Estimate Processing Factor (PF) | RAC STMR/HR (mg/kg) | STMR-P/HR-P (mg/kg) |
|---|---|---|---|---|
| Apple | Wet pomace | 1.1 | 0.07 | 0.077 |
| | Dry pomace | 4.2 | | 0.29 |
| | Juice | 0.4 | | 0.028 |
| | Sauce | 0.6 | | 0.042 |
| Barley | Pearled | 0.7 | 0.063 | 0.044 |
| | Bran | 1.0 | | 0.063 |
| | Flour | 0.8 | | 0.050 |
| | Malt sprouts | 1.3 | | 0.082 |
| | Beer | 0.2 | | 0.013 |
| Cabbage | Sauerkraut | 0.09 | 0.099 | 0.009 |
| Canola (rape seed) | Meal | 1.9 | 0.045 | 0.086 |
| | Oil | 0.3 | | 0.014 |
| Carrot | Juice | 2.4 | 0.01 | 0.024 |
| Cherry | Juice | 0.8 | 0.91/1.2 | 0.73 |
| | Jam | 1.1 | | 1.0 |
| | Dried | 5.1 | | 4.6/6.1 |
| Cotton | Hulls | 1.8 | 0.02 | 0.036 |
| | Meal | 0.8 | | 0.016 |
| | Oil | < 0.1 | | < 0.002 |
| Grape | Raisin | 3.5 | 0.14/1.6 | 0.49/5.6 |
| | Juice | 0.7 | | 0.098 |

| Raw Agricultural Commodity (RAC) | Processed Commodity | Best Estimate Processing Factor (PF) | RAC STMR/HR (mg/kg) | STMR-P/HR-P (mg/kg) |
|---|---|---|---|---|
| | Pomace | 1.0 | | 0.14 |
| | Wine | 0.7 | | 0.098 |
| Orange | Juice | 0.14 | 0.31 | 0.043 |
| | Wet pulp | 2.5 | | 0.78 |
| | Dried pulp | 8.3 | | 2.6 |
| | Oil | < 0.2 | | < 0.062 |
| | Peel | 5.6 | | 1.7 |
| Potato | Flakes | 2.5 | 0.01 | 0.025 |
| | Chips | 2.1 | | 0.021 |
| | Dried | 3.6 | | 0.036 |
| | French Fries | 1.6 | | 0.016 |
| Soya bean | Aspirated grain fractions | 94 | 0.011 | 1.0 |
| | Meal | 1.3 | | 0.014 |
| | Hulls | 1.5 | | 0.017 |
| | Oil | 0.3 | | 0.0033 |
| Strawberry | Juice | 0.3 | 0.19 | 0.057 |
| | Jam | 0.4 | | 0.076 |
| Sugar beet | Thick juice | 4.7 | 0.014 | 0.066 |
| | Raw sugar | 1.8 | | 0.025 |
| | Molasses | 10 | | 0.14 |
| | Dried pulp | 3.0 | | 0.042 |
| Tomato | Juice | 1.0 | 0.11 | 0.11 |
| | Ketchup | 2.1 | | 0.29 |
| | Puree | 2.0 | | 0.22 |
| | Paste | 4.4 | | 0.48 |
| Wheat | Aspirated grain fractions | 21 | 0.025 | 0.53 |
| | Bran | 0.4 | | 0.010 |
| | Middlings | 0.2 | | 0.005 |
| | Shorts | 0.2 | | 0.005 |
| | Flour | 0.2 | | 0.005 |
| | Bread | < 0.2 | | < 0.005 |
| | Starch | < 0.2 | | < 0.005 |
| | Gluten | < 0.2 | | < 0.005 |

In order to determine if a maximum residue level should be recommended for processed commodities, a comparison is made between the STMR-P or HR-P value and the recommended maximum residue level for the RAC from which the processed commodity was obtained. Additionally, the processed commodity must be one that is commonly traded. For sulfoxaflor, the only processed commodity for which a maximum residue level recommendation is appropriate is dried grape, at 6 mg/kg.

### *Residues in animal commodities*

#### *Lactating dairy cattle*

The Meeting received a lactating dairy cow feeding study, which provided information on potential residues resulting in ruminant tissues and milk from sulfoxaflor residues in the animal diet.

Lactating Holstein dairy cows were dosed for 28–30 days once daily via a gelatine capsule with a mixture of sulfoxaflor, X11719474, and X11721061. The sulfoxaflor actual dosing rates were 0.45, 2.4, 6.8, and 35 ppm in the dry-weight diet. Lesser concentrations of the metabolites were dosed in proportion to the potential exposure from formation of these compounds in livestock feedstuffs.

Residues of sulfoxaflor transferred into milk, skim milk, and cream at all dose levels. Residues of sulfoxaflor reached a plateau in milk within 8 days of dosing. There was no evidence of preferential transfer of residues to skim milk or cream; in general, residues of sulfoxaflor were slightly lower in cream than in skim milk at all dose levels. In tissues, residues of sulfoxaflor transferred into muscle, fat, liver, and kidney at all dose levels. Residues were generally highest in liver and kidney and lowest in fat.

*Laying hens*

The Meeting also received a laying hen feeding study, which provided information on potential residues resulting in poultry tissues and egg from sulfoxaflor residues in the animal diet.

Lohman laying hens were dosed for 29 or 30 days once daily via a gelatine capsule with a mixture of sulfoxaflor, X11719474, and X11721061. The sulfoxaflor actual dosing rates were 0.15, 0.76, 2.1, and 10.7 ppm in the dry weight diet. Lesser concentrations of the metabolites were dosed in proportion to the potential exposure from formation of these compounds in the livestock feedstuffs.

In eggs, quantifiable residues of sulfoxaflor were observed at all dose levels except the lowest dose level. Residues of sulfoxaflor after plateau ranged from 0.020 to 0.59 mg/kg and were dependent on dose level. Quantifiable residues of sulfoxaflor transferred into liver at all dose levels and into muscle and fat at dose levels of 0.76 ppm and higher. In general, residues were highest in liver and lowest in fat.

*Farm animal dietary burden*

The Meeting estimated the dietary burden of sulfoxaflor in livestock on the basis of the diets listed in OECD Feed Table 2009[1]. Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating maximum residue levels, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities.

*Estimated maximum and mean dietary burdens of farm animals*

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the livestock diets from US-Canada, EU, Australia and Japan in the OECD Feed Table 2009.

| | | Livestock dietary burden, sulfoxaflor, ppm of dry matter diet | | | |
|---|---|---|---|---|---|
| | | US-Canada | EU | Australia | Japan |
| Max | beef cattle | 0.64 | 2.00 | 3.04 [a] | 0.05 |
| | dairy cattle | 1.23 | 2.68 [c] | 2.31 | 0.04 |
| | poultry - broiler | 0.07 | 0.07 | 0.02 | 0.01 |
| | poultry - layer | 0.07 | 0.89 [e] | 0.02 | 0.00 |
| | | | | | |
| Mean | beef cattle | 0.18 | 0.60 | 0.91 | 0.05 |
| | dairy cattle | 0.57 | 0.77 | 0.90 [b d] | 0.04 |
| | poultry - broiler | 0.07 | 0.07 | 0.02 | 0.01 |
| | poultry - layer | 0.07 | 0.30 [f] | 0.02 | 0.00 |

[a] Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimates for mammalian meat.

[1] Available from: http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmpr/jmpr-docs/en/).

[b] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[c] Highest maximum dairy cattle dietary burden suitable for maximum residue level estimates for milk.

[d] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[e] Highest maximum poultry dietary burden suitable for maximum residue level estimates for poultry meat and eggs.

[f] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

### *Animal commodities, maximum residue level estimation*

*Cattle*

The sulfoxaflor maximum dietary burden for beef and dairy cattle is 3.04 and 2.68 ppm, respectively. The sulfoxaflor mean dietary burden for beef and dairy cattle is 0.91 and 0.90 ppm, respectively.

For maximum residue level estimation, the high residues in the tissues were calculated by multiplying the maximum dietary burden (3.04 ppm) by the higher tissue transfer factor (TF = maximum tissue residue divided by feeding level dose) of the two bracketing feeding levels (2.4 and 6.8 ppm) from the dairy cow feeding study.

The STMR values for the tissues were calculated by multiplying the mean dietary burden (0.91 ppm) by the higher tissue transfer factor (mean tissue residue divided by feeding level dose) of the two bracketing feeding levels (0.45 and 2.4 ppm) from the dairy cow feeding study.

For milk maximum residue level estimation, the high residues in the milk were calculated by multiplying the maximum dietary burden (2.68 ppm) by the higher tissue transfer factor (mean milk residue divided by feeding level dose) of the two bracketing feeding levels (2.4 and 6.8 ppm) from the dairy cow feeding study.

The STMR value for milk was calculated by multiplying the mean dietary burden (0.90 ppm) by the higher tissue transfer factor (mean milk residue divided by feeding level dose) of the two bracketing feeding levels (0.45 and 2.4 ppm) from the dairy cow feeding study.

This process is summarized in the table below, where the selected tissue transfer factor is indicated by shading. The estimated maximum residue levels were based on the higher of the two projected residue levels for each commodity.

| Cattle commodity | | Feeding level (ppm) 0.45 | 2.4 | 6.8 | 35 | Dietary burden (ppm) | Projected residue levels (mg/kg) | Estimated maximum residue level (mg/kg) |
|---|---|---|---|---|---|---|---|---|
| Milk | HR (mg/kg) | 0.038 | 0.123 | 0.288 | 1.679 | | | |
| | TFHR | 0.084 | 0.051 | 0.042 | 0.048 | 2.68 | 0.14 | 0.2 |
| | STMR (mg/kg) | 0.024 | 0.090 | 0.243 | 1.253 | | | |
| | TFSTMR | 0.053 | 0.0375 | 0.036 | 0.036 | 0.90 | 0.048 | |
| Muscle | HR (mg/kg) | 0.026 | 0.155 | 0.311 | 1.691 | | | |
| | TFHR | 0.058 | 0.065 | 0.046 | 0.048 | 3.04 | 0.20 a | 0.3 |
| | STMR(mg/kg) | 0.020 | 0.105 | 0.271 | 1.453 | | | |
| | TFSTMR | 0.044 | 0.044 | 0.040 | 0.042 | 0.91 | 0.040 | |
| Fat | HR (mg/kg) | 0.014 | 0.057 | 0.139 | 0.915 | | | |
| | TFHR | 0.031 | 0.024 | 0.020 | 0.026 | 3.04 | 0.073 a | |
| | STMR (mg/kg) | 0.013 | 0.039 | 0.099 | 0.592 | | | |
| | TFSTMR | 0.029 | 0.016 | 0.015 | 0.017 | 0.91 | 0.026 | |
| Liver | HR (mg/kg) | 0.061 | 0.375 | 0.758 | 4.030 | | | |
| | TFHR | 0.136 | 0.156 | 0.111 | 0.115 | 3.04 | 0.47 | 0.6 |
| | STMR (mg/kg) | 0.057 | 0.283 | 0.744 | 3.766 | | | |
| | TFSTMR | 0.127 | 0.118 | 0.109 | 0.108 | 0.91 | 0.12 | |
| Kidney | HR (mg/kg) | 0.040 | 0.210 | 0.566 | 2.442 | | | |

| Cattle commodity | | Feeding level (ppm) 0.45 | 2.4 | 6.8 | 35 | Dietary burden (ppm) | Projected residue levels (mg/kg) | Estimated maximum residue level (mg/kg) |
|---|---|---|---|---|---|---|---|---|
| | TFHR | 0.089 | 0.088 | 0.083 | 0.070 | 3.04 | 0.27 | 0.4 |
| | STMR (mg/kg) | 0.034 | 0.184 | 0.461 | 2.282 | | | |
| | TFSTMR | 0.076 | 0.077 | 0.068 | 0.065 | 0.91 | 0.070 | |

[a] Considered together for recommending a Meat (from mammals other than marine mammals) maximum residue level.

TF = Transfer factor.

The Meeting estimated the following STMR values: milk of 0.048 mg/kg; edible offal (based on liver) at 0.12 mg/kg; muscle at 0.040 mg/kg; and fat at 0.026 mg/kg.

The Meeting estimated the following HR values: milk, 0.14 mg/kg; edible offal (based on liver), 0.47 mg/kg; muscle, 0.20 mg/kg; and fat, 0.073 mg/kg.

The Meeting estimated the following maximum residue levels: milks, 0.2 mg/kg; edible offal (Mammalian), 0.6 mg/kg; and meat (from mammals other than marine mammals) at 0.3 mg/kg.

*Poultry*

The sulfoxaflor maximum dietary burden for poultry is 0.89 ppm and the mean dietary burden is 0.30 ppm.

For maximum residue level estimation, the high residues in the tissues were calculated by multiplying the maximum dietary burden (0.89 ppm) by the higher tissue transfer factor (maximum tissue residue divided by feeding level dose) of the two bracketing feeding levels (0.76 and 2.1 ppm) from the laying hen feeding study.

The STMR values for the tissues were calculated by multiplying the mean dietary burden (0.30 ppm) by the tissue transfer factor (mean tissue residue divided by feeding level dose) at the 0.76 ppm feeding level from the laying hen feeding study. The tissue transfer factor computed at the 0.15 ppm feeding level was based on < LOQ residue levels and, therefore, was not appropriate for STMR value determinations.

For egg maximum residue level estimation, the high residues in the egg were calculated by multiplying the maximum dietary burden (0.89 ppm) by the higher tissue transfer factor (mean egg residue divided by feeding level dose) of the two bracketing feeding levels (0.76 and 2.1 ppm) from the laying hen feeding study.

The STMR value for egg was calculated by multiplying the mean dietary burden (0.30 ppm) by the egg transfer factor (mean egg residue divided by feeding level dose) at the 0.76 ppm feeding level from the laying hen feeding study. The egg transfer factor computed at the 0.15 ppm feeding level was based on < LOQ residue levels and, therefore, was not appropriate for STMR value determinations.

This process is summarized in the table below, where the selected tissue transfer factor is indicated by shading. The estimated maximum residue levels were based on the higher of the two projected residue levels for each commodity.

| Poultry commodity | | Feeding level (ppm) 0.15 | 0.76 | 2.1 | 10.7 | Dietary burden (ppm) | Projected residue levels (mg/kg) | Estimated maximum residue level (mg/kg) |
|---|---|---|---|---|---|---|---|---|
| Eggs | HR (mg/kg) | 0.01 | 0.059 | 0.099 | 0.594 | | | |
| | $TF_{HR}$ | NC [a] | 0.078 | 0.047 | 0.056 | 0.89 | 0.069 | 0.1 |
| | STMR(mg/kg) | 0.01 | 0.031 | 0.081 | 0.423 | | | |

| Poultry commodity | | Feeding level (ppm) | | | | Dietary burden (ppm) | Projected residue levels (mg/kg) | Estimated maximum residue level (mg/kg) |
|---|---|---|---|---|---|---|---|---|
| | | 0.15 | 0.76 | 2.1 | 10.7 | | | |
| | $TF_{STMR}$ | NC [a] | 0.041 | 0.039 | 0.040 | 0.30 | 0.012 | |
| Muscle | HR (mg/kg) | 0.01 | 0.042 | 0.109 | 0.659 | | | |
| | $TF_{HR}$ | NC [a] | 0.055 | 0.052 | 0.062 | 0.89 | 0.049 [b] | 0.1 |
| | STMR (mg/kg) | 0.01 | 0.035 | 0.086 | 0.448 | | | |
| | $TF_{STMR}$ | NC [a] | 0.046 | 0.041 | 0.042 | 0.30 | 0.014 | |
| Liver | HR (mg/kg) | 0.028 | 0.150 | 0.232 | 1.193 | | | |
| | $TF_{HR}$ | 0.193 | 0.198 | 0.111 | 0.111 | 0.89 | 0.18 | 0.3 |
| | STMR (mg/kg) | 0.015 | 0.110 | 0.171 | 1.118 | | | |
| | $TF_{STMR}$ | 0.103 | 0.145 | 0.082 | 0.104 | 0.30 | 0.044 | |
| Fat | HR (mg/kg) | 0.01 | 0.013 | 0.048 | 0.184 | | | |
| | $TF_{HR}$ | NC [a] | 0.017 | 0.023 | 0.017 | 0.89 | 0.020 [b] | |
| | STMR (mg/kg) | 0.01 | 0.012 | 0.033 | 0.164 | | | |
| | $TF_{STMR}$ | NC [a] | 0.016 | 0.016 | 0.015 | 0.30 | 0.005 | |

[a] NC - not calculated since residues were < 0.01 mg/kg (LOQ).

[b] Considered together for recommending a Poultry meat maximum residue level.

TF = Transfer factor.

The Meeting estimated the following STMR values: egg, 0.012 mg/kg; edible offal of poultry (based on liver), 0.044 mg/kg; muscle, 0.014 mg/kg; and fat, 0.005 mg/kg.

The Meeting estimated the following HR values: egg, 0.069 mg/kg; edible offal of poultry (based on liver), 0.18 mg/kg; muscle, 0.049 mg/kg; and fat, 0.020 mg/kg.

The Meeting estimated the following maximum residue levels: eggs, 0.1 mg/kg; edible offal of poultry, 0.3 mg/kg; and poultry meat, 0.1 mg/kg.

## DIETARY RISK ASSESSMENT

### *Long-term intake*

The International Estimated Daily Intakes (IEDI) for sulfoxaflor was estimated for the 13 GEMS/Food cluster diets using the STMR or STMR-P values estimated by the current Meeting. The results are shown in Annex 3. The IEDI ranged from 1 to 8% of the maximum ADI (0–0.05 mg/kg bw). The Meeting concluded that the long-term intake of residues of sulfoxaflor, from uses that have been considered by the JMPR, is unlikely to present a public health concern.

### *Short-term intake*

The International Estimated Short Term Intake (IESTI) for sulfoxaflor was calculated for the plant and livestock commodities (and their processing factions) for which STMRs and HRs were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI varied from 0 to 70% of the ARfD (0.3 mg/kg bw). The Meeting concluded that the short-term intake of residues of sulfoxaflor, from uses that have been considered by the JMPR, is unlikely to present a public health concern.