5.21 SAFLUFENACIL (251)

RESIDUE AND ANALYTICAL ASPECTS

Saflufenacil is a herbicide belonging to the uracil family of compounds. The biochemical mode of action is a protoporphyrinogen IX oxidase (PPO) inhibitor. Saflufenacil was evaluated as a new compound by the 2011 JMPR. The 2011 Meeting determined that the residue definition for MRL compliance and estimation of dietary exposure for both plant and animal commodities is parent saflufenacil, and that the residue is not fat soluble. The 2011 Meeting also derived an ADI of 0–0.05 mg/kg bw and determined that an ARfD is not necessary.

Saflufenacil was listed by the 47th Session of the CCPR for the evaluation of additional MRLs. The 2016 Meeting received residue data reflecting use of saflufenacil on pomegranate, dessicant uses on barley and wheat, peanut, sunflower, olive, sugarcane, alfalfa, and perennial grasses. In addition, the Meeting received a metabolism study for rice.

Plant metabolism

In a study depicting the metabolism of saflufenacil in rice, upland (dry land) rice (BBCH 22–24) was treated with a single, foliar application of saflufenacil, radiolabelled in either the phenyl or uracil moieties, at a rate of 100 g ai/ha. A sample of rice forage was collected one week after application, and samples of rice grain and straw were collected four to five months after application. Major residues (defined as ≥ 10% TRR and ≥ 0.01 mg/kg) occurred only in forage and straw, and were identified as saflufenacil (ca. 60–80% TRR, ca. 1 mg/kg in forage; ca. 44% TRR, 0.3–1 mg/kg in straw), M800H11 (14% TRR, 0.25 mg/kg in forage (phenyl-label only)), M800H35 (10% TRR, 0.26 mg/kg in straw(phenyl-label only)), M800H02 (16% TRR 0.3 mg/kg in forage (phenyl-label only)), M800H29 (trifluoroacetic acid; 14% TRR, 0.09 mg/kg in straw (uracil-label only)). In grain, radioactivity was associated primarily with carbohydrates (54–62% TRR, 0.02–0.07 mg eq./kg).

As with studies reviewed by the 2011 Meeting, the metabolism study in rice shows that saflufenacil is the predominant residue in matrices where it was found. The metabolism study in rice supports the original conclusion that the residue definition for both compliance and dietary intake is saflufenacil.

Methods of analysis

Analytical methods used for analysis of saflufenacil trials being evaluated by the current Meeting were found to be acceptable by the 2011 Meeting. The reported limit of quantification (LOQ) is based on the lowest limit of method validation and is either 0.01 mg/kg or 0.025 mg/kg, depending on the matrix.

Stability of pesticide residues in stored analytical samples

The stability of saflufenacil, M800H35, and M800H11 in plant matrices was evaluated by the 2011 Meeting, which determined that residues of saflufenacil, M800H11, and M800H35 are stable in maize, soya bean, orange, radish root, raisin, and chickpea matrices for at least 553 days (JMPR, 2011).

The 2016 Meeting received storage stability data for the saflufenacil metabolite M800H02 in cereal, oilseed, legume, and citrus matrices. The data indicate that M800H02 is stable in orange fruit, kidney bean, canola seed, wheat grain, wheat forage, and wheat hay for at least 768 days. In addition, the 2016 Meeting received storage stability data for saflufenacil in bovine muscle, liver, and milk, and in poultry egg. The data demonstrate that saflufenacil is stable in those matrices for at least 125 days.

Results of supervised residue trials on crops

The Meeting received data from supervised residue trials conducted on olive, pomegranate, barley, wheat, sugar cane, peanut, sunflower seed, alfalfa, and perennial forage grass. Field trials were conducted in Brazil, Canada, and the US. All residue results are supported by adequate method and storage stability data, and reflect independent trials unless otherwise noted.

Olives

For olives, the critical GAP is from the registration in the US (four applications at 50 g ai/ha with a 0-day PHI). The Meeting notes that the label directs the applicator to avoid treating tree foliage, flowers, buds, and fruit. Four field trials are available reflecting residues resulting from three applications, each at 50 g a.i/ha and harvest zero days after the last application (DALA). The Meeting determined that a fourth application would be unlikely to significantly impact residues since it would be made early in the growing season and saflufenacil has a relatively short field half-life. The Meeting noted that olives were harvested by hand and pitted in the field prior to being frozen. Given that residues of saflufenacil are stable to hydrolysis at pH ≤ 7 (JMPR 2011) and that no degradation of residues was observed in homogenised, frozen storage stability samples, the current Meeting determined that the field pitting is unlikely to have had a negative impact on the suitability of the trials.

Mean field trial residues of saflufenacil in pitted olives from independent field trials matching the critical GAP (n = 4) were: < 0.01 (4) mg/kg. Furthermore, residues from a single trial conducted at a five-fold exaggerated application rate were also < 0.01 mg/kg.

Olives are considered a major commodity, generally requiring a minimum of six trials to support a recommendation by the Meeting. Furthermore, hand harvesting of the olives precludes contamination from residues on the ground that would be expected to occur based on the use pattern (ground-directed spray, 0-day PHI) and mechanical harvesting techniques that are frequently used. As the trials are unlikely to reflect residues that would be expected following common agricultural practices for olive, the Meeting decided to not make a recommendation for olives.

Pomegranate

For pomegranate, the critical GAP is from the registration in the US (four applications at 50 g ai/ha on a 21-day interval with a 0-day PHI). The Meeting notes that the label directs the applicator to avoid treating tree foliage, flowers, buds, and fruit. Four field trials are available reflecting residues resulting from four applications, each at 50 g ai/ha and harvest 0 DALA. The Meeting noted that pomegranates were quartered in the field prior to being frozen. Given that residues of saflufenacil are stable to hydrolysis at pH ≤ 7 (JMPR 2011) and that no degradation of residues was observed in homogenised storage stability samples, the field quartering is unlikely to have had a negative impact on the suitability of the trials. Furthermore, the Meeting determined that the two trials conducted in Parlier, California are not independent; therefore, only data from only three independent trials are available.

Mean field trial residues of saflufenacil in pomegranate from independent field trials matching the critical GAP (n = 3) were: < 0.01 (3) mg/kg.

The Meeting noted that saflufenacil is a herbicide that is not translocated, that residues would not be expected from the use under consideration, and that all of the available trials had non-quantifiable residues, the Meeting determined that the available data are sufficient. The Meeting estimated a maximum residue level for pomegranate of 0.01* mg/kg and an STMR of 0.

Barley

For barley, the critical GAP is from registration in the US as a harvest aid (one application at 50 g ai/ha with a 3-day PHI). Fifteen field trials are available reflecting residues resulting from one application at 50 g ai/ha and harvest 3 DALA.

Mean field trial residues of saflufenacil in barley grain from independent field trials matching the critical GAP (n = 14) were: 0.08, 0.12, 0.26, 0.28, 0.30, 0.30, 0.32, 0.34, 0.38, 0.38, 0.39, 0.40, 0.48, and 0.54 mg/kg.

The Meeting estimated a maximum residue level for barley grain of 1 mg/kg and an STMR of 0.33 mg/kg.

Wheat

For wheat, the critical GAP is from a registration in the US as a harvest aid (one application at 50 g ai/ha with a 3-day PHI). Twenty-five field trials are available, reflecting residues resulting from one application at 50 g ai/ha and harvest 3 DALA.

Mean field trial residues of saflufenacil in wheat grain from independent field trials matching the critical GAP (n = 25) were: < 0.01 (2), 0.01 (2), 0.02 (7), 0.03 (5), 0.04, 0.06 (2), 0.08, 0.1 (3), 0.22, and 0.50 mg/kg.

The Meeting estimated a maximum residue level for wheat grain of 0.7 mg/kg and an STMR of 0.03 mg/kg. Noting that the GAP in the US includes use on triticale, the Meeting decided to extrapolate the recommendation to triticale.

Sugar cane

For sugar cane, the critical GAP is from registrations in Brazil as a harvest aid (one application at 98 g ai/ha with a 7-day PHI). Nine field trials are available reflecting residues resulting from one application at 98 g ai/ha and harvest 7 DALA.

Mean field trial residues of saflufenacil in sugar cane stalks from independent field trials matching the critical GAP (n = 9) were: < 0.01 (8), and 0.02 mg/kg.

The Meeting estimated a maximum residue level for sugar cane of 0.03 mg/kg, an STMR of 0.01 mg/kg and a highest residue of 0.02 mg/kg.

Peanut

For peanut, the critical GAP is from registrations in Nicaragua (one crop pre-emergence application at 90 g ai/ha).

Mean independent field trial residues of saflufenacil in peanut nutmeat following a single application at 50 g ai/ha with harvest seven days later (n = 8) were: < 0.01 (8) mg/kg.

The meeting concluded that the use pattern used in the field trials is likely to lead to higher residues than the label GAP due to the much shorter time between application and harvest. As all of the residues in the trials were < LOQ, the Meeting decided to make a recommendation for residues in peanut nutmeat.

The Meeting estimated a maximum residue level for peanut nutmeat of 0.01* mg/kg and an STMR of 0 mg/kg.

Sunflower

The GAP for sunflower in Canada and the US is up to two applications on a 7-day interval at up to 50 g ai/ha, with a 7-day PHI. An additional GAP exists in Brazil (one application up to 98 g ai/ha, 7-

day PHI). The 2011 Meeting evaluated eight saflufenacil residue trials on sunflower matching the US GAP (residues ranging from 0.056 to 0.44 mg/kg) and four trials matching the Brazil GAP (residues ranging from < 0.01 to 0.07 mg/kg). The 2011 Meeting noted that there was no GAP corresponding to the Brazil trials. Comparison of the US and Brazil data showed the Canadian/US GAP to be more critical. The current Meeting received three additional field trials on sunflower matching the GAP in Canada and the US as a harvest aid (two applications at 50 g ai/ha with a 7-day PHI).

Mean field trial residues of saflufenacil in sunflower seed from the newly submitted independent field trials matching the GAP (n = 3) were: 0.03, 0.12, and 0.14 mg/kg.

The Meeting recognised that residues found in the newly submitted supervised field trials are covered by the existing MRL, and confirms its previous recommendation for sunflower (maximum residue = 0.7 mg/kg, STMR = 0.12 mg/kg).

Alfalfa

For alfalfa, the critical GAP is from registrations in the US as broadcast applications during the dormant season (not to exceed 50 g ai/ha) and between cuttings (one application per cutting at 25 g ai/ha with a 21-day PHI). Twelve field trials are available reflecting residues resulting from one application at 50 g ai/ha during the dormant period, just prior to green-up and a second application at 25 g ai/ha immediately after the first cutting. Multiple cuttings were harvested, ranging from 21 to 161 DALA. Of those, eight trials had harvest approximating the label PHI (i.e., 21–28 DALA).

Mean field trial residues of saflufenacil in alfalfa forage from independent field trials matching the critical GAP (n = 8) were: < 0.025 (8) mg/kg. Residues were also < 0.025 mg/kg at all other cuttings, regardless of the DALA.

For alfalfa forage the Meeting estimated median and highest residues of 0.025 mg/kg.

Mean field trial residues of saflufenacil in alfalfa fodder (fresh) from independent field trials matching the critical GAP (n = 8) were: < 0.025 (7), and 0.026 mg/kg.

The Meeting estimated a maximum residue level for alfalfa fodder (dry) of 0.06 mg/kg, a median residue of 0.025 mg/kg (fresh), and a highest residue of 0.026 mg/kg (fresh).

Forage grass

For forage grasses, the critical GAP is from registration in the US as a post-crop emergence broadcast application (applications any time during the dormant phase, not to exceed 100 g ai/ha, followed by applications in season, on a 14-day interval, not to exceed 50 g ai/ha; neither a PHI nor a pre-grazing interval (PGI) is specified). Sixteen field trials are available reflecting residues resulting from one application at 100 g ai/ha during the dormant period, just prior to green-up and a second application at 50 g ai/ha at the boot growth stage.

Mean field trial residues of saflufenacil in grass forage from independent field trials matching the critical GAP (n = 16) were: 1.4, 1.6, 1.8, 2.2, 2.3, 2.6, 3.3, 3.6 (2), 3.8, 3.9, 4.0, 4.2, 7.1 (2), and 7.5 mg/kg.

For grass forage (fresh) the Meeting estimated a median residue of 3.6 mg/kg and a highest residue of 7.5 mg/kg.

Hay or fodder (dry) of grasses

Mean field trial residues of saflufenacil in grass hay (as received) from independent field trials matching the critical GAP noted above (n = 16) were: 2.5, 3.2, 3.7, 3.8, 4.1, 4.2, 4.8, 5.0, 5.6, 6.3, 6.8, 6.9, 8.9, 9.8, 10, and 13 mg/kg.

The Meeting estimated a maximum residue level for grass hay (dry) of 30 mg/kg based on a dry matter content of 88%.

For grass hay (as received), the Meeting estimated a median residue of 5.3 and a highest residue of 13 mg/kg.

Barley straw

For barley, the critical GAP is from registrations in Canada and the US as a harvest aid (one application at 50 g ai/ha with a 3-day PHI). Fifteen field trials are available reflecting residues resulting from one application at 50 g ai/ha and harvest 3 DALA.

Mean field trial residues of saflufenacil in barley straw (as received) from independent field trials matching the critical GAP (n = 15) were: 0.10, 0.12, 0.81, 0.86, 0.90, 1.5, 1.6, 2.3, 2.4, 2.5, 4.1, 4.6, 5.7 (2), and 6.6 mg/kg.

Wheat straw

For wheat, the critical GAP is from registrations in Canada and the US as a harvest aid (one application at 50 g ai/ha with a 3-day PHI). Twenty-five field trials are available, reflecting residues resulting from one application at 50 g ai/ha and harvest 3 DALA.

Mean field trial residues of saflufenacil in wheat straw (as received) from independent field trials matching the critical GAP (n = 25) were: 0.07, 0.22 (2), 0.34, 0.82, 0.84, 0.90, 0.92, 1.1, 1.3, 1.4 (2), 1.8, 1.9 (2), 2.0, 2.1, 2.3, 2.4 (2), 2.5, 2.6, 3.0, 3.2, and 3.4 mg/kg.

Noting that it is difficult to discern cereal straws from one another, and that there is no evidence for a difference in the residue populations between straw from barley and hay (Kruskal-Wallis test), the Meeting decided to combine the residues (as received; n = 40): 0.07, 0.10, 0.12, 0.22 (2), 0.34, 0.81, 0.82, 0.84, 0.86, 0.90 (2), 0.92, 1.1, 1.3, 1.4 (2), 1.5, 1.6, 1.8, 1.9 (2), 2.0, 2.1, 2.3 (2), 2.4 (3), 2.5 (2), 2.6, 3.0, 3.2, 3.4, 4.1, 4.6, 5.7 (2), and 6.6 mg/kg.

Based on a dry matter content of 89%, the Meeting estimated a maximum residue level for straw of barley and wheat (dry) of 10 mg/kg.

For barley and wheat straw (as received), the Meeting estimated a median residue of 1.85 mg/kg, and a highest residue of 6.6 mg/kg.

As the GAP in the US includes use on triticale, the Meeting decided to extrapolate the estimates to triticale straw.

Peanut hay

For peanuts, the critical GAP is from registrations in Nicaragua (one crop pre-emergence application at 90 g ai/ha). Eight field trials are available reflecting residues resulting from a single application at 50 g ai/ha with harvest seven days later.

No data are available from trials matching GAP; therefore, the Meeting is not making a recommendation for peanut hay.

Fate of residues during processing

Residues after processing

The Meeting received data depicting the concentration/dilution of residues during processing of barley, wheat, sugar cane, and peanuts. For all crops, processed commodities were derived using simulated commercial practices. The resulting processing factors and STMR-P estimates are summarized below.

Raw agricultural commodity	Processed commodity	Processing factors [median/best estimate][A]	MRL, mg/kg	STMR-P, mg/kg
Barley grain MRL = 1 STMR = 0.33	Pearled barley	0.28, 0.064, 0.084, 0.10 [0.092]	--	0.03
	Bran (unprocessed)	3.1, 1.6, 2.7, 3.5 [2.9]	3	0.96
	Flour	0.22, 0.058, 0.084, 0.11 [0.097]	--	0.032
	Spent grain	0.039, <0.006, <0.009, <0.008 [0.039]	--	0.013
	Beer	0.098, <0.006, <0.009, <0.008 [0.098]	--	0.032
Wheat grain MRL = 0.7 STMR = 0.03	Aspirated grain fraction	245 [245]	--	7.4
	Flour	0.083, 0.24 [0.16]	--	0.0048
	Gluten feed meal	0.50, 0.43 [0.46]	--	0.014
	Shorts	1.0, <0.05 [1.0]	--	0.03
	Whole grain bread	0.50, 0.29 [0.40]	--	0.012
Sugar cane stalk MRL = 0.03 STMR = 0.01	Bagasse	2.5 [2.5]	--	0.025
	Molasses	3.0 [3]	1	0.03

[A] Only finite factors were used to derive the mean processing factor. If no finite factor is available, then the highest factor was used to derive the STMR-P.

Residues in animal commodities

The 2011 Meeting evaluated a cattle feeding study for saflufenacil (feeding levels were 0.15 ppm, 0.48 ppm, and 1.7 ppm), and estimated dietary burdens based on saflufenacil residues in animal feed items from tree nuts, cotton, pulses, cereals, and sunflower. The current Meeting received new feeding studies conducted with lactating cattle and laying hens dosed at higher levels.

In the new cattle feeding study, lactating cows were dosed for 28 days at levels equivalent to ca. 5, 17.8, and 62.5 ppm in the feed. The study is supported by adequate analytical methods and storage stability data. Residues of saflufenacil were < 0.01 mg/kg in all samples from the control group and from all dosing levels in milk, muscle, omental fat, and subcutaneous fat. For other matrices, mean (and maximum) residues of saflufenacil at the 5, 17.8, and 62.5 ppm dose levels, respectively, were:

Perirenal fat = < 0.01 (< 0.01), 0.039, (0.051), and 0.019 (0.027) mg/kg;

Kidney = 0.081 (0.090), 0.26 (0.29), and 0.54 (0.81) mg/kg; and

Liver = 15 (16), 38 (56), and 41 (45) mg/kg.

Residues in kidney increased linearly over the dosing levels used in the study. The levels in perirenal fat and liver indicate that uptake into those commodities reached saturation between the mid- and high-dose levels.

In the new poultry feeding study, laying hens were dosed for 28 days at levels equivalent to ca. 0.98, 9.8, and 49 ppm in the feed. The study is supported by adequate analytical methods and storage stability data. Residues of saflufenacil were < 0.01 mg/kg in all control samples and from samples of eggs, fat, and muscle from the 49 ppm feeding level. Analyses were not conducted for those matrices at lower feeding levels. Residues in liver were < 0.01 mg/kg from the 9.8 ppm dose group; samples from the 0.98 ppm dose group were not analysed. The mean and maximum residues in liver from the 49 ppm dose group were 0.016 and 0.019 mg/kg, respectively.

Estimated maximum and mean dietary burdens of livestock

Dietary burden estimates from the 2011 Meeting have been recalculated by the 2016 Meeting to include contributions from barley, wheat, sugar cane, alfalfa, and forage grasses. Estimated dietary burdens for Australia, the EU, Japan, and Canada/US are summarized below. The livestock diets are listed in Annex 6.

Livestock Dietary Burdens (ppm of dry matter diet) for saflufenacil.

	Australia		EU		Japan		Canada/US	
Livestock	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Cattle (beef)	30	14	15	7.4	7.0	3.1	2.9	1.5
Cattle (dairy)	30	14	18	8.8	12	5.2	14	6.7
Poultry (broiler)	0.083	0.083	0.28	0.28	0.043	0.043	0.31	0.31
Poultry (layer)	0.083	0.083	3.3	1.8	0.060	0.060	0.31	0.31

The bold values, above, reflect the highest burdens for both MRL estimation (maximum diet) and STMR estimation (mean diet).

Animal commodities residue level estimation

Anticipated residues resulting from the dietary burdens and based on the new feeding studies are summarized below.

Saflufenacil feeding study	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat [C]
MRL beef or dairy cattle							
Feeding study [A]	17.8	< 0.01	17.8	< 0.01	56.5	0.29	0.051
	62.5	< 0.01	62.5	< 0.01	45.6	0.81	0.027
Dietary burden and high residue	30	< 0.01	30	< 0.01	54	0.43	0.044
STMR beef or dairy cattle							
Feeding study [B]	5	< 0.01	5	< 0.01	15	0.081	< 0.01
	17.8	< 0.01	17.8	< 0.01	38	0.26	0.039
Dietary burden and residue estimate	14	< 0.01	14	< 0.01	31	0.21	0.03

[A] Highest residues for tissues and mean residues for milk

[B] Mean residues for tissues and mean residues for milk

[C] Based on residue in perirenal fat

The 2011 Meeting recommended maximum residue levels of 0.3 mg/kg in mammalian edible offal and 0.01 mg/kg in each of mammalian fats (except milk fats), meat (from mammals other than marine mammals), and milks. The 2016 Meeting confirms its previous recommendations of 0.01 mg/kg for meat (from mammals other than marine mammals) and 0.01 mg/kg for milks.

The Meeting estimated new maximum residue levels for edible offal, mammalian except marine mammals of 60 mg/kg and for mammalian fats (except milk fats) of 0.05 mg/kg. The Meeting withdrew its previous recommendations for these commodities.

Furthermore, the Meeting estimated STMRs of 31 mg/kg for mammalian edible offal and 0.03 mg/kg for mammalian fat.

In the poultry feeding study, residues in samples from the 49-ppm feeding level were <0.01 in eggs, fat, and muscle; and < 0.01 to 0.019 mg/kg (mean = 0.016 mg/kg) in liver. Based on an estimated maximum dietary burden for poultry of 3.3 ppm, the Meeting estimated maximum residue

levels and STMRs of 0.01* mg/kg and 0 mg/kg, respectively, for poultry meats, fats, and eggs. The Meeting estimated a maximum residue level and STMR of 0.01* mg/kg and 0.01 mg/kg, respectively, for edible offal of poultry.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for IEDI assessment.

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

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The International Estimated Daily Intakes (IEDIs) of saflufenacil were calculated for the 17 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current and previous Meetings. The ADI is 0–0.05 mg/kg bw and the calculated IEDIs were 2–20% of the maximum ADI (0.05 mg/kg bw). The Meeting concluded that the long-term exposure to residues of saflufenacil, when used in ways that have been considered by the JMPR, are unlikely to present a public health concern.

Short-term dietary exposure

The 2011 Meeting determined that establishment of an acute reference dose is not necessary for saflufenacil. The Meeting therefore concluded that the short-term dietary exposure to residues of saflufenacil, resulting from uses that have been considered by the JMPR, is unlikely to present a public health concern.