5.28 PICOXYSTROBIN (258)

RESIDUE AND ANALYTICAL ASPECTS

Picoxystrobin (ISO common name) is a strobilurin type fungicide for use by foliar application in a range of broadacre crops including cereals, sweet corn, soya bean, rape and pulses. At the forty-third session of the CCPR (2011), picoxystrobin was scheduled for evaluation as a new compound by the 2012 JMPR.

Data was provided to the 2012 JMPR on the metabolism of picoxystrobin in food producing animals and plants, methods of analysis, stability of residues in stored analytical samples, GAP information, supervised residue trials, processing, and animal feeding studies.

The 2012 JMPR established an ADI of 0–0.09 mg/kg bw/day and an ARfD of 0.09 mg/kg bw and recommended a residues definition for enforcement in plant and animal commodities. However, the 2012 JMPR was unable to conclude on the toxicological relevance of two plant metabolites, IN-H8612 and IN-QGU64 (2-(2-formylphenyl)-2-oxoacetic acid), both of which had structural alerts for genotoxicity. As a result, the 2012 JMPR could not recommend a residue definition for dietary risk assessment, or maximum residue levels for picoxystrobin.

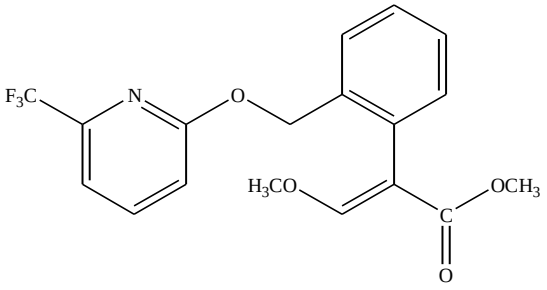
The 2013 JMPR received genotoxicity data for IN-H8612 which showed no evidence of genotoxicity. Chronic and acute exposure calculations showed that exposures were below the relevant TTC values for Cramer class III compounds with no evidence of genotoxicity and there was no concern for dietary exposure to this metabolite. However, no data was provided for IN-QGU64 as the compound could not be synthesised in sufficient amounts.

The 2016 JMPR received an additional metabolism study for soybeans during the meeting, and a preliminary evaluation indicated that that metabolic pathway was broadly similar to that observed in previously submitted plant metabolism studies in soybeans, wheat, and canola. The new study did not identify IN-QGU64 but did report IN-H8612 (a structural isomer of IN-QGU64). However the 2016 JMPR noted that in some chromatograms IN-H8612 eluted as two peaks. The 2016 JMPR concluded that there may be an interconversion between IN-H8612 and IN-QGU64 and requested further information from the Sponsor.

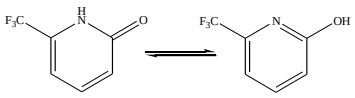
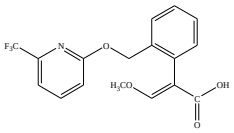
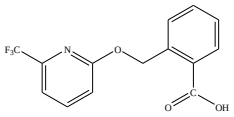
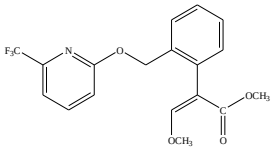
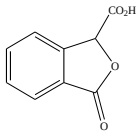
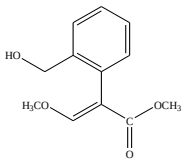
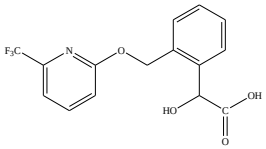
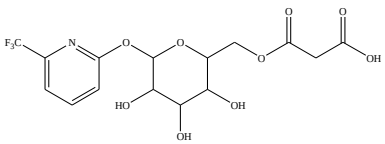
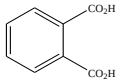
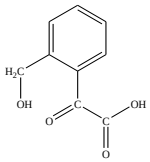
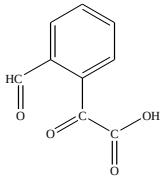
The current Meeting received further plant metabolism studies, for potatoes and tomatoes. Together with the 2016 submitted soybean study, these studies were evaluated for the current Meeting.

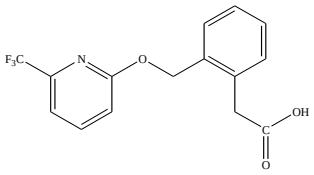
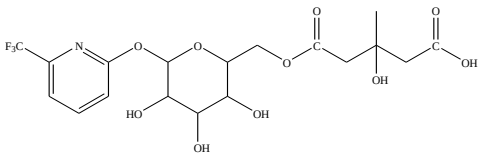
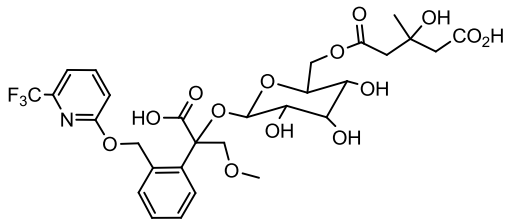
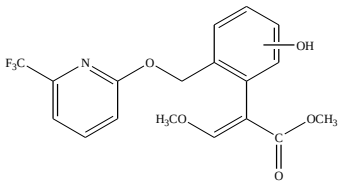
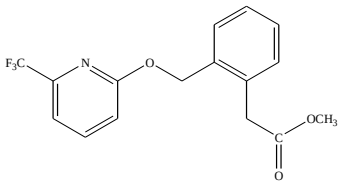
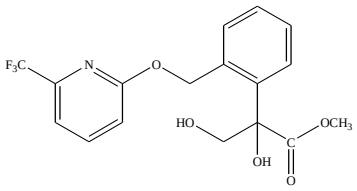
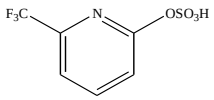
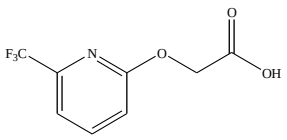
Data on animal metabolism, confined crop rotation, metabolism in plants (wheat, canola and soya bean – 2012 submitted study), environmental fate, analytical methods, storage stability, residues in processing and animal feeding were evaluated in 2012. Conclusions regarding these studies have not changed, and are not reproduced here. The reader is referred to the 2012 JMPR evaluation and appraisal.

The IUPAC name for picoxystrobin is methyl (*E*)-3-methoxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]acrylate



The following abbreviations are used for the metabolites discussed below:

Code	Chemical name	Structure
IN-QDK50	6-(Trifluoromethyl)-1*H*-pyridin-2-one	
IN-QDY62	(*E*)-3-Methoxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]acrylic acid	
IN-QDY63	2-[2-(6-Trifluoromethyl-2-pyridyloxymethyl)] benzoic acid	
IN-QCD12	Methyl (*Z*)-3-methoxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]acrylate	
IN-H8612	1,3-Dihydro-3-oxoisobenzofuran-1-carboxylic acid	
IN-QDY60	Methyl (*E*)-3-methoxy-2-(2-hydroxymethylphenyl)acrylate	
IN-QGS46	2-Hydroxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)phenyl] acetic acid	
IN-QGU72	2-Malonylglucosyl-6-trifluoromethylpyridine	
IN-K2122	Phthalic acid	
PAG3	2-(2-Hydroxymethylphenyl)-2-oxoacetic acid	
IN-QGU64	2-(2-Formylphenyl)-2-oxoacetic acid	

IN-QFA35	2-[2-(6-Trifluoromethyl-2-pyridyloxymethyl)phenyl] acetic acid	
IN-QGU73	Mixture of isomers, where n=3, 4 or 6 2-{n-(3-Hydroxy-3-methylglutaryl)glucosyl}-6-trifluoromethylpyridine	
Hydroxy IN-QDY62 3-hydroxymethyl glutaryl glucoside		
R290447	Methyl (*E*)-3-methoxy-2-[n-hydroxy-2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]acrylate	
IN-QCD09	Methyl 2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]acetate	
IN-QGU70, R290461	Methyl 2,3-dihydroxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl)-phenyl]propionate	
PYST2	6-Trifluoromethyl-2-pyridylsulfuric acid	
IN-U3E08, R409665, metabolite 30	2-(6-Trifluoromethyl-2-pyridyloxy)acetic acid	

Plant metabolism

In a study in soya bean submitted to the 2016 JMPR, plants raised outdoors were treated with 3 × 220 g ai/ha foliar applications at BBCH 65–67, 9 days later, and finally at BBCH 85, 49 days after the second application (DAA2). Forage samples were collected immediately after the first application (0 DAA1), and 7 and 19 days after the second application (7 DAA2 and 19 DAA2). At 49 days after the second application (49 DAA2, immediately before the final application) forage and immature pods with seeds were collected, then a final collection of mature seeds, pods without seeds and straw (the last was not analysed) was made 14 days after the third application (14 DALA).

Total radioactive residues (TRRs) in forage ranged from 2.0–8.8 mg eq/kg, in immature pods with seeds were 0.18 mg eq/kg, in mature pods without seeds were 3.2–11 mg eq/kg, and mature seeds were 0.076–0.78 mg eq/kg. Extractability of residues from the matrices using acetonitrile/water were generally high, at 93–99% TRR for 0DAA1, 7 DAA2 and 19 DAA2 forage, 86–90% TRR for 49 DAA2 forage, 87–89% TRR 49 DAA2 immature pods plus seeds, 82–93% TRR for mature pods (without seeds), and 80–90% TRR for mature seeds. A further 3.4–6.7% TRR was released from 49 DAA2 forage using enzymatic, acid and base hydrolyses, while from mature seed, a further 7–12% TRR was released using these techniques.

Parent ranged from 0.016–0.037 mg eq/kg (4.8–21%) in mature seed. Major components of the residue in mature seed in the second soybean study were phthalic acid (0.39 mg eq/kg, 50% TRR), and IN-H8612 (0.16 mg eq/kg, 20% TRR). In forage, parent was a major component of the residue at 0.45–7.54 mg eq/kg (23–86% TRR), while the sum of IN-QGS46 and its conjugates ranged from 0.12–0.84 mg eq/kg (1.9–17% TRR) and IN-QGU70 plus conjugates ranged from 0.11–0.53 mg eq/kg (1.9–11% TRR).

The current Meeting received additional plant metabolism data in potatoes and tomatoes.

In tomatoes, outdoor grown plants were treated with 3 × 333 g ai/ha applications at 7-day intervals between BBCH 62–64 and 71–73. Fruit and leaves were sampled at 1, 7, and 14 DALA, with stems additionally being collected at 14 DALA.

TRRs in fruit ranged from 0.51–1.1 mg eq/kg, TRRs in leaves ranged from 25–38 mg eq/kg, and in stems, TRRs ranged from 2.8–3.2 mg eq/kg. Extractabilities using acetonitrile/water were high, with the combined solvent rinses and extractions releasing 96–98% TRR from fruit, 92–97% TRR from leaves, and 92–94% TRR from stems. A further 4.0–5.7% TRR was released from 14 DALA leaves using enzymatic, acid and base hydrolyses.

Parent was a major residue component in tomato fruit at 0.20–0.72 mg eq/kg (30–80% TRR), along with phthalic acid at 0.08–0.23 mg eq/kg (7.3–29% TRR) and IN-H8612 at 0.08–0.19 mg eq/kg (7.5–28% TRR). The metabolic profile in leaves and stems was similar, except metabolism occurred to a lesser extent, with parent being present at a higher percentage, and being the only major component in any of the leaf/stem matrices except phenyl label stems, in which phthalic acid was present at 20% TRR.

In potatoes, three applications were made, the first an in-furrow soil application at 440 g ai/ha on the day of planting and the second and third being made as foliar applications at 220 and 440 g ai/ha at 8 and 3 days before harvest maturity. Foliage and tubers were collected immediately before the second application and 3 days after the last application.

TRRs in potato tubers were 0.027–0.039 mg eq/kg for the phenyl label and 0.12–0.13 mg eq/kg for the pyridyl label. In the foliage collected just before the second application, TRRs ranged from 0.12–0.44 mg eq/kg, while in the final harvest forage, TRRs were 42 mg eq/kg. Solvent extractability was high, at 86–87% TRR for phenyl label tubers, 96–97% TRR for pyridyl label tubers, and 95–99% TRR for foliage.

In tubers, parent ranged from 0.003–0.008 mg eq/kg (4.6–18% TRR), while the only other major components of the residue were hydroxy IN-QDY62 3-hydroxymethylglutaryl glucoside at 0.006–0.010 mg eq/kg (6.7–26% TRR) and IN-QDK50, the pyridyl-label specific soil metabolite, at 0.068–0.072 mg eq/kg (55–56% TRR). In foliage, the metabolic pattern was similar, with parent, IN-QDK50, hydroxy IN-QDY62 3-hydroxymethylglutaryl glucoside, IN-QGS46 glucosides and another pyridyl label specific metabolite, IN-U3E08 being observed as major metabolites.

The major metabolic pathways for picoxystrobin in plants (wheat, rapeseed and soya bean evaluated for the 2012 JMPR and soya bean, potatoes and tomatoes evaluated for the current Meeting) were:

- Oxidative cleavage of the molecule at the ether bridge to yield IN-QDK50 and IN-QDY60. IN-QDK50 was subsequently conjugated with glucose and malonic or glutaric acid, while the

phenacrylate cleavage product was subject to further oxidation and cleavage giving phthalic acid or IN-H8612;

- Loss of the methoxy methyl group followed by reduction of the enol, further hydroxylation of the side chain, and conjugation of the hydroxyl groups with glucose and malonic acid (IN-QGU70 and conjugates); and
- Hydrolysis of the ester, followed by oxidation and cleavage of the acrylate moiety ultimately yielding the benzoic acid metabolite IN-QDY63 or a phenyl-acetic acid metabolite (IN-QFA35), with or without glucose conjugation of the hydroxyl or carboxylic acid functionalities.

Hydroxylation of the phenyl ring was also observed in wheat, while small amounts of the *Z*-isomer of picoxystrobin (IN-QCD12) were found in soybeans, tomatoes, rape and wheat.

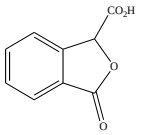
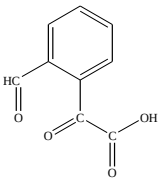
Definition of the residue

The 2012 JMPR recommended a residue definition for enforcement in plant and animal commodities of picoxystrobin, with residues being fat soluble. However, as the 2012 JMPR was unable to conclude on the toxicological relevance of two plant metabolites, IN-H8612 and IN-QGU64, a residue definition for dietary risk assessment could not be recommended.

Data provided to the 2013 JMPR together with dietary exposure calculations enabled the 2013 JMPR to conclude that there was no toxicological concern regarding IN-H8612.

With respect to IN-QGU64, the current Meeting notes that IN-QGU64 was not identified in seed in an additional metabolism study in soybeans that was provided to the 2016 JMPR. Further, IN-QGU64 was not reported in four other plant metabolism studies now available to the current Meeting, in wheat, oilseed rape, potatoes, and tomatoes. IN-H8612 is a structural isomer of IN-QGU64, and was identified in the additional soybean study, in wheat (both as a primary and a rotational crop), in tomatoes, and in potatoes. In the additional soybean study, and the metabolism studies in potatoes and tomatoes, IN-H8612 was identified with the aid of reference standards, while in the first soybean study, the structure of IN-QGU64 was proposed on the basis of mass spectral studies of a butyl ester derivative, reference standards not being available. The 2016 JMPR noted that IN-H8612 eluted as two peaks with some HPLC methods in the soya bean study provided to the 2016 JMPR. However, the current Meeting notes that IN-H8612 elutes as a single peak using other HPLC methods, indicating that the double peak is a method artefact.

Further, the Sponsor has made a number of attempts to synthesise IN-QGU64 in order to conduct toxicity tests, eventually succeeding in synthesising only small amounts of the lithium salt. This suggests that IN-QGU64 is not a stable compound.

	
IN-H8612 (1,3-dihydro-3-oxoisobenzofuran-1-carboxylic acid), C9H6O4	IN-QGU64 (2-(2-Formylphenyl)-2-oxoacetic acid), C9H6O4

On the weight of evidence the Meeting therefore concluded that in the 2006 soybean metabolism study, IN-H8612 had been incorrectly characterised as IN-QGU64.

Plant commodities

The newly submitted metabolism data for soya beans, tomatoes, and potatoes supports the conclusion of the 2012 JMPR that picoxystrobin is a suitable marker residue in plant commodities, and the previous recommendation for parent only as a residue definition for enforcement in plant commodities remains appropriate. The 2012 JMPR concluded that picoxystrobin breaks down rapidly in soil and does not accumulate in following crops.

In addition to IN-H8612 and IN-QGU64, which were identified as being of toxicological concern by the 2012 JMPR (and have now been resolved), the current Meeting noted that the toxicological aspects of a further three metabolites identified in the potato metabolism study required consideration (hydroxy IN-QDY62 3-hydroxymethylglutaryl glucoside, IN-QDK50, and IN-U3E08).

The metabolite hydroxy IN-QDY62 3-hydroxymethylglutaryl glucoside is a major metabolite in potatoes, but is a conjugate of IN-QDY62 (previously considered by the 2012 JMPR) and is not of toxicological concern.

IN-QDK50 and IN-U3E08 were observed as major metabolites in the potato metabolism study as well as in the previously considered rotational crop metabolism studies.

Genotoxicity studies for IN-QDK50 were provided to the current Meeting, and these indicated that IN-QDK50 is not genotoxic. A conservative calculation of the chronic dietary intake of IN-QDK50 (including its conjugates converted back to equivalents of unconjugated IN-QDK50) was carried out using data from field trials for crops with direct uses, expected residues in rotational crops based on the confined crop rotation study, and residues in animal commodities based on metabolism data and adjusted for expected feeding levels). The expected chronic intake of IN-QDK50 is 1.46 µg/kg bw/day, below the Threshold of Toxicological Concern (TTC) for a Cramer Class III compound (1.5 µg/kg bw/day).

The results of a Quantitative Structure-Activity Relationships (QSAR) analysis were provided for IN-U3E08, which did not indicate structural alerts for genotoxicity. A conservative calculation of the chronic dietary intake of IN-U3E08 was carried out using the expected residues in rotational crops based on the confined crop rotation study. IN-U3E08 has not been found in animal metabolism studies, and although significant levels of this metabolite were seen in the potato metabolism study, no GAPs for direct use of picoxystrobin on root vegetables have been provided to the Meeting. The expected chronic intake of IN-U3E08 is 0.2 µg/kg bw/day, below the Threshold of Toxicological Concern (TTC) for a Cramer Class III compound (1.5 µg/kg bw/day).

The conclusions regarding the metabolites considered using the TTC approach, including IN-H8612, IN-QDK50, and IN-U3E08 will need to be re-evaluated if additional use patterns are presented to the JMPR in the future.

Noting that there are no longer any outstanding plant metabolites of toxicological concern, the Meeting proposed a residue definition for dietary risk assessment in plant commodities of parent compound only.

Animal commodities

No new information regarding metabolism of picoxystrobin in animals has been provided to the JMPR since the 2012 Meeting. The conclusion of the 2012 JMPR that parent compound only is a suitable residue definition for enforcement in animal commodities, with residues being fat soluble, is supported.

Noting that the 2012 JMPR did not identify any toxicological concern regarding any of the major metabolites in food producing animals, a residue definition of parent only for dietary risk assessment in animal commodities is supported.

Residue definition for picoxystrobin in plant and animal commodities (for compliance with maximum residue levels and dietary risk assessment): *picoxystrobin.*

Picoxystrobin residue is fat soluble.

Results of supervised residue trials on crops

The 2012 JMPR received supervised trial data for application of picoxystrobin on sweet corn, peas (dry), beans (dry), soya bean (dry), wheat, barley and rape conducted in the USA and Canada.

In all trials, duplicate field samples were collected at each sampling interval and separately analysed. The mean result of the duplicate analyses were taken as the best estimate of the residue.

Pulses

Trials in peas (dry), and beans (dry) were conducted in the USA and Canada and were evaluated against the Canadian GAP for pulses except soya bean (2 × 0.22 kg ai/ha with a 14 day PHI).

Residues in pea seed from trials (n=11) at the Canadian GAP were: < 0.01 (4), 0.010, 0.012, 0.013, 0.016 (2), 0.025 and 0.033 mg/kg.

Residues in bean seed from trials (n=11) at the Canadian GAP were: < 0.01 (6), 0.011 (2), 0.016 and 0.038 (2) mg/kg.

Given the similarity of the data sets (confirmed by the Mann-Whitney U test), and the identical GAPs, the Meeting decided to combine the data sets for peas (dry) and beans (dry) for mutual support and to obtain more robust estimates of the maximum residue levels: < 0.01 (10), 0.010, 0.011 (2), 0.012, 0.013, 0.016 (3), 0.025, 0.033, and 0.038 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.06 mg/kg for the subgroup of dry peas along with an STMR of 0.0105 mg/kg.

Trials were conducted in soya bean in the USA and Canada and were assessed against the critical Canadian GAP (3 × 0.22 kg ai/ha and a 14-day PHI).

Residues in soya bean (dry) from trials (n=20) at the Canadian GAP were ≤ 0.01 (13), 0.010, 0.011, 0.012, 0.019, 0.031, 0.035, and 0.039 mg/kg.

The Meeting noted that the combined dry peas and dry beans data, and the soya bean data both yield an estimation of 0.06 mg/kg for the maximum residue level despite the differing GAPs.

Therefore, the Meeting agreed that a maximum residue level for the subgroup of dry beans could be supported, and estimated a maximum residue level of 0.06 mg/kg for the subgroup of beans, together with an STMR of 0.0105 mg/kg.

Cereals

Wheat, barley, oats, rye and triticale

Trials were conducted in wheat and barley in the USA and Canada and were assessed against the critical GAP of Canada for wheat, barley, triticale, oats and rye (3 × 0.22 kg ai/ha applications, with a PHI of 45 days).

Residues in wheat grain from trials (n=23) matching Canadian GAP were ≤ 0.01 (15), 0.010 (2), 0.013, 0.014, 0.019, 0.022, 0.025, and 0.028 mg/kg.

Residues in barley grain from trials (n=17) matching the Canadian GAP were < 0.01 (4), 0.011, 0.014, 0.016 (2), 0.017, 0.022, 0.028 (2), 0.029, 0.047, 0.087, 0.12, and 0.22 mg/kg.

The Meeting estimated a maximum residue level of 0.04 mg/kg for picoxystrobin in wheat, with an STMR of 0.01 mg/kg. Given the GAPs in Canada are the same for wheat, rye and triticale and the similarity of the crops, the Meeting decided to extrapolate from the wheat residue data to estimate maximum residue levels and STMRs of 0.04 and 0.01 mg/kg respectively for rye and triticale.

The Meeting estimated a maximum residue level of 0.3 mg/kg for barley, with an STMR of 0.017 mg/kg. Given the GAPs are the same for barley and oats and the similarity of the crops, the Meeting decided to extrapolate from the barley residue data to estimate a maximum residue level and an STMR of 0.3 and 0.017 mg/kg respectively for oats.

Sweet corn

Residues in sweet corn cobs from trials (n=11) in the USA and Canada matching the critical Canadian GAP of 4 × 0.22 kg ai/ha applications and a 7-day PHI were < 0.01 (11) mg/kg.
The meeting estimated a maximum residue level of 0.01* mg/kg for picoxystrobin in sweet corn (corn-on-the-cob) (kernels plus cob with husk removed), together with an STMR of 0.01 mg/kg and an HR of 0.01 mg/kg.

Maize

Trials were conducted in maize in the USA and Canada. Residues in maize grain from trials (n=15) matching the critical Canadian GAP for maize, including field, seed and popcorn (3 × 0.22 kg ai/ha applications, and a 7-day PHI) were < 0.01 (13), 0.011, and 0.012 mg/kg.

The Meeting estimated a maximum residue level of 0.015 mg/kg for picoxystrobin in maize, together with an STMR of 0.01 mg/kg.

Noting that the GAP in Canada covered popcorn, the Meeting agreed that these values could be extrapolated to popcorn. The Meeting estimated a maximum residue level and an STMR of 0.015 and 0.01 mg/kg respectively in popcorn.

Rape seed

The GAP for oilseed rape in the USA and Canada is 2 × 0.22 kg ai/ha applications with a 28-day PHI.

Trials were conducted in oilseed rape in the USA and Canada, and were evaluated against the Canadian GAP. Residues in seed from trials (n=3) at the Canadian GAP were < 0.01, 0.012, and 0.031 mg/kg.

The Meeting concluded that there were insufficient trials at GAP to estimate a maximum residue level for oilseed rape.

Animal feedstuffs

Soya bean forage and hay

The Canadian GAP for soya bean (when forage is to be grazed or hay is to be harvested) is 1 × 0.22 kg ai/ha with a 14-day PHI.

Residue data for soya bean forage and hay were collected for the USA and Canadian soya bean residue trials.

Residues of picoxystrobin in soya bean forage from trials (n=19) matching GAP were < 0.01, 0.25, 0.46, 0.57 (2), 0.80, 0.84, 0.88, 0.93, 1.4, 1.6 (3), 1.9, 2.0 (2), 2.1, 2.9, and 3.5 mg/kg (dry weight basis).

Residues of picoxystrobin in soya bean hay from trials (n=19) matching GAP were < 0.01, 0.14, 0.39, 0.50, 0.51, 0.52, 0.59, 0.73, 0.81, 1.2, 1.6 (2), 1.7 (2), 1.8, 2.0, 2.1, 2.3, and 2.7 mg/kg (dry weight basis).

The Meeting estimated a maximum residue level of 5 mg/kg for picoxystrobin in soya bean fodder, together with a median and a highest residue of 1.2 and 2.7 mg/kg respectively.

The Meeting estimated a median and a highest residue of 1.4 and 3.5 mg/kg respectively for soya bean forage (dry weight).

Pea vines and hay

The GAP for picoxystrobin in pulses (except soya bean) in Canada is 2 × 0.22 kg ai/ha, with a 0-day PHI for vines (forage) and hay.

Data for pea vines and pea hay were collected for selected sites in the USA and Canadian pulse residue trials.

At a 0-day PHI, residues of picoxystrobin (n=6) in pea vines were 9.5, 14, 19, 22, 35 and 55 mg/kg (dry weight basis).

Residues of picoxystrobin in pea hay from trials (n=6) matching GAP were 4.1, 7.1, 11, 14, 18, and 64 mg/kg (dry weight basis).

The Meeting estimated a maximum residue level of 150 mg/kg for pea hay or pea fodder (dry), together with a median and a highest residue of 12.5 and 64 mg/kg respectively (dry weight basis).

The Meeting estimated median and highest residues for pea vines of 20.5 and 55 mg/kg respectively (dry weight basis).

Wheat, barley, oat, rye and triticale forage,

The Canadian GAP for wheat, barley, oat, rye and triticale forage is 1 × 0.22 kg ai/ha, with a 7-day PHI.

Residues of picoxystrobin in wheat forage from trials (n=25) at GAP were: 1.1, 1.3, 1.6, 1.7, 1.9, 2.2, 2.3, 3.6 (2), 3.7, 3.8, 3.9, 4.5, 4.6, 4.8, 6.3, 6.4, 7.0, 7.4, 8.9, 9.7, 11 (2), 12, and 31 mg/kg (dry weight basis).

A median and a highest residue value of 4.5 and 31 mg/kg (dry weight) respectively were estimated for wheat forage for use in livestock dietary burden calculations. The Meeting agreed that these values could be extrapolated to barley, oat, rye and triticale forage for the purposes of the livestock dietary burden calculations.

Wheat, barley, oat, rye and triticale hay and straw

The Canadian GAP for wheat, barley, oat, rye and triticale hay is 3 × 0.22 kg ai/ha, with a 14-day PHI.

The Canadian GAP for wheat, barley, rye, oat and triticale straw is 3 × 0.22 kg ai/ha, with a 45-day PHI.

Residue data for wheat hay and straw, and barley hay and straw were generated in the USA and Canada in accordance with the Canadian GAPs.

Residues of picoxystrobin in wheat hay from trials (n=25) at GAP were: 0.18, 0.19, 0.24, 0.41, 0.48, 0.51, 0.61, 0.68, 0.72, 0.78, 0.81, 0.90, 1.0, 1.1 (2), 1.4, 1.5, 1.7, 1.8, 2.4, 2.5, 2.8, 3.4, 3.6, and 4.0 mg/kg (dry weight basis).

Residues of picoxystrobin in barley hay from trials (n=19) at GAP were: 0.20, 0.32, 0.34, 0.38, 0.39, 0.46, 0.55, 0.66, 0.77, 0.78, 0.86, 1.3, 1.4, 1.7 (2), 2.3, 2.4, 3.5, and 5.5 mg/kg (dry weight basis).

Residues of picoxystrobin wheat straw from trials (n=24) at GAP were: < 0.01, 0.016, 0.022 (2), 0.029, 0.033, 0.043, 0.079, 0.10 (2), 0.11, 0.15, 0.28, 0.29, 0.32, 0.36, 0.49, 0.50, 0.52, 0.62, 0.86, 1.2 (2), and 1.7 mg/kg (dry weight basis).

Residues of picoxystrobin in barley straw from trials (n=16) were: 0.049, 0.050, 0.066, 0.069, 0.082, 0.087, 0.13, 0.22, 0.23, 0.24, 0.28, 0.35, 0.40, 0.41, 0.80, and 1.2 mg/kg (dry weight basis).

Hay and straw of different cereal grains are generally indistinguishable in trade.

The Meeting determined that the residue data sets for wheat and barley hay, and for wheat and barley straw were similar (Mann-Whitney U test).

The Meeting agreed to combine the data sets for wheat and barley hay for the purposes of estimating maximum residue levels for cereal fodders. The combined data set for wheat and barley hay is: 0.18, 0.19, 0.20, 0.24, 0.32, 0.34, 0.38, 0.39, 0.41, 0.46, 0.48, 0.51, 0.55, 0.61, 0.66, 0.68, 0.72,

0.77, 0.78 (2), 0.81, 0.86, 0.90, 1.0, 1.1 (2), 1.3, 1.4 (2), 1.5, 1.7 (3), 1.8, 2.3, 2.4 (2), 2.5, 2.8, 3.4, 3.5, 3.6, 4.0, and 5.5 mg/kg.

The Meeting agreed to combine the data sets for wheat and barley straw for the purposes of estimating median and highest residue values for cereal straws. The combined data set for wheat and barley straw is: < 0.01, 0.016, 0.022 (2), 0.029, 0.033, 0.043, 0.049, 0.050, 0.066, 0.069, 0.079, 0.082, 0.087, 0.10 (2), 0.11, 0.13, 0.15, 0.22, 0.23, 0.24, 0.28 (2), 0.29, 0.32, 0.35, 0.36, 0.40, 0.41, 0.49, 0.50, 0.52, 0.62, 0.80, 0.86, 1.2 (3), and 1.7 mg/kg.

Using the combined wheat and barley hay data set, the Meeting estimated maximum residue levels of 7 mg/kg for barley straw and fodder, dry and for wheat straw and fodder, dry, with median and highest residue values of 0.88 and 5.5 mg/kg (dry weight basis) respectively, for wheat and barley hay.

The Meeting agreed that these recommendations could be extrapolated to the other cereal crops with the same GAP in Canada and estimated maximum residue levels of 7 mg/kg for oat straw and fodder, dry, for rye straw and fodder, dry, and for triticale straw and fodder, dry, together with median and highest residue values of 0.88 and 5.5 mg/kg (dry weight basis) respectively, for oat, rye and triticale hay.

Using the combined wheat and barley straw data set, the Meeting estimated median and highest residue values of 0.225 and 1.7 mg/kg (dry weight basis) respectively, for wheat and barley straw, and agreed to extrapolate these values to oat, rye and triticale straw.

Sweet corn forage

The GAP for sweet corn in Canada is 4 × 0.22 kg ai/ha, with a 0-day grazing interval. Residue data for sweet corn forage was collected for the USA and Canadian sweet corn trials. However, most samples were collected 7 days after treatment, which is not consistent with Canadian GAP.

Residues in sweet corn forage at 0 days after treatment (DAT) were 8.4 and 17 mg/kg.

The Meeting concluded that there were insufficient data points to estimate a median or a highest residue for sweet corn forage.

Maize forage and stover

The GAP for picoxystrobin in maize in Canada is 3 × 0.22 kg ai/ha, with a 0-day PHI for grazing of forage, and a 7-day PHI for grain and stover.

Residue data for maize forage and maize stover were collected for the USA and Canadian trials.

Residues in maize forage from trials (n=15) in accordance with the Canadian GAP were: 3.5, 4.6, 5.0, 5.7, 6.2, 6.3, 6.7, 7.1, 8.0, 8.5, 9.7, 11, 12, 13, and 14 mg/kg (dry weight basis).

Residues in maize stover from trials (n=15) in accordance with the Canadian GAP were: 0.023, 0.94, 1.0, 2.1, 2.2, 3.2, 3.5, 3.8, 5.7, 6.0, 6.6, 7.4, 8.2, 8.5 and 8.6 mg/kg (dry weight basis).

A median and a highest residue value of 7.1, and 14 mg/kg (dry weight) respectively were estimated for maize forage for use in livestock dietary burden calculations.

The Meeting determined a maximum residue level of 20 mg/kg for picoxystrobin in maize fodder, together with a median and a highest residue of 3.8 and 8.6 mg/kg (dry weight) respectively.

Fate of residues during processing

Processing studies were conducted in wheat, barley, soya bean, and maize.

Processing factors in accordance with the residue definition (parent only) are tabulated below.

Raw agricultural commodity (RAC)	Processed commodity	Processing factors	Best estimate processing factor	RAC STMR (mg/kg)	RAC MRL (mg/kg)	STMR-P (mg/kg)	PF × RAC MRL, where required
Barley	Beer	< 0.05, < 0.25 (2), < 0.5	0.26	0.017	0.3	0.01	-
	Malt	0.48, < 0.5, < 0.5	0.48			0.01	-
	Spent grain	0.5, 0.81	0.66			0.011	-
Wheat	Bran	1.9, 2.1, 3.0, 3.8	2.7	0.01	0.04	0.027	0.108
	Germ	2.6, 3.8	3.2			0.032	0.128
	Wholemeal flour	1.1, 1.3	1.2			0.012	-
	Flour	0.21, 0.26	0.24			0.01	-
	Type 550 (white) flour	0.83, 1.1	0.97			0.01	-
	Patent flour	1.1, 1.2	1.2			0.012	-
	Wholemeal bread	0.45, 1.0	0.73			0.01	-
	Type 550 (white) bread	0.64, 0.67	0.66			0.01	-
	Screenings	1.7, 5.1	3.4			0.034	-
Soya bean	Refined oil (solvent extracted)	0.93, 1.0, 1.6, 2.2	1.4	0.01	0.06	0.014	0.084
	Refined oil (mechanically extracted)	3.4, 3.4	3.4			0.034	0.204
	Meal (solvent extracted)	0.03, 0.06, < 0.09, 1.1	0.32			0.01	-
	Meal (mechanically extracted)	0.36, 0.60	0.48			0.01	-
	Aspirated grain fractions	190, 320	260			2.6	-
	Hulls	2.2, 4.4, 5.1, 5.6	4.3			0.043	-
Maize	Starch	0.025, < 0.068	0.047	0.01	0.02	0.01	-
	Grits	0.34, 0.51	0.43			0.01	-
	Flour	1.0, 1.2	1.1			0.011	-
	Refined oil (wet milled)	6.4, 7.3	6.9			0.069	0.138
	Refined oil (dry milled)	3.4, 5.4	4.4			0.044	0.088
	Meal	0.77, 0.79	0.78			0.01	-
	Aspirated grain fractions	13, 17	15			0.15	

Picoxystrobin concentrated significantly in wheat bran, wheat germ, soya bean refined oil, and maize refined oil.

The Meeting therefore estimated maximum residue levels of 0.15, 0.15, 0.2, and 0.15 mg/kg for wheat bran, processed, wheat germ, soya bean oil, refined, and maize oil, edible, respectively, based on the best estimate processing factors and the raw agricultural commodity maximum residue levels.

Residues in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of picoxystrobin in farm animals on the basis of the OECD diets listed in Appendix IX of the FAO Manual 2016. Calculation from highest residue, STMR (some bulk commodities), and STMR-P values provides 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. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed on a dry weight basis.

	US/Canada		EU		Australia		Japan	
	Max.	Mean	Max.	Mean	Max.	Mean	Max.	Mean
Beef cattle	2.33	1.30	31.6	10.1	64[a]	17.3[e]	0.102	0.102
Dairy cattle	18.2	5.43	32.7	9.63	54.1[b]	14.1[f]	7.93	3.63
Poultry (broiler)	0.095	0.095	0.052	0.052	0.046	0.046	0.01	0.01
Poultry (layer)	0.095	0.095	9.55[c,d]	2.81[g,h]	0.046	0.046	0.059	0.059

[a] Maximum calculated dietary burden for beef cattle, used for calculation of mammalian tissue MRLs.

[b] Maximum calculated dietary burden for dairy cattle, used for calculation of the milk MRL.

[c] Maximum calculated dietary burden for laying hens, used for calculation of egg MRL.

[d] Maximum calculated dietary burden for broiler hens, used for calculation of poultry tissue MRLs.

[e] Highest calculated mean dietary burden for beef cattle, used for calculation of mammalian tissue STMRs.

[f] Highest calculated mean dietary burden for dairy cattle, used for calculation of milk STMR.

[g] Highest calculated mean dietary burden for laying hens, used for calculation of egg STMR.

[h] Highest calculated mean dietary burden for broiler hens, used for calculation of poultry tissue STMRs.

The detailed dietary burden calculations are provided in Annex 6.

Animal commodity maximum residue levels

Mammals

The maximum dietary burdens for beef and dairy cattle are 64 and 54 ppm dry weight in feed respectively. HR and STMR values calculated by interpolation or using transfer factors for picoxystrobin in mammalian animal matrices are tabulated below.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat
HR determination (beef or dairy cattle)							
Feeding study	120	< 0.01	120	< 0.01	0.017	< 0.01	0.026
	40	< 0.01	40	< 0.01	< 0.01	< 0.01	< 0.01
Dietary burden and estimate of highest residue	54	0	64	0	0.012	0	0.015
STMR determination (beef or dairy cattle)							
Feeding study	40	< 0.01	40	< 0.01	< 0.01	< 0.01	< 0.01
Dietary burden and estimate of median residue	14	0	17	0	0.01	0	0.01

Residues of picoxystrobin were not detected in milk from cattle at the two feeding levels bracketing the calculated maximum dietary burden for dairy animals. A maximum residue level of 0.01* mg/kg is therefore recommended for picoxystrobin in milk.

Residues of picoxystrobin were not detected in muscle or kidney from cattle at the two feeding levels bracketing the calculated maximum dietary burden for beef cattle. Residues were found at low levels above the LOQ in fat and liver of cattle at the next highest feeding level above the maximum dietary burden for beef cattle, and were below the LOQ for the next lowest feeding level.

Maximum residue levels of 0.02 mg/kg are therefore recommended for edible offal (mammalian), meat (from mammals other than marine mammals) (fat), and mammalian fats (except milk fats).

The mean dietary burdens for beef and dairy cattle are 17 and 14 ppm in feed respectively. Residues are not expected in milk, or muscle at these feeding levels, so STMRs for these commodities are 0 mg/kg. For offal and fat, the estimated STMRs are 0.01 mg/kg.

Poultry

The maximum dietary burdens for broiler chickens and laying hens is 9.6 ppm dry weight in feed. HR and STMR values calculated by interpolation or using transfer factors for picoxystrobin in poultry animal matrices are tabulated below.

	Feed level (ppm) for egg residues	Residues (mg/kg) in egg	Feed level (ppm) for tissue residues	Residues (mg/kg)		
				Muscle	Liver	Fat
HR determination (broiler or laying hens)						
Feeding study	15	< 0.01	15	< 0.01	< 0.01	< 0.01
Dietary burden and estimate of highest residue	9.6	0	9.5	0	0	< 0.01
STMR determination (broiler or laying hens)						
Feeding study	15	< 0.01	15	< 0.01	< 0.01	< 0.01
Dietary burden and estimate of median residue	2.8	0	2.8	0	0	0.01

Residues of picoxystrobin were not detected in the eggs, muscle or liver of hens fed at the next highest feeding level (15 ppm) above the maximum poultry dietary burden (9.5 ppm). Residues were detectable, but below the LOQ, in the fat of birds fed at 15 ppm.

MRLs of 0.01* mg/kg are therefore recommended for picoxystrobin in eggs, poultry meat, and poultry, edible offal of. An MRL of 0.01 mg/kg is recommended for picoxystrobin in poultry fats.

The mean dietary burdens for broiler chickens and laying hens are 2.8 ppm. Residues are not expected in poultry muscle, liver or eggs at this feeding level and the STMRs for poultry meat, poultry, edible offal of, and eggs are all 0 mg/kg. The STMR for poultry fats is 0.01 mg/kg.

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/IESTI assessment.

Definition of the residue for compliance with the maximum residue levels and for estimation of dietary intake for animal and plant commodities: *picoxystrobin*.

Picoxystrobin residues are considered fat soluble.

DIETARY RISK ASSESSMENT

Long-term intake

The 2012 JMPR established an Acceptable Daily Intake (ADI) of 0–0.09 mg/kg bw for picoxystrobin.

The International Estimated Dietary Intakes (IEDI) of picoxystrobin for the 17 GEMS/Food cluster diets, based on estimated STMRs were in the range 0–0.1% of the maximum ADI of 0.09 mg/kg bw.

The Meeting concluded that the long-term dietary exposure to residues of picoxystrobin from uses that have been considered by the 2017 JMPR is unlikely to present a public health concern. The results are shown in Annex 3 of the JMPR 2017 Report.

Short-term intake

The 2012 JMPR established an Acute Reference Dose (ARfD) of 0.09 mg/kg bw for picoxystrobin.

The International Estimated Short Term Intakes (IESTIs) for picoxystrobin were calculated for the commodities for which STMRs/STMR-Ps and HRs/HR-Ps were estimated by the current

Meeting. The IESTIs represented 0–3% and 0–1% of the ARfD for the general population and for children respectively. The Meeting concluded that the short-term dietary exposure to residues of picoxystrobin from uses considered by the current Meeting was unlikely to present a public health concern. These results are shown in Annex 4 of the JMPR 2017 Report.