### PENTHIOPYRAD (253)

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#### **EXPLANATION**

Penthiopyrad is a locally systemic carboxamide fungicide used for control of foliar and soil-borne plant diseases. The IUPAC name for penthiopyrad is (RS)-N-[2-(1, 3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl) pyrazole-4-carboxamide. Penthiopyrad was first evaluated in 2011 for toxicology, and an ADI of 0–0.1 mg/kg bw and an ARfD of 1 mg/kg bw were established. For residues, penthiopyrad was first evaluated by the 2012 JMPR. The residue definition for compliance with the MRL for plant commodities is *penthiopyrad*. For compliance with the MRL for animal commodities and dietary risk assessment for plant and animal commodities, the residue definition is the *sum of penthiopyrad and 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide (PAM)*, *expressed as penthiopyrad*. The residue is not fat-soluble. Additional uses were evaluated by the 2013 JMPR.

Penthiopyrad was scheduled at the Fiftieth Session of the CCPR for evaluation of additional uses by the 2019 JMPR. The Meeting received information on supervised residue trials and GAP information for caneberry and blueberry.

### **METHODS OF RESIDUE ANALYSIS**

#### Analytical methods

In the submitted residue trials on caneberry and blueberry, penthiopyrad and its metabolites (PAM and PCA, 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxylic acid) were analysed using the method CEMR 3727, which was considered as valid by the 2012 JMPR. The method involves extraction with acetonitrile/water (4:1, v/v), partitioning with ethyl acetate after addition of 10% sodium chloride solution and concentrated HCl solution, and determination by LC-MS/MS: ion transitions monitored, m/z 358 $\rightarrow$ 149 (quantification) and 358 $\rightarrow$ 208 (confirmation) for penthiopyrad; m/z 194 $\rightarrow$ 174 (quantification) and 194 $\rightarrow$ 134 (confirmation) for PAM; m/z 193 $\rightarrow$ 149 (quantification) and 193 $\rightarrow$ 109 (confirmation) for PCA. In the method validation recovery tests, conducted prior to analyses of sample, the recoveries of the analytes were satisfactory and the LOQ values were 0.01 mg/kg for all analytes and matrices. Further concurrent recovery test results were also satisfactory. The recovery test results are shown in Table 1.

Table 1 Recoveries of penthiopyrad and its metabolites in caneberry and blueberry

Sample	Analyte	Fortification level	n	Recovery			
_		(mg/kg)		Range (%)	Mean (%)	RSD (%)	
Method valie	dation recoveries						
Caneberry	Penthiopyrad	0.01	3	79-86	83	4	
		0.02	3	89-92	90	2	
		0.1	3	89-96	92	4	
		22	3	102-107	104	3	
	PAM	0.01	3	80-87	84	4	
		0.02	3	84-89	87	3	
		0.1	3	79-87	83	4	
	PCA	0.01	3	78-92	87	8	
		0.02	3	96-109	101	7	
		0.1	3	89-106	96	9	
Blueberry	Penthiopyrad	0.010	3	74-90	85	11	
		0.020	3	82-91	88	5	
		0.10	3	85-93	89	4	
		5.0	3	100-102	101	1	
	PAM	0.010	3	81-83	82	1	
		0.020	3	79-85	82	3	

Sample	Analyte	Fortification level	n	Recovery			
-		(mg/kg)		Range (%)	Mean (%)	RSD (%)	
		0.10	3	83-105	93	11	
	PCA	0.010	3	95-102	98	4	
		0.020	3	92-95	93	1	
		0.10	3	97-100	98	2	
Concurrent r	recoveries	•		•	•	•	
Caneberry	Penthiopyrad	0.01	7	69-104	85	12	
		0.1	4	89-120	105	13	
		1	3	112-117	115	3	
	PAM	0.01	7	57, 78-93 (n=6)	80	15	
		0.1	4	82-85	83	2	
		1	3	97-100	98	2	
	PCA	0.01	7	58, 75-96 (n=6)	81	14	
		0.1	4	77-87	82	6	
		1	3	86-92	89	3	
Blueberry	Penthiopyrad	0.010	6	84-91	88	3	
		0.020	2	94-96	95		
		0.10	2	94-97	96		
		5.0	1	106			
	PAM	0.010	6	74-102	93	10	
		0.020	2	73-84	79		
		0.10	2	83-97	90		
	PCA	0.010	6	76-97	90	8	
		0.020	2	85-91	88		
		0.10	2	82-95	89		

### **USE PATTERN**

Penthiopyrad is a curative and protectant fungicide. It inhibits fungal respiration by binding to mitochondrial respiratory complex II. The Meeting received GAP information (Canada) on the use of penthiopyrad relevant to the submission to the 2019 JMPR. The information is summarized in Table 2.

Table 2 Registered uses of penthiopyrad on caneberry and blueberry in Canada

Crop	Formulation	Applicatio		PHI			
		Method	kg ai/ha	L/ha	No.	Interval (days)	(days)
Caneberry (blackberry; loganberry; raspberry, black and red, Wild raspberry and cultivars, varieties and/or hybrids of these)	SC 200 g/L	Field spray	0.20-0.35	min 100	3-5	7-10 or shorter interval	0
Blueberry, highbush; Currant, black and red; Elderberry; Huckleberry; Aronia berry; Chilean guava; European barberry; Highbush cranberry; Honeysuckle, edible; Jostaberry; Juneberry; Lingonberry; Native currant; Salal; Sea buckthorn; Cultivars, varieties and/or hybrids of these	SC 200 g/L	Field spray	0.20-0.35	min 100	3-5	7-10 or shorter interval	0

Maximum seasonal rate is 1.0 kg ai/ha, with no more than 5 applications.

### RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

The Meeting received supervised residue trials on caneberry (blackberry, raspberry) and blueberry conducted in Canada or the USA. The detailed information is summarized in Table 3 and 4 as shown below.

CODEX Group	Commodity	Table No.
Group 004 Berries and other small fruits	Subgroup 004A Caneberries	Table 3
	FB 2005 Subgroup of caneberries	
	FB 0264 Blackberries	
	FB 0272 Raspberries, Red, Black	
Group 004 Berries and other small fruits	Subgroup 004B Bush berries	Table 4
	FB 2006 Subgroup of bush berries	
	FB 0020 Blueberries	

In all trials, two replicate field samples were taken randomly through a whole plot and analysed separately. The Meeting used an average residue for the samples for estimation of maximum residue levels, which were underlined in the tables. In cases of non-independent trials, the plot in which the highest residue level is observed was selected for maximum residue level estimation.

### Berries and other small fruits

# Caneberries (blackberry, raspberry)

A total of seven residue trials on caneberry (six raspberry and one blackberry) were conducted in Canada (five trials) and the USA (2 trials), during the 2011 growing season [Ballantine, J., 2014, Report No.AAFC11-006R]. An SC formulation of penthiopyrad (200 g/L) was applied to caneberry as a foliar directed application at a rate ranging from 0.35 to 0.41 kg ai/ha in 3 applications with retreatment intervals of 5 to 8 days. The total seasonal application rate ranged from 1.0–1.1 kg ai/ha. Adjuvants were included in the spray mixtures and the spray volumes, ranging from 513 to 996 L/ha, were sufficient to provide adequate dispersal of the test substance on to the caneberry plants. Samples were harvested on the day of the final application, shortly after the spray solution had dried. One decline trial was conducted, with samples collected at 0, 1, 3, 10 and 15 days after the last application. All samples were transported to freezers in coolers after harvest and then frozen as soon as possible, and remained frozen (<-18 °C) until analysis. The maximum storage period of the samples was 551 days.

### **Blueberries**

A total of nine residue trials on blueberry (highbush) were conducted in Canada (two trials) and the USA (seven trials), during the 2012 growing season [Malegus, R., 2015, Report No. AAFC12-061R]. An SC formulation of penthiopyrad (200 g/L) was applied to highbush blueberries as a foliar directed application at a rate ranging from 0.34–0.38 kg ai/ha in 3 applications with re-treatment intervals of 6 to 10 days. The total seasonal application rate ranged from 1.0–1.1 kg ai/ha. An adjuvant was included in the spray mixtures and the spray volume was 179–920 L/ha. Samples were harvested on the day of the final application, after the spray had dried on the plants. One decline trial was conducted, with samples collected at 0, 1, 4, 9 and 14 days after the last application. All samples were transported to freezers in coolers after harvest and then frozen as soon as possible, and remained frozen (<-18 °C) until analysis. The maximum storage period of the samples was 530 days.

Table 3 Residues in caneberry (raspberry, blackberry) following foliar application of penthiopyrad in Canada and USA (Report No. AAFC11-006R)

Location, Year (Crop/Variety)	Appl	lication a			DALA	Residues, mg/kg <sup>b</sup>			
Trial ID	n	kg ai/ha	L/ha	Inter. days		Penthiopyrad	PAM	PCA	Total <sup>c</sup>
Canada Frelighsburg, QC (Raspberry, Nova)	3	0.35- 0.36	601- 617	7	0	3.5	0.011	< 0.01	3.5
241*						3.9	0.011	< 0.01	4.0
						3.7 <sup>d</sup>	0.012	< 0.01	3.8
					1	3.8	0.013	< 0.01	3.8
						2.9	0.012	< 0.01	2.9
						3.3	0.013	< 0.01	3.4
					3	2.0	0.015	< 0.01	2.04
						1.9	0.013	< 0.01	2.0
						2.0	0.014	< 0.01	2.0
					7	0.90	0.014	< 0.01	0.93
					'	0.97	0.014	< 0.01	1.0
						0.94	0.015	< 0.01	0.97
					15	0.52	0.013	< 0.01	0.55
					13	0.48	0.014	0.011	0.53
G 1	2	0.27	(20	7	0	0.50	0.015	< 0.01	0.53
Canada Frelighsburg, QC (Raspberry, Killarney) 242*	3	0.37	628- 638	7	0	3.3	0.014	< 0.01	3.3
						2.9	0.016	< 0.01	2.9
						3.1	0.015	< 0.01	3.1
Canada Agassiz, BC (Raspberry/ Chemanius) 243	3	0.36- 0.41	764- 868	7	0	2.2°	<0.01	< 0.01	2.2
						1.7	< 0.01	< 0.01	1.7
						2.0	< 0.01	< 0.01	2.0
Canada Aldergrove, BC (Raspberry/ Cascade Delight) 244**	3	0.35- 0.36	593- 620	5-6	0	2.1	< 0.01	< 0.01	2.1
						2.0	< 0.01	< 0.01	2.1
						2.1	< 0.01	< 0.01	2.1
Canada Aldergrove, BC (Raspberry/ Coho) 245**	3	0.37- 0.38	621- 640	5-7	0	3.6	< 0.01	< 0.01	3.6
						3.2	< 0.01	< 0.01	3.2
					ļ	3.4	< 0.01	< 0.01	3.4
USA Cream Ridge, NJ (Raspberry/Heritage) 246	3	0.36- 0.37	513- 541	7	0	4.0	0.012	< 0.01	4.0
						3.4	0.010	< 0.01	3.4
USA Parlier, CA (Blackberry/ Natchez) 247	3	0.36	962- 996	6-8	0	3.7 3.9	0.011	< <b>0.01</b> 0.016	3.7 3.9
						4.7	0.014	0.013	4.8
						4.3	0.014	0.014	4.3

<sup>&</sup>lt;sup>a</sup> 200 SC (200 g/L) formulation was used.

<sup>&</sup>lt;sup>b</sup> mg of the specific analyte per kg sample

- <sup>c</sup> Total residue: sum of penthiopyrad and PAM, expressed as parent equivalents. Conversion factor for PAM into penthiopyrad is 1.86. The <LOQ values were handled as their numeric value (e.g. <0.01 mg/kg as 0.01 mg/kg), except that
- if both analytes are <0.01 mg/kg, the sum residue is <0.01 mg/kg.
- <sup>d</sup> Bold letter: mean of replicate samples
- <sup>e</sup> In one of two control samples, residue value of penthiopyrad was determined as 0.016 mg/kg.
- \*: Not independent trials, due to the same place and the same application dates
- \*\*: Not independent trials, due to the same place and close application dates

Table 4 Residues in blueberry following foliar application of penthiopyrad in Canada and USA (Report No. AAFC12-061R)

Location, Year (Variety)	Appl	lication a			DALA	Residues, mg/kg <sup>b</sup>			
Trial ID	n	kg ai/ha	L/ha	Inter. days		Penthiopyrad	PAM	PCA	Total <sup>c</sup>
USA Cream Ridge, NJ (Highbush, Duke ) 245*	3	0.35	179- 191	6-7	0	3.9	0.037	0.032	3.9
						3.9	0.043	0.035	4.0
						3.9 <sup>d</sup>	0.040	0.033	4.0
USA Cream Ridge, NJ (Highbush, Bluecrop) 246*	3	0.36	296- 313	6-7	0	2.5	0.017	0.014	2.5
						2.6	0.019	0.015	2.7
						2.5	0.018	0.014	2.6
USA Alapaha, GA (Highbush, TH667) 247	3	0.34	277- 280	6	0	2.6	0.021	0.014	2.7
						2.5	0.022	0.014	2.6
						2.6	0.022	0.014	2.6
USA Castle Hayne, NC (Highbush, Croatan) 248	3	0.36- 0.37	194- 196	7-8	0	2.0	0.013	<0.01	2.0
						1.5	0.011	<0.01	1.5
						1.7	0.012	<0.01	1.7
USA Fennville, MI (Highbush, Jersey) 249**	3	0.35	523- 529	7	0	1.6	0.012	<0.01	1.6
						1.3	0.012	<0.01	1.4
						1.5	0.012	<0.01	1.5
USA Fennville, MI (Highbush, Jersey) 250**	3	0.35	477- 509	7	0	1.3	0.012	<0.01	1.3
						1.3	0.011	< 0.01	1.3
						1.3	0.012	< 0.01	1.3
Canada Frelighsburg, QC (Highbush, Bluecrop) 251	3	0.34- 0.38	686- 750	7	0	1.6	<0.01	<0.01	1.7
						1.8	<0.01	<0.01	1.8
						1.7	< 0.01	<0.01	1.7
Canada	3	0.36	913-	0	7-10	0.50	< 0.01	< 0.01	0.51

Location, Year (Variety)	Application <sup>a</sup>				DALA	Residues, mg/k			
Trial ID	n	kg ai/ha	L/ha	Inter. days		Penthiopyrad	PAM	PCA	Total <sup>c</sup>
Langley, BC (Highbush, Brigitta) 252			920						
						0.65	< 0.01	< 0.01	0.67
						0.57	< 0.01	< 0.01	0.59
USA Aurora, OR (Highbush, Bluecrop) 253	3	0.35-	469- 485	0	8	1.3	<0.01	<0.01	1.3
						1.2 1.2	<0.01 <0.01	<0.01 < <b>0.01</b>	1.2 1.3
				1	-	1.2	<0.01	<0.01	1.2
				1		0.86	<0.01	<0.01	0.88
						1.0	<0.01	<0.01	1.0
				4		1.3	0.013	< 0.01	1.3
						1.1	0.012	< 0.01	1.1
						1.2	0.013	< 0.01	1.2
				9		0.68	0.013	< 0.01	0.70
						0.70	< 0.01	< 0.01	0.72
					_	0.69	0.011	< 0.01	0.71
				14		0.35	< 0.01	0.0114	0.37
						0.34	< 0.01	0.0104	0.35
						0.34	< 0.01	0.011	0.36

<sup>&</sup>lt;sup>a</sup> 200 SC (200 g/L) formulation was used.

if both analytes are <0.01 mg/kg, the sum residue is <0.01 mg/kg.

# **APPRAISAL**

Penthiopyrad is a locally systemic carboxamide fungicide used for the control of foliar and soil-borne plant diseases. Penthiopyrad was first evaluated in 2011 for toxicology, and an ADI of 0–0.1 mg/kg bw and an ARfD of 1 mg/kg bw were established. For residues, penthiopyrad was first evaluated by the 2012 JMPR. The residue definition for compliance with the MRL for plant commodities is penthiopyrad. For compliance with the MRL for animal commodities and dietary risk assessment for plant and animal commodities, the residue definition is the sum of penthiopyrad and 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide (PAM), expressed as penthiopyrad. The residue is not fat-soluble. Additional uses were evaluated by the 2013 JMPR.

Penthiopyrad was scheduled at the Fiftieth Session of the CCPR for evaluation of additional uses by the 2019 JMPR. The Meeting received information on supervised residue trials and GAP information for caneberry and blueberry.

<sup>&</sup>lt;sup>b</sup> mg of the specific analyte per kg sample

<sup>&</sup>lt;sup>c</sup> Total residue is the sum of penthiopyrad and PAM, expressed as parent equivalents. Conversion factor for PAM into penthiopyrad is 1.86. The <LOQ values were handled as their numeric value (e.g. <0.01 mg/kg as 0.01 mg/kg), except that

<sup>&</sup>lt;sup>d</sup> Bold letter: mean of replicate samples

<sup>\*:</sup> Not independent trials, due to the same place and close application dates

<sup>\*\*:</sup> Not independent trials, due to close place and application dates

### Methods of analysis

Residues of penthiopyrad and its metabolites (PAM and PCA, 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxylic acid) were analysed by the method evaluated by the 2012 JMPR. The current Meeting received additional method validation and concurrent recovery data on caneberry and blueberry. The method involving extraction and partitioning with organic solvent and determination by LC-MS/MS, was sufficiently validated for caneberry and blueberry. Mean recoveries ranged from 80-115% (RSDs  $\leq 15\%$ ). The LOQs for the analytes were 0.01 mg/kg.

### Stability of residues in stored analytical samples

The 2012 JMPR agreed that penthiopyrad; PAM and PCA are stable for at least 18 months in frozen plant matrices. The residue sample storage intervals used in the field trials considered by the current Meeting were covered by the demonstrated stability period.

### Results of supervised residue trials on crops

Supervised trials were available for the use of penthiopyrad on caneberry and blueberry. Product labels were available from Canada.

For dietary risk assessment, the sum of penthiopyrad and PAM (conversion factor into penthiopyrad, 1.86) is referred to as "total". If both analytes were below LOQs (< 0.01 mg/kg), the total residues were assumed to be < 0.01 mg/kg, and for all other cases, <LOQ values were handled as their numeric value (e.g. < 0.01 mg/kg as 0.01 mg/kg).

# Cane berries, Subgroup of

# Blackberry and raspberry

The critical GAP for penthiopyrad on caneberries in Canada is 3 foliar spray applications of 0.35 kg ai/ha each with a minimum retreatment interval of 7 days and a PHI of 0 days. One field trial on blackberry conducted in the USA and four independent field trials on raspberry conducted in Canada or the USA matched the critical GAP. Noting that the cGAP was for caneberries, the Meeting decided to combine the data from raspberries and blackberries to consider a group maximum residue level.

For the purposes of maximum residue level estimation penthiopyrad residues in raspberries and blackberries from trials matching the Canadian GAP were (n = 5): 2.0, 3.4, 3.7, 3.7 and 4.3 (blackberry) mg/kg.

For the dietary risk assessment purposes the total residues in caneberry were (n = 5): 2.0, 3.4, 3.7, 3.8 and 4.3 mg/kg (highest individual value was 4.8 mg/kg).

The Meeting estimated a maximum residue level of 10 mg/kg, a STMR of 3.7 mg/kg and a HR of 4.8 mg/kg for penthiopyrad in the Subgroup 004A Caneberries.

### **Blueberries**

The critical GAP for penthiopyrad on bushberries is 3 spray applications at a rate of 0.35 kg ai/ha with a minimum retreatment interval of 7 days and a PHI of 0 days. Seven independent trials on highbush blueberry conducted in Canada or the USA matched the critical GAP.

For the purposes of maximum residue level estimation penthiopyrad residues in blueberry were (n = 7): 0.57, 1.2, 1.5, 1.7, 1.7, 2.6 and 3.9 mg/kg.

For the dietary risk assessment purposes the total residues in blueberry were (n = 7): 0.59, 1.3, 1.5, 1.7, 1.7, 2.6 and 4.0 mg/kg.

Noting that blueberry is a representative crop for bushberries, the Meeting estimated a maximum residue level of 7 mg/kg, a STMR of 1.7 mg/kg and a HR of 4.0 mg/kg for penthiopyrad in the Subgroup 004B Bush berries.

The Meeting noted that the Canadian bushberries group includes highbush cranberries, listed in The Codex Classification as Guelder rose (*Vibernum opulus* L.) and Elderberries (*Sambucus* spp.) in the subgroup of large shrub/tree berries, and agreed to extrapolate the maximum residue level of 7 mg/kg, the STMR of 1.7 mg/kg and the HR of 4.0 mg/kg for penthiopyrad to Guelder rose and Elderberries.

#### Residues in animal feeds

The additional uses submitted to the current Meeting are not relevant to animal feeds.

### **RECOMMENDATIONS**

On the basis of the data obtained from supervised trials, the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI and IESTI assessments.

Definition of the residue for compliance with the MRL for plant commodities: penthiopyrad

Definition of the residue for compliance with the MRL for animal commodities and for dietary risk assessment for plant and animal commodities: sum of penthiopyrad and 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide (PAM), expressed as penthiopyrad

The residue is not fat-soluble.

Table 1 Residue levels suitable for establishing maximum residue limits and for IEDI and IESTI assessments

CCN	Commodity	Recommended		STMR or	HR or
		Maximum residue level		STMR-P	HR-P
		(mg/kg)		mg/kg	mg/kg
		New	Previous		
FB 2005	Subgroup of caneberries	10		3.7	4.8
FB 2006	Subgroup of bush berries	7		1.7	4.0
FB 0267	Elderberries	7		1.7	4.0
FB 2254	Guelder rose	7		1.7	4.0

#### **DIETARY RISK ASSESSMENT**

### Long-term dietary exposure

The ADI for penthiopyrad is 0–0.1 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for penthiopyrad were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR values estimated by the JMPR. The results are shown in Annex 3 of the 2019 JMPR Report.

The IEDIs ranged from 1-8% of the maximum ADI. The Meeting concluded that long-term dietary exposure to residues of penthiopyrad from uses considered by the JMPR is unlikely to present a public health concern.

### Acute dietary exposure

The ARfD for penthiopyrad is 1 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for penthiopyrad were calculated for the food commodities for which HRs were estimated by the

present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2019 JMPR Report.

The IESTIs varied from 0–5% of the ARfD for children and general population. The Meeting concluded that acute dietary exposure to residues of penthiopyrad from uses considered by the present Meeting is unlikely to present a public health concern.

# **REFERENCES**

Author	Report No.	Year	Study title
Ballantine, J.	AAFC11-006R	2014	Penthiopyrad: Magnitude of the Residue on Caneberry. Minor Use Pesticide Program, Pest Management Centre, Agriculture and Agri-Food Canada, Building 57, 960 Carling Ave., Ottawa, ON K1A 0C6; Dated: 5 November, 2014
Malegus, R.	. AAFC12-061R	2015	Penthiopyrad: Magnitude of the Residue on Blueberry, Highbush. Minor Use Pesticide Program, Pest Management Centre, Agriculture and Agri-Food Canada, Building 57, 960 Carling Ave., Ottawa, ON K1A 0C6; Dated: 15 June 2015.