

## 5.28 PENTHIOPYRAD (253)

### RESIDUE AND ANALYTICAL ASPECTS

Penthiopyrad (ISO common name) is a carboxamide fungicide used to control a broad spectrum of diseases on a large variety of crops. Penthiopyrad inhibits fungal respiration by binding to mitochondrial respiratory complex II. It was considered for the first time by the 2011 JMPR for toxicology, establishing an acceptable daily intake (ADI) of 0–0.1 mg/kg bw and an acute reference dose (ARfD) of 1 mg/kg bw. In 2012, the Meeting evaluated uses from the USA for residues, resulting in the recommendation of various maximum residue levels for plant and poultry commodities.

However, the Meeting estimated a maximum and mean dietary burden for beef and dairy cattle above the highest dose level administered in livestock animal feeding studies on cows and concluded, that no recommendations on mammalian animal products and milk could be made based on the available data. The maximum and mean dietary burden was calculated based on the Australian diet for beef and dairy cattle (main contributor: soya bean hay).

The Forty-fifth Session of the CCPR scheduled penthiopyrad for the evaluation of additional labels from Australia, Ireland, Italy, New Zealand, United Kingdom and the USA. In addition, following official communication from Australia that no fodder crops are imported, a re-evaluation of the dietary burden for livestock animals was requested. No additional residue data were provided to the 2013 Meeting.

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

As indicated the present Meeting did not receive additional supervised trial data for penthiopyrad. New European GAPs residue data was previously presented in the 2012 Evaluation for penthiopyrad, which at the time could not be taken into account as label authorisations had not been finalised.

For the new labels registered for penthiopyrad in Australia, New Zealand and the USA the Meeting noted that none of the GAPs involves higher application rates or shorter PHIs than evaluated in 2012. Since no additional supervised field trial data were submitted, no re-evaluation of these uses was conducted by the 2013 JMPR.

For dietary intake assessment the residue is defined as the sum of penthiopyrad and PAM, expressed as penthiopyrad (referred to as “total”). Since residue data were expressed in mg of the specific analyte per kg sample, PAM needs to be converted into penthiopyrad equivalents. The corresponding factor is: PAM → penthiopyrad =  $359.42 \text{ g/mol} \div 193.13 \text{ g/mol} = 1.86$ . In supervised field trials PAM residues were normally found at much lower levels than parent penthiopyrad. As a result, no adjustment of PAM or addition of LOQs was conducted, if both analytes were below the LOQ. For all other purposes of calculation < LOQ values were handled as their numeric value (e.g., < 0.01 mg/kg as 0.01 mg/kg).

This is illustrated below:

Penthiopyrad [mg/kg]	PAM [mg/kg]	Total [mg/kg]* (Sum of penthiopyrad and PAM, expressed as penthiopyrad equivalents)
< 0.01	< 0.01	< 0.01
0.1	< 0.01	0.12 (0.1 + 1.86 × 0.01)
< 0.01	0.1	0.2 (0.01 + 1.86 × 0.1)
0.1	0.1	0.29 (0.1 + 1.86 × 0.1)

\* rounded to two significant figures above the LOQ

*Cucurbits with edible peel*

In Italy penthiopyrad is registered for the use on cucumber and summer squash (zucchini) with one foliar application of 0.04 kg ai/hL with a 3 day PHI. Supervised field trial data on courgettes (zucchini) and cucumbers involving two treatments at the registered spray concentration were available for glasshouse use (Belgium, France, Greece, Italy and Spain) and field application (France, Greece, Italy and Spain). The analysis of samples collected directly before the second treatment indicates a contribution by the previous application of < 25% to the final residue, making these trials acceptable for evaluation.

For the purposes of MRL estimation penthiopyrad residues in protected summer squash were (n=2): 0.13 and 0.23 mg/kg.

For the dietary intake purposes the total residues in protected summer squash were (n=2): 0.15 and 0.25 mg/kg.

For the purposes of MRL estimations penthiopyrad residues in field summer squash were (n=2): 0.075, 0.12 mg/kg.

For the dietary intake purposes the total residues in field summer squash were (n=2): 0.095 0.14 mg/kg.

For the purposes of MRL estimations penthiopyrad residues in protected cucumber were (n=4): 0.031, 0.041, 0.053, 0.058 mg/kg.

For the dietary intake purposes the total residues in protected cucumber were (n=4): 0.051, 0.061, 0.073, 0.078 mg/kg.

For the purposes of MRL estimations penthiopyrad residues in field cucumber were (n=5): 0.013, 0.019, 0.082, 0.13, 0.3 mg/kg.

For the dietary intake purposes the total residues in field cucumber were (n=5): 0.033, 0.039, 0.1, 0.15, 0.32 mg/kg.

The Meeting decided that the previous recommendation for a maximum residue level of 0.5 mg/kg for penthiopyrad in fruiting vegetables, cucurbits also covered residues in cucumber and summer squash resulting from the new uses considered.

*Tomato and eggplants*

In Italy penthiopyrad is registered for the use on tomato and eggplants with one foliar application of 0.04 kg ai/hL with a 3 day PHI. Supervised field trial data on tomato involving two treatments at the registered spray concentration were available for glasshouse (Belgium, France, Greece, Italy, Spain) and field application (France, Greece, Italy, Spain). The analysis of samples collected directly before the second treatment indicates a contribution by the previous application of < 25% to the final residue, making these trials acceptable for evaluation.

For the purposes of MRL estimations penthiopyrad residues in protected tomato were (n=7): 0.15, 0.24, 0.31, 0.38, 0.55, 0.76, 0.76 mg/kg.

For the dietary intake purposes the total residues in protected tomato were (n=7): 0.17, 0.26, 0.33, 0.4, 0.57, 0.78, 0.78 mg/kg.

For the purposes of MRL estimations penthiopyrad residues in field tomato were (n=5): 0.11, 0.18, 0.22, 0.29, 0.32 mg/kg.

For the dietary intake purposes the total residues in field tomato were (n=5): 0.13, 0.2, 0.24, 0.31, 0.34 mg/kg.

The Meeting recognized that residue data on tomato can also be extrapolated to eggplants.

The Meeting decided that the previous recommendation for a maximum residue level of 2 mg/kg for penthiopyrad in fruiting vegetables, other than cucurbits, except sweet corn and mushrooms also covers residues in tomatoes and eggplants resulting from the new uses considered.

#### *Barley and oats*

In Ireland and the UK penthiopyrad is registered for the use on barley and oats with two foliar application up to 0.3 kg ai/ha each. The PHI is covered by a specified growth stage (BBCH 61). Supervised residue trials approximating this GAP were submitted to the 2012 Meeting from France, Germany, Hungary and the UK.

For the purposes of MRL estimations penthiopyrad residues in barley grain were (n=14): < 0.01(3), 0.01, 0.01, 0.039, 0.057, 0.063, 0.069, 0.071, 0.076, 0.1, 0.12 mg/kg.

For the dietary intake purposes the total residues in barley grain were (n=14): < 0.01(3), 0.03, 0.03, 0.059, 0.083, 0.089, 0.091, 0.096, 0.1, 0.12, 0.14 mg/kg.

The Meeting recognized that barley and oats share an identical GAP and decided to extrapolate residue data from barley to oats.

The Meeting estimated a maximum residue level and an STMR of 0.2 mg/kg and 0.086 mg/kg for penthiopyrad in barley and oats, respectively, replacing its previous recommendation of a maximum residue level of 0.15 mg/kg for barley and oats.

#### *Wheat, rye and triticale*

In Ireland and the UK penthiopyrad is registered for the use on rye, triticale and wheat with two foliar application up to 0.3 kg ai/ha each. The PHI is covered by a specified growth stage (BBCH 71). Supervised residue trials approximating this GAP were submitted to the 2012 Meeting from France, Germany, Hungary and UK.

For the purposes of MRL estimations penthiopyrad residues in wheat grain were (n=13): < 0.01(9), 0.013, 0.015, 0.015, 0.081 mg/kg.

For the dietary intake purposes the total residues in wheat grain were (n=13): < 0.01(9), 0.033, 0.035, 0.035, 0.1 mg/kg.

The Meeting recognized that wheat, rye and triticale share an identical GAP and decided to extrapolate residue data from wheat to rye and triticale.

The Meeting estimated a maximum residue level of 0.1 mg/kg and confirmed its previous estimate of an STMR of 0.01 mg/kg for penthiopyrad in wheat, rye and triticale, respectively, replacing its previous recommendation of a maximum residue level of 0.04 mg/kg for wheat, rye and triticale.

#### *Animal feeds*

##### *Barley, oats, rye, triticale and wheat forage*

In Ireland and the UK penthiopyrad is registered for the use on barley, oats, rye, triticale and wheat with two foliar application up to 0.3 kg ai/ha each. The PHI is covered by specified growth stages (BBCH 61 & 71). Supervised residue trials approximating this GAP were submitted to the 2012 Meeting from France, Germany, Hungary and the UK.

For the calculation of the livestock animal dietary burden total residues in barley forage (fresh) were (n=6): 2.0, 3.5, 3.9, 3.9, 4.0 and 4.5 mg/kg.

For the calculation of the livestock animal dietary burden total residues in wheat forage (fresh) were (n=6): 2.2, 3.0, 3.8, 4.3, 5.3 and 5.7 mg/kg.

The Meeting decided that the previously estimated median and highest residues in barley, oats, rye, triticale and wheat forage (fresh) of 10 mg/kg and 17 mg/kg, respectively, covered residues resulting from the new uses considered by the present Meeting.

*Barley, oats, rye, triticale and wheat straw and fodder of cereals*

In Ireland and the UK penthiopyrad is registered for the use on barley, oats, rye, triticale and wheat with two foliar application up 0.3 kg ai/ha each. The PHI is covered by specified growth stages (BBCH 61 & 71). Supervised residue trials approximating this GAP were submitted to the 2012 Meeting from France, Germany, Hungary and the UK.

For the purposes of MRL estimations penthiopyrad residues in barley straw (fresh) were (n=12): < 0.05, 0.051, 0.11, 0.13, 0.15, 0.2, 0.25, 0.28, 0.28, 0.36, 0.57 and 0.68 mg/kg.

For the calculation of the livestock animal dietary burden total residues in barley straw (fresh) were (n=12): < 0.05, 0.15, 0.21, 0.23, 0.25, 0.3, 0.35, 0.38, 0.38, 0.46, 0.67, 0.78 and 1.0 mg/kg.

For the purposes of MRL estimations penthiopyrad residues in wheat straw (fresh) were (n=13): 0.05, 0.052, 0.059, 0.067, 0.077, 0.12, 0.13, 0.16, 0.21, 0.26, 0.75, 1.1 and 2.3 mg/kg.

For the calculation of the livestock animal dietary burden total residues in wheat straw (fresh) were (n=13): 0.15, 0.16, 0.16, 0.17, 0.18, 0.22, 0.23, 0.26, 0.31, 0.36, 0.85, 1.2 and 2.6 mg/kg.

The Meeting decided that the previously estimated maximum residue level, median and highest residue in barley, oats, rye, triticale and wheat straw of 80 mg/kg (DM based), 21 mg/kg and 54 mg/kg, respectively, covered residues resulting from the new uses considered by the present Meeting.

*Fate of residues during processing*

The Meeting estimated new maximum residue levels for barley, oats, rye, triticale and wheat and a new STMR for barley and oats.

The estimation of maximum residue levels is based on the parent substance only, whereas for the dietary intake assessment the total residue needs to be taken into account. Based on the processing factors derived by the 2012 Meeting the following residues in processed products were estimated:

Commodity	Processing factor	Processing factor (median or best estimate)	MRL / STMR (mg/kg)	MRL, STMR-P (mg/kg)
Barley beer	Total: < 0.11, < 0.36	Total: < 0.24	STMR: 0.086	STMR-P: 0.021
Pot barley	Total: 0.67, 0.68	Total: 0.68	STMR: 0.086	STMR-P: 0.058
Wheat bran	Penthiopyrad: 1.8	Penthiopyrad: 1.8	MRL: 0.1	MRL: 0.2
Wheat germ	Penthiopyrad: 2.1	Penthiopyrad: 2.1	MRL: 0.1	MRL: 0.2

For wheat processed into wheat bran and wheat germ the Meeting estimated maximum residue levels of 0.2 mg/kg, respectively, and agreed to withdraw its previous recommendations of 0.1 mg/kg.

### ***Residues in animal commodities***

#### ***Livestock dietary burden***

Livestock feeding studies involving administration of penthiopyrad to lactating cows and laying hens were reported in the 2012 JMPR Report.

#### ***Estimated maximum and mean dietary burdens of livestock***

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6.

The Meeting received official communication from Australia that no fodder crops are imported. The Meeting therefore decided to make a refined calculation of the livestock dietary burden based using the following parameters:

For the Australian diet only feed commodities corresponding to Australian authorisations plus globally traded non-fodder commodities are taken into account (e.g., grains and seeds).

For US-Canada, EU and Japan the calculation was conducted according to the usual procedure described in FAO Manual and amended by the new estimated median residue of 0.086 mg/kg for barley and oats. However, in contrast to 2012, forage crops were only included in the dietary burden for regions with corresponding labels (e.g. barley, oats, rye, triticale and wheat forage for Europe).

The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2009 edition of the FAO Manual.

<b>Livestock dietary burden, total residue*, ppm of dry matter diet</b>								
	US-Canada		EU		Australia		Japan	
	max.	mean	max.	mean	max.	mean	max.	mean
Beef cattle	12	4.5	23	12	1.3	1.3	1.9	0.46
Dairy cattle	55 <sup>a,c</sup>	26 <sup>b,d</sup>	30	13	1.1	1.1	4.6	0.9
Poultry - broiler	0.2	0.2	0.19	0.19	0.19	0.19	0.17	0.17
Poultry - layer	0.2	0.2	22 <sup>e</sup>	11 <sup>f</sup>	0.19	0.19	0.14	0.14

<sup>a</sup> Highest maximum beef or dairy cattle burden suitable for MRL estimates for mammalian meat

<sup>b</sup> Highest mean beef or dairy cattle burden suitable for STMR estimates for mammalian meat

<sup>c</sup> Highest maximum dairy cattle burden suitable for MRL estimates for milk

<sup>d</sup> Highest mean dairy cattle burden suitable for STMR estimates for milk

<sup>e</sup> Highest maximum broiler or laying hen burden suitable for MRL estimates for poultry products and eggs

<sup>f</sup> Highest mean broiler or laying hen burden suitable for STMR estimates for poultry products and eggs

\* total residue: sum of penthiopyrad and PAM, expressed as penthiopyrad

#### ***Animal commodities, MRL estimation***

For beef and dairy cattle maximum and mean dietary burdens of 55 ppm and 26 ppm were estimated, respectively. The calculation to estimate highest total residues for use in estimating maximum residue levels, STMR and HR values were shown below.

Penthiopyrad feeding study	Feed level (ppm)	Total residue				
		(mg/kg) in milk	(mg/kg) in muscle	(mg/kg) in kidney	(mg/kg) in liver	(mg/kg) in fat
<b>Maximum residue level: dairy cattle</b>						
Feeding study	21.4 74.6	< 0.01 0.042	< 0.01 0.036	0.03 0.07	0.04 0.08	0.03 0.04
Dietary burden and residue estimate	55	0.03	0.026	0.055	0.065	0.036
<b>STMR dairy cattle</b>						
Feeding study	21.4 74.6	< 0.01 0.042	< 0.01 0.036	0.03 0.07	0.04 0.08	0.03 0.04
Dietary burden and residue estimate	26	0.013	0.012	0.033	0.043	0.031

For beef and dairy cattle the Meeting estimated HR values for penthiopyrad (total residue) of 0.026 mg/kg in muscle, of 0.065 mg/kg in edible offal (based on liver) and of 0.036 mg/kg in fat. STMR values were estimated at levels of 0.013 mg/kg for milk, 0.012 mg/kg for meat, 0.043 mg/kg for edible offal (based on liver) and 0.031 mg/kg for fat.

The Meeting also estimated the following maximum residue levels: milk 0.04 mg/kg, meat (mammalian except marine mammals) 0.04 mg/kg, mammalian fat 0.05 mg/kg and edible offal 0.08 mg/kg.

For poultry the mean and maximum dietary burden differed insignificantly compared to the calculation by the 2012 Meeting (Max/Mean; 2012: 22ppm/10ppm; 2013: 22ppm/11ppm). The previous recommendations for penthiopyrad in poultry tissues and eggs are confirmed.

## RECOMMENDATIONS

The Meeting estimated the STMR, HR and MRL values shown below.

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

Definition of the residue for compliance with MRL for animal commodities and for the estimation of dietary intake 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.

## DIESTARY RISK ASSESSMENT

### *Long-term intake*

The WHO Panel of the 2011 JMPR established an Acceptable Daily Intake (ADI) of 0-0.1 mg/kg bw/day for penthiopyrad.

The 2013 evaluation of penthiopyrad resulted in new recommendations for MRLs and STMR values for barley, oats, rye, triticale, wheat and mammalian animal products. Where data on consumption were available for the listed food commodities evaluated in 2012 or 2013, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3.

The IEDIs in the thirteen Cluster Diets, based on the estimated STMRs were 0-6% of the maximum ADI (0.1 mg/kg bw). The Meeting concluded that the long-term intake of residues of penthiopyrad from uses that have been considered by the JMPM is unlikely to present a public health concern.

#### ***Short-term intake***

The WHO Panel of the 2011 JMPM established an Acute Reference Dose (ARfD) of 1 mg/kg bw for penthiopyrad.

The International Estimated Short-Term Intake (IESTI) for penthiopyrad was calculated for the food commodities for which STMRs or HRs were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4. The IESTI for children and for the general population was 0% of the ARfD.

The Meeting concluded that the short-term intake of residues of penthiopyrad resulting from uses that have been considered by the 2013 JMPM is unlikely to present a public health concern.

