BIXAFEN (262)

The first draft was prepared by Mr Christian Sieke, Federal Institute for Risk Assessment, Berlin, Germany

EXPLANATION

Bixafen (ISO common name) is a pyrazole-carboxamide fungicide used to control diseases on rape plants and cereals. Bixafen inhibits fungal respiration by binding to mitochondrial respiratory complex II. It was considered for the first time by the 2013 JMPR for toxicology and residues, when an ADI of 0–0.02 mg/kg bw and an ARfD of 0.2 mg/kg bw were established.

The 2013 Meeting also recognized that bixafen residues are persistent in soil and may lead to significant residues in rotational crops. Since no field rotational crop studies addressing estimated soil plateau levels were available, no recommendations on maximum residue levels in plant or animal commodities could be given and consequently a dietary risk assessment was not conducted.

However, the 2013 Meeting recommended the following residue definition for bixafen:

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

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 bixafen and N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1H-pyrazole-4-carboxamide (bixafen-desmethyl), expressed as bixafen*

The residue is fat-soluble.

The current Meeting received new information on residues in rotational crops grown in the field supported by additional analytical methods and storage stability data.

METABOLISM AND ENVIRONMENTAL FATE

Field rotational crop studies

A field rotational crop study investigating residues in cereal grains, carrots and lettuce grown as succeeding crops was conducted by Schöning and van Berkum (2015, BIXAFEN_074). In three trials bare soil was treated once with an application rate equivalent to 0.93 kg ai/ha and incorporated into the first 20 cm soil layer. In one additional trial a plot previously used for the long-term soil accumulation study by Heinemann, O. and Weuthen, M. (2013, BIXAFEN_027, please refer to 2013 JMPR Report) was selected. Before treatment, aged soil residues still present from the long-term accumulation study were measured (Freitag T., 2014, BIXAFEN_075) and an amount of bixafen was freshly applied which resulted in a combined soil concentration equivalent to a single bare soil application rate of 0.93 kg ai/ha (based on the 0-20 cm layer).

After 19-31 days the first following crops were sown and grown to maturity. Second and third crop rotations were only conducted at one location with sowing at 100-240 days after treatment (DAT) and 300-365 DAT. Samples were collected at selected immature stages as well as for the mature crops ready for commercial harvest. The collected plant samples as well as soil samples were analysed for residues of parent bixafen and its metabolite M21 (bixafen-desmethyl) as well as for M43 (bixafen-pyrazole-4-carboxamide) and M44/M45 (bixafen-desmethyl-pyrazole-4-carboxylic acid).

Analytical methods used were all based on LC-MS/MS techniques. For plant matrices method MR-06/138 (BIXAFEN_043) and for soil analysis method MR-07/289 (BIXAFEN_048) were used. Both methods are described in the 2013 JMPR Evaluation on bixafen. For Method 01366, which is suitable for the analysis of M43 and M44/45 in plant matrices, please refer to the analytical methods section below.

In the following table the trial layout used on the four locations is summarized. Analysis of soil residues (0-20 cm layer) directly after treatment showed bixafen residues between 0.18–

0.27 mg/kg for trial 13-2502-01, 0.22–0.29 mg/kg for trial 13-2502-02, 0.22–0.26 mg/kg for trial 13-2502-03 and 0.25–0.26 mg/kg for trial 13-2502-04.

Table 1 Rotational crop layout for four supervised field rotational crop studies involving application of bixafen to bare soil at rates up to 0.93 kg ai/ha

Trial no. Location	Application to bare soil	1st Crop Rotation	2nd Crop Rotation	3rd Crop Rotation
13-2502-01 United Kingdom, Little Shelford	1 × 0.93 kg ai/ha, 200 L water/ha	Carrot (PBI 31 d)	Carrot (PBI 124 d)	Carrot (PBI 336 d)
		Lettuce (PBI 31 d)	Lettuce (PBI 137 d)	Lettuce (PBI 363 d)
		Wheat (PBI 24 d)	Wheat (PBI 181 d)	Barley (PBI 332 d)
13-2502-02 Germany, Monheim (combined trial with aged soil residues and freshly applied active substance)	Aged residue (0-20cm layer): 0.47 kg ai/ha eq. Freshly applied: 1 × 0.46 kg ai/ha, 300 L water/ha	Carrot (PBI 19 d)	Not performed	Not performed
		Lettuce (PBI 19 d)		
	Aged residue (0-20cm layer): 0.43 kg ai/ha eq. Freshly applied: 1 × 0.50 kg ai/ha, 300 L water/ha	Wheat (PBI 21 d)		
13-2502-03 Germany, Monheim	1 × 0.93 kg ai/ha, 300 L water/ha	Carrot (PBI 19 d)	Not performed	Not performed
		Lettuce (PBI 19 d)		
		Wheat (PBI 21 d)		
13-2502-04 Germany, Burscheid	1 × 0.93 kg ai/ha, 300 L water/ha	Carrot (PBI 21 d)	Not performed	Not performed
		Lettuce (PBI 21 d)		
		Wheat (PBI 21 d)		

In the following tables the analytical results for bixafen and its metabolites found in samples of rotational crops are summarized:

Table 2 Residues in samples obtained from rotational crops grown in the field after application of bixafen to bare soil at rates up to 0.93 kg ai/ha

Trial no. Location	Bare soil rate	Crop and plant back interval	Sample material	DALT	Residues in mg bixafen eq./kg			
					Bixafen	M21	M44/45	M43
13-2502-01 United Kingdom, Little Shelford	1 × 0.93 kg ai/ha	Carrot (PBI 31 d)	Leaf	136 166	0.015 0.021	< 0.01 < 0.01	0.18 0.095	< 0.01 < 0.01
			Root	136 166	0.028 0.016	< 0.01 < 0.01	0.044 0.033	< 0.01 < 0.01
		Lettuce (PBI 31 d)	Head	68 77	< 0.01 < 0.01	< 0.01 < 0.01	0.024 0.031	< 0.01 < 0.01
		Wheat (PBI 24 d)	Green material Grain Straw	200 301 301	< 0.01 < 0.01 0.049	< 0.01 < 0.01 0.07	0.025 < 0.01 0.082	< 0.01 < 0.01 < 0.01
		Carrot (PBI 124 d)	Leaf	391 406	< 0.01 < 0.01	< 0.01 < 0.01	0.12 0.086	< 0.01 < 0.01
			Root	391 406	< 0.01 0.01	< 0.01 < 0.01	0.043 0.036	< 0.01 < 0.01
		Lettuce (PBI 137 d)	Head	192 206	< 0.01 < 0.01	< 0.01 < 0.01	0.021 0.021	< 0.01 < 0.01
		Wheat (PBI 181 d)	Green material Grain Straw	357 458 458	< 0.01 < 0.01 0.034	< 0.01 < 0.01 0.048	0.048 < 0.01 0.07	< 0.01 < 0.01 < 0.01
		Carrot (PBI 336 d)	Leaf	476 495	< 0.01 < 0.01	< 0.01 < 0.01	0.094 0.12	< 0.01 < 0.01
			Root	476 495	0.018 0.012	< 0.01 < 0.01	0.018 0.022	< 0.01 < 0.01
		Lettuce (PBI 363 d)	Head	402 418	< 0.01 < 0.01	< 0.01 < 0.01	0.092 0.047	< 0.01 < 0.01
		Barley (PBI 332 d)	Green material	382	< 0.01	< 0.01	0.044	< 0.01

Trial no. Location	Bare soil rate	Crop and plant back interval	Sample material	DALT	Residues in mg bixafen eq./kg			
					Bixafen	M21	M44/45	M43
			Grain Straw	458 458	< 0.01 0.013	< 0.01 0.024	< 0.01 0.07	< 0.01 < 0.01
13-2502-02 Germany, Monheim (combined trial with aged soil residues and freshly applied active substance)	[A]	Carrot (PBI 19 d)	Leaf	104 120	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
			Root	104 120	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
		Lettuce (PBI 19 d)	Head	55 69	< 0.01 < 0.01	< 0.01 < 0.01	0.012 < 0.01	< 0.01 < 0.01
	[B]	Wheat (PBI 21 d)	Green material Grain Straw	190 330 330	< 0.01 < 0.01 0.012	< 0.01 < 0.01 0.023	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01
13-2502-03 Germany, Monheim	1 × 0.93 kg ai/ha	Carrot (PBI 19 d)	Leaf	104 120	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
			Root	104 120	0.014 0.012	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
		Lettuce (PBI 19 d)	Head	55 69	< 0.01 < 0.01	< 0.01 < 0.01	0.017 0.015	< 0.01 < 0.01
		Wheat (PBI 21 d)	Green material Grain Straw	190 330 330	< 0.01 < 0.01 0.019	< 0.01 < 0.01 0.043	0.02 < 0.01 0.014	< 0.01 < 0.01 < 0.01
13-2502-04 Germany, Burscheid	1 × 0.93 kg ai/ha	Carrot (PBI 21 d)	Leaf	105 123	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
			Root	105 123	0.012 0.019	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
		Lettuce (PBI 21 d)	Head	64 78	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
		Wheat (PBI 21 d)	Green material Grain Straw	196 322 322	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 0.036	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01

[A] Aged residue (0-20cm layer): 0.47 kg ai/ha eq. plus freshly applied: 1 × 0.46 kg ai/ha, 300 L water/ha

[B] Aged residue (0-20cm layer): 0.43 kg ai/ha eq. plus freshly applied: 1 × 0.50 kg ai/ha, 300 L water/ha

M21: bixafen-desmethyl

M43: bixafen-pyrazole-4-carboxamide

M44/45: bixafen-desmethyl-pyrazole-4-carboxylic acid

RESIDUE ANALYSIS

Methods of analysis

Plant materials

For bixafen one additional analytical method was provided for the determination of M43 and M44/45 in plant matrices. All plant matrices were validated with an LOQ of 0.01 mg/kg for each analyte.

Method 01366 (Schoening, Willmes and Oel, 2015, BIXAFEN_076; Schoening, R., Willmes, J, 2015, BIXAFEN_077)

All analytes are extracted from plant materials using a mixture of acetonitrile/water (4/1; v/v) assisted by microwave irradiation. After filtration of the extract, the solution is made up to volume, diluted and subjected to reversed phase HPLC-MS/MS without further clean-up. Both analytes are detected using electrospray ionization in the Multiple Reaction Monitoring mode (MRM). Residues are quantified against matrix-matched standards. Results are expressed as bixafen equivalents.

The stability of extracts was demonstrated within the studies for a storage period of at least one up to four weeks for the matrices investigated.

Table 3 Recovery data for method 01366 measuring M43 and M44/45 in plant matrices

Matrix	Fortification level (mg/kg)[a]	n	Recovery range (%)	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Schoening, Willmes and Oel, 2015, BIXAFEN_076						
Orange fruit	0.056 0.56	5 5	95-104 93-100	100 97	3.3 3.0	M43: m/z: 176 → 136
	0.056 0.56	5 5	98-104 94-99	102 97	2.5 2.2	M43: m/z: 176 → 156
	0.065 0.65	5 5	101-107 95-104	104 102	2.1 4.4	M44: m/z: 163 → 68
	0.065 0.65	5 5	101-105 93-107	104 102	1.7 5.3	M44: m/z: 161 → 66
Tomato	0.056 0.56	5 5	101-113 99-113	106 107	4.2 5.3	M43: m/z: 176 → 136
	0.056 0.56	5 5	103-113 97-111	108 105	4.2 5.5	M43: m/z: 176 → 156
	0.065 0.65	5 5	100-106 102-108	103 104	2.2 2.1	M44: m/z: 163 → 68
	0.065 0.65	5 5	94-100 103-109	99 104	3.8 2.5	M44: m/z: 163 → 123
Potato tuber	0.056 0.56	5 5	86-100 75-80	92 78	6.2 3.3	M43: m/z: 176 → 136
	0.056 0.56	5 5	85-101 75-80	92 78	6.5 3.0	M43: m/z: 176 → 156
	0.065 0.65	5 5	91-103 83-93	96 89	5.1 4.2	M44: m/z: 163 → 68
	0.065 0.65	5 5	92-103 82-92	96 89	5.0 4.3	M44: m/z: 163 → 123
Dry bean seed	0.056 0.56	5 5	95-103 108-119	101 112	3.5 3.8	M43: m/z: 176 → 136
	0.056 0.56	5 5	97-105 107-119	102 112	3.1 4.0	M43: m/z: 176 → 156
	0.065 0.65	5 5	84-103 99-106	95 102	7.5 2.9	M44: m/z: 163 → 68
	0.065 0.65	5 5	82-101 100-105	95 102	7.9 2.0	M44: m/z: 163 → 123
Soya bean seed	0.056 0.56	5 5	91-97 94-102	94 97	3.0 3.7	M43: m/z: 176 → 136
	0.056 0.56	5 5	91-99 92-102	95 96	3.8 4.1	M43: m/z: 176 → 156
	0.065 0.65	5 5	84-87 89-91	85 90	1.5 0.8	M44: m/z: 163 → 68
	0.065 0.65	5 5	83-87 89-92	85 91	1.7 1.3	M44: m/z: 163 → 123
Schoening, R., Willmes, J, 2015, BIXAFEN_077						
Orange fruit	0.01 0.1	5 5	99-100 101-105	99 104	0.5 1.7	M43: m/z: 176 → 136
	0.01 0.1	5 5	94-100 103-106	97 105	2.5 1.1	M43: m/z: 176 → 156
	0.01	5	93-107	101	5.9	M44: m/z: 163 → 68

Matrix	Fortification level (mg/kg)[a]	n	Recovery range (%)	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
	0.1	5	99-103	101	1.5	
	0.01 0.1	5 5	95-105 99-105	99 102	3.9 2.5	M44: m/z: 163 → 123
Tomato	0.01 0.1	5 5	88-99 89-99	93 95	5.1 4.4	M43: m/z: 176 → 136
	0.01 0.1	5 5	88-96 87-99	92 95	3.6 5.3	M43: m/z: 176 → 156
	0.01 0.1	5 5	87-107 83-100	97 94	7.4 7.5	M44: m/z: 163 → 68
	0.01 0.1	5 5	89-96 85-98	91 93	3.1 5.8	M44: m/z: 163 → 123
Potato tuber	0.01 0.1	5 5	99-103 91-99	101 95	1.8 3.4	M43: m/z: 176 → 136
	0.01 0.1	5 5	102-105 91-98	103 95	1.3 2.9	M43: m/z: 176 → 156
	0.01 0.1	5 5	92-106 89-94	97 92	5.8 2.3	M44: m/z: 163 → 68
	0.01 0.1	5 5	96-104 94-98	99 96	3.2 1.8	M44: m/z: 163 → 123
Dry bean seed	0.01 0.1	5 5	100-109 73-78	104 76	3.1 3.3	M43: m/z: 176 → 136
	0.01 0.1	5 5	100-106 74-79	103 77	2.2 3.6	M43: m/z: 176 → 156
	0.01 0.1	5 5	83-98 70-72	90 71	6.9 1.3	M44: m/z: 163 → 68
	0.01 0.1	5 5	83-85 66-68	84 67	1.0 1.2	M44: m/z: 163 → 123
Soya bean seed	0.01 0.1	5 5	93-98 96-100	95 98	2.4 3.0	M43: m/z: 176 → 136
	0.01 0.1	5 5	92-98 96-101	95 99	2.6 2.1	M43: m/z: 176 → 156
	0.01 0.1	5 5	78-95 84-88	85 86	8.0 2.1	M44: m/z: 163 → 68
	0.01 0.1	5 5	86-89 81-86	88 84	1.7 2.3	M44: m/z: 163 → 123

[a] expressed as bixafen equivalent

Stability of pesticides in stored analytical samples

Plant matrices

Schoening, R. and Diehl, P. (2015, BIXAFEN_078)

The stability of the bixafen metabolites M43 and M44 was investigated in orange fruit, tomato fruit, potato tuber, dry bean seed and soya bean seed representing commodities of high acid, high water, high starch, high protein and high oil content, respectively. The storage stability was investigated for about 24 months (720 days) under frozen storage conditions.

All samples were homogenized with dry ice and fortified with M43 and M44 at concentrations of 0.56 g/kg and 0.65 mg/kg, respectively. The samples were stored in glass vessels at -

18 °C. Samples were taken for analysis at intervals up to 24 months in parallel to freshly fortified samples to estimate the procedural recovery. Analysis of the samples was performed according to the method 01366.

In the study report the results for the stored samples are only reported as percentage of the fortified level corrected by the procedural recoveries. No measured concentrations were described.

Table 4 Recovered M43 residues in stored plant commodities after storage up to 24 months (Schoening, R. and Diehl, P., 2015, BIXAFEN_078)

Matrix	Forti-fication level (mg/kg)[a]	Storage period (months)	Residue level in stored samples		Procedural recovery	
			Individual values (% fortified)	Mean (%)	Individual values (%)	Mean (%)
Orange fruit	0.56	0	90, 96, 93, 95, 104	96	100, 82[a]	91[a]
		1	104, 99, 92	98	99, 101	100
		3	97, 99, 96	97	96, 97	97
		6	103, 101, 102	102	101, 102	102
		12	100, 100, 98	99	103, 103	103
		18	95, 96, 93	95	100, 94	97
		24	96, 94, 93	94	94, 92	93
Tomato	0.56	0	99, 99, 97, 101, 103	100	88, 81[b]	85[a]
		1	88, 94, 92	91	96, 95	96
		3	106, 108, 110	108	102, 92	97
		6	103, 107, 103	104	101, 108	105
		12	103, 104, 104	104	104, 103	104
		18	101, 94, 103	99	100, 101	101
		24	103, 101, 97	100	101, 101	101
Potato tuber	0.56	0	103, 106, 115, 82, 115	104	98, 108[a]	103[a]
		1	97, 97, 98	97	104, 100	102
		3	100, 99, 101	100	103, 97	100
		6	105, 104, 107	105	108, 105	107
		12	107, 104, 100	104	108, 104	106
		18	96, 99, 100	98	101, 94	98
		24	95, 94, 93	94	93, 92	93
Dry bean seed	0.56	0	104, 115, 113, 114, 115	112	114, 106[a]	110[a]
		1	71, 76, 77	75	81, 82	82
		3	109, 98, 103	103	119, 113, 108	113
		6	97, 90, 94	94	99, 103	101
		12	96, 100, 100	99	103, 103	103
		18	101, 99, 99	100	95, 99	97
		24	95, 92, 95	94	96, 96	96
Soya bean seed	0.56	0	96, 94, 90, 89, 91	92	95, 106[a]	101[a]
		1	93, 95, 93	94	99, 101	100
		3	97, 98, 95	97	103, 97	100
		6	88, 90, 91	90	92, 93	93
		12	100, 101, 101	101	98, 99	99
		18	91, 90, 93	91	95, 97	96
		24	96, 92, 98	95	93, 95	94

[a] expressed as bixafen equivalent

[b] fortified with 0.056 mg/kg only

Table 5 Recovered M44 residues in stored plant commodities after storage up to 24 months (Schoening, R. and Diehl, P., 2015, BIXAFEN_078)

Matrix	Forti-fication level	Storage period	Residue level in stored samples	Procedural recovery

	(mg/kg)[a]	(months)	Individual values (% fortified)	Mean (%)	Individual values (%)	Mean (%)
Orange fruit	0.65	0 1 3 6 12 18 24	93, 92, 94, 91, 90 96, 98, 96 96, 98, 96 101, 101, 106 95, 95, 96 93, 91, 91 95, 93, 96	92 97 97 103 95 92 95	101, 89 [b] 95, 96 95, 96 95, 98 95, 96 98, 94 96, 95	95 [a] 96 96 97 96 96 96
Tomato	0.65	0 1 3 6 12 18 24	105, 103, 100, 97, 105 96, 97, 96 105, 108, 105 107, 105, 110 96, 97, 97 97, 95, 97 97, 97, 97	102 96 106 107 97 96 97	103, 96 [a] 99, 96 106, 95 96, 99 100, 99 98, 100 97, 97	100 [a] 98 101 98 100 99 97
Potato tuber	0.65	0 1 3 6 12 18 24	106, 102, 105, 104, 104 95, 100, 98 98, 102, 101 97, 92, 93 94, 93, 97 98, 95, 93 92, 95, 95	104 98 100 94 95 95 94	96, 107 [a] 98, 98 101, 99 99, 94 102, 99 100, 93 96, 94	102 [a] 98 100 97 101 97 95
Dry bean seed	0.65	0 1 3 6 12 18 24	108, 111, 86, 114, 106 84, 90, 97 107, 106, 104 83, 93, 89 95, 88, 91 94, 96, 90 91, 92, 94	105 90 106 88 91 93 92	104, 104 [a] 87, 87 117, 115, 111 95, 97 100, 100 95, 99 95, 94	104 [a] 87 114 96 100 97 95
Soya bean seed	0.65	0 1 3 6 12 18 24	75, 77, 77, 76, 76 63, 75, 74 84, 81, 82 78, 81, 81 69, 74, 74 69, 72, 65 72, 76, 78	76 71 82 80 72 69 75	82, 90 [a] 82, 87 96, 93 84, 85 84, 81 86, 86 81, 84, 90	86 [a] 85 95 85 83 86 85

[a] expressed as bixafen equivalent

[b] fortified with 0.056 mg/kg only

APPRAISAL

Bixafen is a pyrazole-carboxamide fungicide used to control diseases on rape plants and cereals. It inhibits fungal respiration by binding to mitochondrial respiratory complex II. It was considered for the first time by the 2013 JMPR for toxicology and residues, when an ADI of 0–0.02 mg/kg bw and an ARfD of 0.2 mg/kg bw were established.

The 2013 Meeting also recognized that bixafen residues are persistent in soil and may lead to significant residues in rotational crops. Since no field rotational crop studies addressing estimated soil plateau levels were available, no recommendations on maximum residue levels in plant or animal commodities could be given and consequently a dietary risk assessment was not conducted.

However, the 2013 Meeting recommended the following residue definition for bixafen:

Definition of the residue (for compliance with MRLs) for plant commodities: *bixafen*

Definition of the residue (for compliance with MRLs) for animal commodities and (for dietary exposure assessment) for plant and animal commodities: *sum of bixafen and N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1H-pyrazole-4-carboxamide (bixafen-desmethyl), expressed as bixafen*

The residue is fat soluble.

At the 47th Session of CCPR, bixafen was scheduled for the evaluation of additional data in the 2016 JMPR. The current Meeting received new information on residues in rotational crops grown in the field supported by additional analytical methods and storage stability data for the metabolites M43 and M44/45. Since the current residue definition includes residues of parent bixafen and bixafen-desmethyl only, they are not discussed further in the appraisal.

Environmental fate in soil

For bixafen the Meeting concluded in 2013 that the active substance is persistent in soil, accumulating after subsequent years of annual treatment. Confined rotational crop studies indicate a potential uptake of residues for bixafen and M21 (bixafen-desmethyl) into plant commodities.

The Meeting also recognized that field rotational crop studies involve soil treatment rates not addressing the soil concentrations expected after subsequent annual treatment. The Meeting concluded that bixafen residues accumulate in soil after subsequent annual treatments. Under consideration of the highest annual application rate reported in the authorised GAPs of 0.25 kg ai/ha, soil residue concentrations equivalent to single application rates to bare soil of 0.9 kg ai/ha could be reached.

Additional field rotational crop studies were submitted to the present Meeting. In three trials conducted in Europe (2 from Germany and one from the UK), the ground was treated with rates equivalent to 0.93 kg ai/ha and carrots, lettuce or wheat/barley were grown as rotational crops at plant-back intervals (PBI) of 19–31 days. In the UK trial the same crops (but in different order) were additionally sown as second and third rotations with PBIs of 124–181 days and 332–363 days, respectively. For the first rotation, residues for bixafen and bixafen-desmethyl (M21) in the rotated crops were:

Commodity	Residue in mg bixafen equivalents per kg (mean value)		
	Bixafen	Bixafen-desmethyl (M21)	Total
Carrot, tops	2 × < 0.01, 0.021 (0.014)	3 × < 0.01	2 × < 0.02, 0.031 (0.024)
Carrot, roots	0.014, 0.019, 0.028 (0.02)	3 × < 0.01	0.024, 0.029, 0.038 (0.03)
Lettuce, head	3 × < 0.01	3 × < 0.01	3 × < 0.02
Wheat, forage	3 × < 0.01	3 × < 0.01	3 × < 0.02
Wheat, straw	< 0.01, 0.019, 0.049 (0.026)	0.036, 0.043, 0.07 (0.05)	0.036, 0.062, 0.12 (0.076)
Wheat, grain	3 × < 0.01	3 × < 0.01	3 × < 0.02

For the second and third rotation, which was conducted in one trial only, residues of bixafen and M21 were generally below 0.01 mg/kg, except for carrot roots (bixafen: 0.018 mg/kg, M21:

< 0.01 mg/kg, total: 0.018 mg/kg) and wheat/barley straw (bixafen: 0.034 mg/kg, M21: 0.048 mg/kg, total: 0.082 mg/kg).

One additional trial utilized test-sites from long-term soil accumulation studies, which were treated with bixafen subsequently for over six years. Before sowing, the soil was analysed for the accumulated residues of bixafen still present at concentrations equivalent to 0.43–0.47 kg ai/ha (based on the first 20 cm layer). The residues being subject to sorption/desorption effects in soil (“aging”) were complemented with an additional treatment of bixafen to bare soil for a total nominal soil concentration equivalent to 0.93 kg ai/ha (e.g., 0.43 kg ai/ha aged residue plus 1 × 0.5 kg ai/ha new treatment). Again, carrot, lettuce and wheat were grown in one crop rotation with PBIs of 19–21 days.

In carrots and lettuce, no residues of bixafen or M21 above the LOQ of 0.01 mg/kg were found. Wheat forage and grain were also < 0.01 mg/kg for all analytes, except for 0.012 mg/kg bixafen and 0.023 mg/kg M21 in the straw (total: 0.035 mg/kg).

The Meeting concluded that the transfer of bixafen and its metabolites bixafen-desmethyl (M21) into rotational crops is low. In aerial parts of rotated crops, residues of both compounds were mostly below the LOQ of 0.01 mg/kg, except for a single sample of carrot tops (0.021 mg/kg for bixafen) and in wheat straw (< 0.01–0.05 mg/kg). In soil covered parts (carrot roots), residues of bixafen were found in almost all samples analysed, but also at levels near the LOQ (0.014–0.028 mg/kg). M21 was not found in these samples.

Taking into account the very conservative basis for the estimated soil plateau concentration equivalent to 0.93 kg ai/ha, which addresses many years of subsequent application at the maximum annual GAP rate (up to 0.25 kg ai/ha and year), the Meeting concluded that under realistic field conditions no significant uptake (≥ 0.01 mg/kg) of bixafen or bixafen-desmethyl from soil into plants is to be expected.

No representative crops from the group of pulses/oilseeds or fruiting vegetables have been investigated as rotational crops to date. In view of the low transport of bixafen residues from soil into the investigated crops (root crops, leafy crops and cereal grains), significant residues at or above the LOQ are also not expected for pulses/oilseeds and fruiting vegetables.

Results of supervised residue trials on crops

The 2013 JMPR Meeting already assessed uses of bixafen on rape, barley and wheat according to European GAP.

The 2013 Meeting concluded that field rotational crop studies did not address residues in soil expected after subsequent annual application of bixafen and decided that no recommendations on maximum residue levels and median/highest residues could be made for bixafen in non-permanent crops.

Since such studies were submitted to the current Meeting, which indicate no significant contribution to plant residues by soil uptake, maximum residue levels and STMR values can be estimated based on the 2013 Report.

Therefore, median and highest residues already estimated by the 2013 Meeting for rape seed, small cereal grains (barley, wheat) and feed commodities thereof were directly transferred into estimations of maximum residue levels, STMR values and median/highest residue values by the present Meeting.

Residue values referred to as “total” describe the sum of bixafen and M21 (bixafen-desmethyl), expressed as bixafen.

Barley and oats

In 2013 the Meeting identified the following residues of bixafen and total bixafen for barley grain based on a GAP on barley and oats from the UK:

For MRL compliance purposes residues of parent bixafen in barley grain in the whole of Europe were (n = 19): 0.02, 0.03, 0.04(5), 0.05, 0.06, 0.06, 0.07, 0.08, 0.08, 0.09, 0.09, 0.1, 0.1, 0.25 and 0.34 mg/kg.

For dietary intake purposes the total residues in barley grain in the whole of Europe were (n = 19): 0.03, 0.04, 0.05(5), 0.06, 0.08(3), 0.1(3), 0.11(3), 0.29 and 0.38 mg/kg.

The 2016 Meeting estimated a maximum residue level of 0.4 mg/kg and an STMR value of 0.08 mg/kg for barley grain and decided to extrapolate its estimations to oats.

Wheat, rye and triticale

In 2013 the Meeting identified the following residues of bixafen and total bixafen for wheat grain based on a GAP for rye, triticale and wheat from the UK:

For monitoring purposes residues of parent bixafen in wheat grain in the whole of Europe were (n = 20): < 0.01(12), 0.01(3), 0.02, 0.02, 0.03, 0.03 and 0.03 mg/kg.

For dietary intake purposes the total residues in wheat grain in the whole of Europe were (n = 20): < 0.02(12), 0.02(3), 0.03, 0.03, 0.04, 0.04 and 0.04 mg/kg.

The 2016 Meeting estimated a maximum residue level of 0.05 mg/kg and an STMR value of 0.02 mg/kg for wheat grain and decided to extrapolate its estimations to rye and triticale grain also.

Rape seed

In 2013 the Meeting identified the following residues of bixafen and total bixafen for rape seed based on a GAP for oilseed rape from the UK:

For MRL compliance purposes residues of parent bixafen in rape seeds were (n = 10): < 0.01(6), 0.01(3), 0.017 mg/kg.

For dietary intake purposes the total residues in rape seeds were (n = 10): < 0.02(5), 0.02(4), 0.028 mg/kg.

The 2016 Meeting estimated a maximum residue level of 0.04 mg/kg and an STMR value of 0.02 mg/kg for rape seed.

Animal feeds

Barley, oats, rye, triticale and wheat – forage of cereals

In 2013 the Meeting identified the following residues of total bixafen in barley and wheat forage based on GAPs from the UK for barley/oats and rye/triticale/wheat:

For the calculation of the livestock animal dietary burden the total residues in barley forage (as received) in Europe were (n = 19): 2.1, 2.5, 2.6, 2.7, 2.9, 3.0, 3.2, 3.4, 3.4, 3.5, 3.7, 3.8, 3.9, 4.0, 4.3, 4.4, 4.5, 6.0, 7.3 mg/kg.

For the calculation of the livestock animal dietary burden the total residues in wheat forage (as received) in Europe were (n = 20): 1.5, 2.4, 2.6, 2.7, 2.8, 2.9, 2.9, 3.0, 3.1, 3.4, 3.6, 3.8, 3.9, 4.2, 4.5, 4.7, 4.8, 5.2, 5.5, 7.3 mg/kg.

The 2016 Meeting estimated a highest residue of 7.3 mg/kg and a median residue of 3.5 mg/kg for barley and wheat forage (as received) and decided to extrapolate the estimations to oats, rye and triticale forage also.

Oilseed rape, forage

The 2013 Meeting concluded that the reported GAP for bixafen is not relevant for the utilisation of oilseed rape as an animal forage crop.

Barley, oats, rye, triticale and wheat-straw and fodder

In 2013 the Meeting identified the following residues of bixafen and total bixafen for barley and wheat straw:

For MRL compliance purposes residues of parent bixafen in barley straw (as received) in Europe were (n = 19): 0.46, 0.64, 0.7, 0.76, 0.77, 0.86, 1.1, 1.1, 1.2, 1.5, 1.9, 3.1, 3.7, 4.8, 5.2, 5.4, 5.7, 6.2, 10 mg/kg.

For the calculation of the livestock animal dietary burden the total residues in barley straw (as received) in Europe were (n = 19): 0.5, 0.72, 0.74, 0.85, 1.0, 1.0, 1.2, 1.2, 1.3, 1.6, 2.1, 3.3, 3.9, 5.2, 5.6, 5.6, 6.1, 6.7, 11 mg/kg.

For MRL compliance purposes residues of parent bixafen in wheat straw (as received) in Europe were (n = 20): 0.52, 0.79, 0.93, 0.95, 1.3, 1.4, 1.7, 1.8, 1.8, 1.9, 2.6, 3.2, 3.3, 3.6, 3.6, 4.1, 5.4, 5.7, 8.4, 10 mg/kg.

For the calculation of the livestock animal dietary burden the total residues in wheat straw (as received) in Europe were (n = 20): 0.78, 1.2, 1.2, 1.3, 1.5, 1.9, 1.9, 2.1, 2.2, 2.5, 3.2, 3.7, 3.9, 3.9, 4.1, 4.4, 6.0, 6.2, 9.6, 11 mg/kg.

The 2016 Meeting noted that straw and fodder of small cereal grains (barley, oats, rye, triticale and wheat) are very similar and difficult to distinguish. Therefore it was decided to consider residue distributions in barley and wheat straw for mutual support. Since the residue populations for barley and wheat straw reported in the 2013 Report are not significantly different (Kruskal-Wallis-Test), residues were combined for a more robust estimate:

For MRL compliance purposes residues of parent bixafen in barley and wheat straw (as received) in Europe were (n = 39): 0.46, 0.52, 0.64, 0.7, 0.76, 0.77, 0.79, 0.86, 0.93, 0.95, 1.1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.7, 1.8, 1.8, 1.9, 1.9, 2.6, 3.1, 3.2, 3.3, 3.6, 3.6, 3.7, 4.1, 4.8, 5.2, 5.4, 5.4, 5.7, 5.7, 6.2, 8.4, 10 and 10 mg/kg.

For the calculation of the livestock animal dietary burden the total residues in barley and wheat straw (as received) in Europe were (n = 39): 0.5, 0.72, 0.74, 0.78, 0.85, 1.0, 1.0, 1.2(4), 1.3, 1.3, 1.5, 1.6, 1.9, 1.9, 2.1, 2.1, 2.2, 2.5, 3.2, 3.3, 3.7, 3.9(3), 4.1, 4.4, 5.2, 5.6, 5.6, 6.0, 6.1, 6.2, 6.7, 9.6, 11 and 11 mg/kg.

The 2016 Meeting estimated a maximum residue level of 20 mg/kg (dry-weight basis, based on 89% DM content), a highest residue of 11 mg/kg (as received) and a median value of 2.2 mg/kg (as received) for barley and wheat, straw and fodder, and decided to extrapolate the estimations to oats, rye and triticale straw and fodder, also.

Fate of residues during processing

The 2013 Meeting received information on the hydrolysis of radio-labelled bixafen as well as processing studies using unlabelled material on grown residues in oilseed rape, barley and wheat.

In a hydrolysis study using radio-labelled bixafen typical processing conditions were simulated (pH 4,5 and 6 with 90 °C, 100 °C and 120 °C for 20, 60 and 20 minutes). In duplicate samples of sterile buffer solution no degradation was observed.

The 2013 Meeting received information on the fate of bixafen and bixafen-desmethyl residues following simulating household and commercial processing of rape seed. Processing factors estimated by the 2013 Meeting, maximum residue levels and STMR-P values for the commodities considered by the 2016 Meeting are summarized below.

Raw commodity	Processed commodity	Bixafen		Total bixafen	
		Processing factor	Maximum residue level in mg/kg	Processing factor	STMR-P in mg/kg
Rape seed (STMR: 0.02 mg/kg, MRL: 0.04 mg/kg)	Oil, crude	0.75	n.n.	0.83	0.016
	Oil, refined	2	0.08	1.5	0.03
	Meal	2	n.n.	1.5	0.03

Raw commodity	Processed commodity	Bixafen Processing factor	Maximum residue level in mg/kg	Total bixafen Processing factor	STMR-P in mg/kg
Barley (STMR: 0.08 mg/kg, MRL: 0.4 mg/kg)	Pearl barley	0.22	n.n.	0.25	0.02
	Beer	< 0.065	n.n.	< 0.11	0.009
	Brewers grain	0.93	n.n.	0.93	0.074
	Brewers malt	0.86	n.n.	0.95	0.076
Wheat (STMR: 0.02 mg/kg, MRL: 0.05 mg/kg)	Flour	0.23	n.n.	0.37	0.007
	Bran, processed	2.7	0.15	2.6	0.052
	White bread	0.2	n.n.	< 0.37	0.007
	Wholemeal	0.9	n.n.	0.91	0.018
	Wholemeal bread	0.5	n.n.	0.63	0.012
	Germs	1	n.n.	1.1	0.022

n.n. not necessary, covered by the maximum residue level for the raw commodity or commodity is not relevant in trade

Residues in animal commodities

Farm animal feeding studies

The 2013 Meeting received feeding studies involving bixafen on lactating cows and laying hens. In the 2013 Report the following conclusions were presented:

"Three groups of lactating cows were dosed daily at levels of 4, 12 and 40 ppm in the diet (0.15, 0.45 and 1.5 mg/kg bw) for 28 consecutive days. Milk was collected throughout the whole study and tissues were collected on day 29 within 24 hrs after the last dose.

In milk highest mean total residues were 0.039 mg/kg for the 4 ppm group, 0.077 mg/kg for the 12 ppm group and 0.218 mg/kg for the 40 ppm group. Investigation of the distribution of the residue in cream gave a 9.9 fold higher concentration than in whole milk (15 between whole milk and milk fat).

Total residues in muscle for the 4, 12 and 40 ppm groups were 0.039–0.065 mg/kg (mean: 0.052 mg/kg), 0.081–0.26 mg/kg (mean: 0.162 mg/kg) and 0.63–1.0 mg/kg (mean: 0.82 mg/kg), respectively. In liver residues were 0.42–0.69 mg/kg (mean: 0.57 mg/kg) for the 4 ppm group, 1.2–1.7 mg/kg (mean: 1.4 mg/kg) for the 12 ppm group and 4.8–5.4 mg/kg (mean: 5.0 mg/kg) for the 40 ppm group. Kidney contained total residues of 0.1–0.15 mg/kg (mean: 0.14 mg/kg), 0.28–0.37 mg/kg (mean: 0.34 mg/kg) and 1.0–1.3 mg/kg (mean: 1.2 mg/kg) for the for the 4, 12 and 40 ppm group.

For fat three different tissues were analysed (perirenal, mesenteric and subcutaneous fat). Highest residues were found in perirenal fat with 0.14–0.21 mg/kg (mean: 0.18 mg/kg) for the 4 ppm group, 0.33–0.48 mg/kg (mean: 0.43 mg/kg) for the 12 ppm group and 0.8–1.9 mg/kg (mean: 1.4 mg/kg) for the 40 ppm group.

For laying hens three groups of animals were dosed with rates of 1.5, 4.5 and 15 ppm in the dry weight feed (0.1, 0.3 and 1.0 mg/kg bw) for 28 consecutive days. Eggs were collected throughout the whole study and tissues were collected on day 29 after the last dose.

In eggs total residues at the plateau phase were < 0.02–0.02 mg/kg (highest daily mean: 0.02 mg/kg) for the 1.5 ppm group and ranged between 0.05 to 0.07 mg/kg (highest daily mean: 0.063 mg/kg) for the 4.5 ppm and between 0.13 to 0.22 mg/kg (highest daily mean: 0.178 mg/kg) for the 15 ppm group.

In tissues no residues above the LOQ were found in muscle. Total residues in fat for the 1.5, 4.5 and 15 ppm groups were < 0.02–0.02 mg/kg (mean: 0.02 mg/kg), 0.05–0.06 mg/kg (mean: 0.057 mg/kg) and 0.06–0.09 mg/kg (mean: 0.07 mg/kg), respectively. In liver residues were < 0.02–0.02 mg/kg (mean: 0.02 mg/kg) for the 1.5 ppm group, 0.02–0.04 mg/kg (mean: 0.03 mg/kg) for the 4.5 ppm group and 0.03–0.05 mg/kg (mean: 0.04 mg/kg) for the 15 ppm group."

Estimated maximum and mean dietary burdens of livestock and animal commodities maximum residue levels

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex IX. The calculations were made according to the livestock diets from US-Canada, EU, Australia and Japan in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Livestock dietary burden, Total bixafen, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max.	mean	max.	mean	max.	mean	max.	mean
Beef cattle	2.0	0.45	8.3	4.0	29 [A]	14 [C]	0.09	0.09
Dairy cattle	8.3	4.0	8.3	4.0	27 [B]	13 [D]	1.3	0.65
Poultry-broiler	0.07	0.07	0.07	0.07	0.03	0.03	0.01	0.01
Poultry-layer	0.07	0.07	3.0 [E]	1.5 [F]	0.05	0.02	0.005	0.05

[A] Highest maximum beef cattle burden suitable for MRL estimates for mammalian meat

[B] Highest maximum dairy cattle burden suitable for MRL estimates for milk

[C] Highest mean beef cattle burden suitable for STMR estimates for mammalian meat

[D] Highest mean dairy cattle burden suitable for STMR estimates for mammalian meat and milk

[E] Highest maximum broiler or laying hen burden suitable for MRL estimates for poultry products and eggs

[F] Highest mean broiler or laying hen burden suitable for STMR estimates for poultry products and eggs

Animal commodities maximum residue levels

For beef cattle a maximum and mean dietary burden of 29 ppm and 14 ppm were estimated, respectively. For dairy cattle a maximum and mean dietary burden of 27 ppm and 13 ppm were estimated. The estimated dietary burdens are evaluated against the dose levels of 12 and 40 ppm from a lactating cow feeding study.

Bixafen feeding study	Feed level	Total residue				
	(ppm)	(mg/kg) in milk	(mg/kg) in muscle	(mg/kg) in kidney	(mg/kg) in liver	(mg/kg) in fat
Maximum residue level: dairy cattle						
Feeding study (HR for each dose group, except for milk)	12 40	0.077 0.218	0.26 1.0	0.37 1.3	1.7 5.4	0.48 1.9
Dietary burden and residue estimate	29 (beef) 27 (dairy)	0.15	0.71	0.93	3.9	1.3
STMR dairy cattle						
Feeding study (Mean for each dose group)	12 40	0.077 0.218	0.16 0.82	0.34 1.2	1.4 5.0	0.43 1.4
Dietary burden and residue estimate	14 (beef) 13 (dairy)	0.082	0.21	0.4	1.7	0.5

The Meeting estimated HR and STMR values of 0.71 and 0.21 mg/kg for muscle, 3.9 and 1.7 mg/kg for liver, 0.93 and 0.4 mg/kg for kidney and 1.3 and 0.5 mg/kg for fat. Corresponding maximum residue levels were estimated at 4 mg/kg for edible offal, mammalian (based on liver) and 2 mg/kg for meat (based on the fat) and mammalian fat (except for milk fat).

For milk, a STMR value and a maximum residue level of 0.082 mg/kg and 0.2 mg/kg were estimated, respectively. Based on an average fat content in whole milk of 4%, the Meeting also estimated a STMR value and a maximum residue level of 2.05 mg/kg and 5 mg/kg for bixafen in milk fat, respectively.

For poultry (laying hens) a maximum and mean dietary burden of 3 ppm and 1.5 ppm were estimated, respectively. The estimated dietary burdens are evaluated against the dose levels of 1.5 and 4.5 ppm from a laying hen feeding study.

Bixafen feeding study	Feed level	Total residue			
	(ppm)	(mg/kg) in eggs	(mg/kg) in muscle	(mg/kg) in liver	(mg/kg) in fat
Maximum residue level: laying hens					
Feeding study (HR)	1.5 4.5	0.02 0.07	< 0.02 < 0.02	0.02 0.04	0.02 0.06
Dietary burden and residue estimate	3	0.047	0.02* (<LOQ at all dose levels)	0.03	0.04
STMR laying hens					
Feeding study (Mean for each dose group)	1.5	0.02	< 0.02	0.02	0.02
Dietary burden and residue estimate	1.5	0.02	0 (< LOQ at all dose levels)	0.02	0.02

The Meeting estimated HR and STMR values of 0 and 0 mg/kg for poultry muscle, 0.03 and 0.02 mg/kg for poultry, edible offal of and 0.04 and 0.02 mg/kg for poultry fat. Corresponding maximum residue levels were estimated at 0.05 mg/kg for poultry, edible offal of, 0.02* mg/kg for poultry meat and 0.05 mg/kg for poultry fat.

For eggs, a STMR value, a HR value and a maximum residue level of 0.02 mg/kg, 0.047 mg/kg and 0.05 mg/kg were estimated, respectively.

RECOMMENDATIONS

Definition of the residue (for compliance with MRLs) for plant commodities: *bixafen*

Definition of the residue (for compliance with MRLs) for animal commodities and (for dietary exposure assessment) for plant and animal commodities: *sum of bixafen and N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1H-pyrazole-4-carboxamide (bixafen-desmethyl), expressed as bixafen*

The residue is fat soluble.

Maximum residue levels and dietary intake

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	Highest residue, mg/kg
CCN	Name	New	Previous		
GC 0640	Barley	0.4	-	0.08	-
AS 0640	Barley, straw and fodder	20 (dw)	-	2.2 (ar)	11 (ar)
MO 0105	Edible offal (mammalian)	4	-	kidney: 0.4 liver: 1.7	kidney: 0.93 liver: 3.9
PE 0112	Eggs	0.05	-	0.02	0.047
MF 0100	Mammalian fats (except milk fats)	2	-	0.5	1.3
MM 0095	Meat (from mammals other than marine mammals)	2 (fat)	-	muscle: 0.21 fat: 0.5	muscle: 0.71 fat: 1.3
FM 0183	Milk fat	5	-	2.05	-
ML 0106	Milks	0.2	-	0.082	-
GC 0647	Oats	0.4	-	0.08	-
AS 0647	Oats, straw and fodder	20 (dw)	-	2.2 (ar)	11 (ar)
PO 0111	Poultry, edible offal of	0.05	-	0.02	0.03
PF 0111	Poultry, fats	0.05	-	0.02	0.04

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	Highest residue, mg/kg
CCN	Name	New	Previous		
PM 0110	Poultry, meat	0.02 *	-	0	0
SO 0495	Rape seed	0.04	-	0.02	-
OR 0495	Rape seed oil, refined	0.08	-	0.03	-
GC 0650	Rye	0.05	-	0.02	-
AS 0650	Rye, straw and fodder	20 (dw)	-	2.2 (ar)	11 (ar)
GC 0653	Triticale	0.05	-	0.02	-
AS 0653	Triticale, straw and fodder	20 (dw)	-	2.2 (ar)	11 (ar)
GC 0654	Wheat	0.05	-	0.02	-
CF 0654	Wheat bran, processed	0.15	-	0.052	-
AS 0654	Wheat, straw and fodder	20 (dw)	-	2.2 (ar)	11 (ar)

Dietary intake and feed burden only

Commodity		Median, mg/kg	Highest residue, mg/kg
CCN	Name		
-	Barley, forage	3.5 (ar)	7.3 (ar)
-	Barley, pearl	0.02	-
-	Beer	0.009	-
-	Brewer´s grain	0.074	-
-	Brewer´s malt	0.076	-
-	Oats, forage	3.5 (ar)	7.3 (ar)
-	Rape seed, meal	0.03	-
-	Rye, forage	3.5 (ar)	7.3 (ar)
-	Triticale, forage	3.5 (ar)	7.3 (ar)
-	Wheat, forage	3.5 (ar)	7.3 (ar)
CF 1211	Wheat flour	0.007	-
CF 1210	Wheat germ	0.022	
CP 1211	White bread	0.007	-
CF 1212	Wheat wholemeal	0.018	-
CP 1212	Wholemeal bread	0.012	-

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The International Estimated Daily Intakes (IEDI) for bixafen was calculated from recommendations for STMRs for raw and processed commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 3.

The IEDI of the 17 GEMS/Food cluster diets, based on the estimated STMRs represented 1% to 9% of the maximum ADI of 0.02 mg/kg bw. The Meeting concluded that the long-term exposure to residues of bixafen from uses considered by the Meeting is unlikely to present a public health concern.

Short-term dietary exposure

The International Estimated Short term Intake (IESTI) for bixafen was calculated for all food commodities and their processed fractions for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI represented 0–20% of the ARfD (0.2 mg/kg bw) for the general population and 0–20% of the ARfD for children. The Meeting concluded that the short-term dietary exposure to residues of bixafen, when used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

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BUPROFEZIN (173)

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EXPLANATION

Buprofezin, an insecticide, was first evaluated by the JMPR in 1991 and then in subsequent years. The compound was reviewed under the Periodic Re-evaluation Programme in 2008 for toxicity and residues, when an ADI of 0–0.009 mg/kg bw and an ARfD of 0.5 mg/kg bw were established. Buprofezin was scheduled at the 47th session of the CCPR (2015) for the evaluation of additional data on residues by the 2016 JMPR. Residue data were submitted on basil by the government of Thailand, and on mango, papaya and soya bean by the company.

The residue definition for compliance with the MRL and estimation of dietary intake in plant commodities is buprofezin.

RESIDUE ANALYSIS

Analytical Methods

Recovery data of the method RAM no. BF/10/97 for determination of buprofezin in papaya were available to the Meeting (Samoil, 2005). The method involves sample extraction with acetone, acidification, partitioning with hexane, the residues present in acidified aqueous phase partitioned into dichloromethane, dried and dissolved in hexane for analysis by GC-NPD. The lowest validated level was 0.05 mg/kg, and the calculated LOQ was reported as 0.02 mg/kg.

Method VR-023/14 was validated for the analysis of buprofezin in mango (Tomaz M.L., 2015). The method involves extraction with acetonitrile and a salt-mixture (magnesiun sulphate, trisodium citrate dihydrate and sodium hydrogencitrate sesquihydrate) and analysis by LC-MS/MS (m/z: 306 → 201 (quantifier) and m/z: 306 → 116 (qualifier)). A similar method (VR.062/2015) was validated for the analysis of buprofezin in soya bean, however using m/z: 306→116 as a quantifier ion and m/z: 306 →201 as the qualifier ion (Vitti, 2015). The method LOQ was 0.01 mg/kg.

In another method for determination of buprofezin in soya bean (VR-046/2008; Maldonado Ribeiro Lopez, 2008), the sample was extracted with dichloromethane for 30 minutes, the extract evaporated, the residues reconstituted in 40 mL hexane/acetone (95:5), and cleaned-up on deactivated florisil. The eluate was dried and the residue re-dissolved in toluene for analysis by GC-ECD. The method was validated at a LOQ of 0.02 mg/kg.

Table 1 summarizes the recovery data for buprofezin in mango, papaya, and soya bean.

Table 1 Recovery data for buprofezin in mango, papaya, and soya bean

Commodity	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Study
Papaya	0.051	4	75-79	78	2.6	BF/10/97 GC-NPD	IR-4 PR No.: 07024
	0.51	4	75-85	82	5.5		
	2.04	4	79-90	85	5.4		
Mango	0.01	5	78-84	80	2.9	VR-023/14 LC-MS/MS	RF-1059.034.217.13
	0.1	5	79-91	86	5.9		
Soya bean (seeds)	0.01	5	91-102	95	4.1	VR.062/15 LC-MS/MS	RF-14677.034.074.15
	1.0	5	81-108	97	10		
Soya bean (seeds)	0.02	5	87-93	90	2.5	VR.046/08 GC-ECD	RF-0018.034.114.08 RF-0018.034.123.08 RF-0018.034.172.08 RF-0018.034.209.08
	0.2	5	79-87	82	4.6		