REASONED OPINION

Setting of new MRLs for bixafen in certain cereals and products of animal origin[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

According to Article 6 of the Regulation (EC) No 396/2005, the United Kingdom, hereafter referred to as the Evaluating Member State (EMS), received an application from Bayer CropScience AG to set new MRLs for bixafen for certain crops for which authorisations will be requested. In order to accommodate for intended uses in France and the United Kingdom, it is proposed to set MRLs for cereals (wheat, rye, barley and oats) and for certain products of animal origin. The United Kingdom drafted according to Article 8 of Regulation (EC) No 396/2005 an evaluation report, consisting of chapter 5, 6 and 7 of the Draft Assessment Report, which was submitted to the European Commission and forwarded to EFSA on 8 July 2009. It is noted that bixafen is a new active substance for which the peer review process under Directive 91/414/EEC is at an early stage.

Based on the relevant chapters of the advanced copy of the Draft Assessment Report prepared by the United Kingdom as designated Rapporteur Member State (RMS) under Directive 91/414/EEC, EFSA derived the following conclusions regarding this application:

The toxicological profile of bixafen was assessed by the EMS in the framework of the preparation of the Draft Assessment Report. The data were sufficient to conclude on an ADI value of 0.02 mg/kg and an ARfD of 0.2 mg/kg. Since the peer review is not yet finalised for this active substance, the toxicological reference values should be considered as provisional only.

The metabolism of bixafen was investigated in primary and rotational crops. In addition, livestock metabolism studies were performed with lactating goats and laying hens which were exposed to bixafen residues via feed. Based on the results of these studies the following residue definitions were derived:

Commodities	**Residue definition risk assessment**	**Residue definition enforcement**
Cereals, pulses and oilseeds	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen	Bixafen

1 On request from the European Commission, Question No EFSA-Q-2009-00722, issued on 16 December 2009.
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Commodities	Residue definition risk assessment	Residue definition enforcement
Animal commodities	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen

Analytical methods are available which can be used for enforcement of MRLs according to the proposed residue definitions. For plant matrices, validation data demonstrated that an LOQ of 0.01 mg/kg is achievable. For animal matrices the validated LOQ is 0.02 mg/kg for the proposed residue definition sum of bixafen and desmethyl bixafen, expressed as bixafen.

The supervised field trials submitted in support of the intended uses in wheat and barley were sufficient to derive MRL proposals for these crops. However, it is noted that for the NEU GAP for barley the data package was not complete and 3 additional trials have to be provided. It is concluded that for wheat an MRL of 0.05 mg/kg would be required to accommodate for the intended use, for barley (SEU GAP) an MRL proposal of 0.5 mg/kg could be derived. According to the EC guidance documents, these MRLs can be extrapolated to rye and oats, respectively. Under processing conditions simulating pasteurisation, baking/brewing/boiling and sterilisation bixafen residues are stable. Specific processing studies were performed with barley treated with the two-fold application rate compared with the intended GAP. The processed products derived from barley and by-products from the brewing process (pearl barley, brewer's malt, beer and brewer's yeast) all contained significantly lower residues compared with unprocessed barley, except pearl barley rub off in which the residues increased by a factor of *ca.* 4.

The rotational crop studies demonstrated that the occurrence of bixafen related residues in rotational crops grown in crop rotation after primary crops treated with bixafen in accordance with the intended GAP is low.

The calculation of the expected dietary burden for ruminants, poultry and pigs, taking into account the residues of bixafen on cereals grain, straw or bran, revealed that for ruminants and pigs a significant intake is expected. Thus, feeding studies with cows which received bixafen residues via feed were used to estimate the residue concentrations in animal tissues and milk. These studies were adequate to derive MRL proposals for these commodities.

The consumer exposure assessment was performed with revision 2 of the EFSA PRIMo (Pesticide Residue Intake Model), taking into account the residues in wheat, rye, barley, oats and the animal commodities for which MRL proposals were derived. The long-term dietary intake for all diets included in the EFSA PRIMo was low (below 4% of the ADI). The highest contributors were milk (2.9%), wheat (0.9%) and barley (0.7%). Regarding the short term dietary intake, the expected exposure was well below the ARfD for all food commodities concerned. The highest intake were calculated for bovine liver (4.2% of the ARfD for the UK infant), milk (0.9% of the ARfD for UK infants), bovine meat (0.9% of the ARfD) and sheep meat (0.7%of the ARfD). For all other commodities the exposure was calculated to be below 0.5% of the ARfD.

EFSA concludes that the intended uses of bixafen on cereals (wheat, rye, barley and oats) are acceptable from a consumer safety point of view, since the residues expected after treatment of the crops according to the intended GAP will not lead to an unacceptable consumer exposure.

In conclusion, the following temporary MRLs are proposed for the intended uses assessed in this reasoned opinion which are recommended to be included in Annex III of Regulation 396/2005:

Code number	Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Justification for the proposal
	Bixafen			
0500010	Barley	Currently the default MRL of 0.01 mg/kg is applicable (Art. 18(1) (b)).	0.5	The proposed MRLs are sufficiently supported by data. The dietary risk assessment did not reveal a potential consumer health concern. The proposed MRL for barley and oats represent the SEU GAP only. For the NEU GAP, three additional supervised field trials are required to complete the data set as required in the EC guidance document.
0500050	Oats		0.5	
0500070	Rye		0.05	
0500090	Wheat		0.05	
	Sum of bixafen and desmethyl bixafen, expressed as bixafen			
1011010	Swine meat	Currently the default MRL of 0.01 mg/kg is applicable (Art. 18(1) (b)).	0.02 (*)	The proposed MRLs are sufficiently supported by data. No consumer health risk was identified.
1011020	Swine fat		0.02 (*)	
1011030	Swine liver		0.02 (*)	
1011040	Swine kidney		0.02 (*)	
1012010	Bovine meat		0.15	
1012020	Bovine fat		0.4	
1012030	Bovine liver		1.5	
1012040	Bovine kidney		0.3	
1013010	Sheep meat		0.15	
1013020	Sheep fat		0.4	
1013030	Sheep liver		1.5	
1013040	Sheep kidney		0.3	
1014010	Goat meat		0.15	
1014020	Goat fat		0.4	
1014030	Goat liver		1.5	
1014040	Goat kidney		0.3	
1020010	Cattle milk		0.04	
1020020	Sheep milk		0.04	
1020030	Goat milk		0.04	
Not yet allocated	Barley straw	Currently no MRLs are established for feed items	15	In view of future needs to establish MRLs for feed items, EFSA derived MRL proposals for straw.
	Oats straw		15	
	Rye straw		20	
	Wheat straw		20	

(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.

As the Draft Assessment Report has not yet been peer reviewed, the conclusions reached in this reasoned opinion have to be considered as provisional and might have to be reconsidered once the peer review under Directive 91/414/EEC has been finalised.

KEY WORDS

Bixafen, wheat, rye, oats, barley, MRL application, Regulation (EC) No 396/2005, consumer risk assessment

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BACKGROUND

Regulation (EC) No 396/2005 establishes the rules governing the setting of pesticide MRLs at Community level. Article 6 of that regulation lays down that a party requesting an authorisation for the use of a plant protection product in accordance with Directive 91/414/EEC, shall submit to a Member State, when appropriate, an application to set or modify an MRL in accordance with the provisions of Article 7 of that regulation.

The United Kingdom, hereafter referred to as the evaluating Member State (EMS), received an application from the company Bayer CropScience AG[3] to set a new MRLs for the active substance bixafen in wheat, rye, barley, oats, and for several products of animal origin. This application was notified to the European Commission and EFSA and subsequently evaluated by the EMS in accordance with Article 8 of the Regulation.

After completion, the evaluation report of the EMS was submitted to the European Commission who forwarded the application, the evaluation report and the supporting dossier to EFSA on 20 October 2009. The application was included in the EFSA Register of Question with the reference number EFSA-Q-2009-00722 and the following subject:

Bixafen - Application to set new MRLs for bixafen in wheat grain at 0.05 mg/kg, in rye grain at 0.05 mg/kg, in barley grain at 0.5 mg/kg, in oats grain at 0.5 mg/kg, for bixafen plus its metabolite desmethyl- bixafen expressed as bixafen in bovine fat at 0.5 mg/kg, in bovine kidney at 0.5 mg/kg, in bovine liver at 2 mg/kg, in bovine meat at 0.2 mg/kg, in cattle milk at 0.05 mg/kg, in goat fat at 0.2 mg/kg, in goat kidney at 0.2 mg/kg, in goat liver at 1 mg/kg, in goat meat at 0.1 mg/kg, in goat milk at 0.05 mg/kg, in poultry fat at 0.02 mg/kg, in poultry liver at 0.02 mg/kg, in poultry meat at 0.02 mg/kg, in birds' eggs at 0.02 mg/kg, in sheep fat at 0.5 mg/kg, in sheep kidney at 0.5 mg/kg, in sheep liver at 2 mg/kg, in sheep meat at 0.2 mg/kg, in sheep milk at 0.1 mg/kg, in swine fat (free of lean meat) at 0.02 mg/kg, in swine kidney at 0.02 mg/kg, in swine liver at 0.1 mg/kg and in swine meat at 0.02 mg/kg, horse meat at 0.2 mg/kg, horse milk at 0.05 mg/kg

EFSA then proceeded with the assessment of the application as required by Article 10 of the Regulation.

Upon request of EFSA, the EMS submitted additional information needed to complete the assessment. This information was provided on 24 November 2009.

TERMS OF REFERENCE

According to Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

According to Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within 3 months from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

In this particular case the calculated deadline for providing the reasoned opinion is 20 October 2009.

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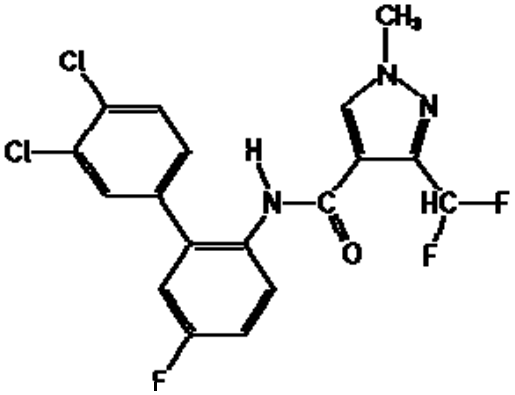
THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Bixafen is the ISO common name for *N*-(3′,4′-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide (IUPAC).



Molecular weight: 414.2

Bixafen is a new broad spectrum fungicide belonging to the group of anilides and pyrazoles. It was developed to control leaf and stem diseases in cereals.

Bixafen is evaluated in the framework of Directive 91/414/EEC as new active substance with the United Kingdom acting as the designated Rapporteur Member State (RMS). The European Commission has confirmed the recognition of a complete application dossier from Bayer CropScience in Decision 2009/700/EC which entered into force on 12 September 2009. The dossier will now undergo a detailed evaluation by the RMS who has to prepare the Draft Assessment Report within one year. The representative uses supported by the manufacturer in the peer review are the foliar application on wheat, rye, triticale, barley and oats. Since the RMS is currently in the stage of drafting of the Draft Assessment Report and the subsequent steps of the peer review procedure have not yet been initiated, a final decision regarding the inclusion in Annex I of Directive 91/414/EEC is not expected within the next months.

Currently no specific bixafen MRLs are established in Regulation (EC) No 396/2005. Therefore the default MRL of 0.01 mg/kg is applicable for all crops. No CXLs are established by Codex Alimentarius.

The applicant Bayer CropScience intends to request provisional authorisations for wheat (including triticale), rye, barley and oats in France and the United Kingdom. The GAPs for these intended uses concern two foliar applications with application rate of 125 g a.s./ha at growth stages between BBCH 25 (5 tillers detectable) and 61 for barley and oats (beginning of flowering) or 69 for wheat and rye (end of flowering). The pre harvest interval (PHI) is defined as 35 days. The summary of the GAPs is presented in Appendix A. It is noted that the GAPs are identical with the GAPs supported in the peer review process.

Currently no information is available to EFSA whether provisional authorisations have already been requested in the Member States concerned.

EFSA bases its risk assessment on the relevant chapters of the advanced copy of the Draft Assessment Report which was submitted by the United Kingdom. The complete DAR is not yet finalised. The assessment is performed in accordance with the legal provisions of the uniform principles for the evaluation of authorisation of plant protection products set out in Annex VI of Directive 91/414/EEC and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a to 1997g, 2008).

ASSESSMENT

1. Methods of analysis

1.1. Methods for enforcement of residues in food of plant origin

The EMS reported an analytical method for the determination of bixafen residues in samples of plant origin. After a microwave extraction with acetonitrile/water the resulting extracts are filtered and analysed by LC/MS/MS, using a C18 column. Validation data in wheat grain, wheat foliage, orange and rape seed demonstrated that a LOQ of 0.01 mg/kg is achievable. The method was also tested in an independent laboratory validation.

The applicant stated that bixafen could not be determined by the German DFG method S19 due to lack of sufficient sensitivity.

EFSA concludes that an analytical method is available for dry commodities and crops with high acid content which can be used for enforcement of MRLs according to the residue definition. However, a multi-residue method, using standard extraction techniques would be desirable.

1.2. Methods for enforcement of residues in food of animal origin

For the determination of residues in products of animal products an analytical method is available which has been evaluated by the RMS. The extraction depends on the matrix: for fat and cream the extraction is done with acetonitrile/hexane, followed by acetonitrile/water; liver is extracted with acetonitrile/water by microwave extraction. For other tissues and milk an extraction with acetonitrile/water is sufficient. After having cleaned the extracts with a C18-cartridge, the eluant is analysed by LC/MS/MS. The method allows separate determination of bixafen and desmethyl-bixafen, each compound with a LOQ of 0.01 mg/kg. Validation data for bixafen and desmethyl-bixafen were presented for eggs, milk, muscle, kidney, fat and liver. An independent laboratory validation was also reported.

Thus, EFSA concludes that for animal tissues, milk and eggs a sufficiently validated analytical method is available.

2. Mammalian toxicology

The toxicological properties of bixafen were assessed by the EMS in the framework of the preparation of the DAR. Although the DAR is not yet completed, the chapter on mammalian toxicology was submitted as part of the Evaluation Report to EFSA (United Kingdom, 2009a). The EMS considered the studies sufficient to derive toxicological reference values. The proposed ADI and ARfD are reported in Table 2-1. These toxicological reference values should be considered as provisional until they are confirmed by the peer review experts.

Table 2-1. Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
Bixafen					
ADI	UK	2009	0.02 mg/kg bw/d	2 year male rat feeding study	100
ARfD	UK	2009	0.2 mg/kg bw	Rat developmental study	100

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

The nature of residues resulting from foliar applications was investigated in wheat and soybeans. The studies were evaluated by the RMS and the conclusions are reported in the residue chapter of the draft assessment report (United Kingdom, 2009a). The studies were conducted using [pyrazole-5-^{14}C]-bixafen (pyrazol-label) and [dichlorophenyl]-UL-^{14}C]-bixafen (dichlorophenyl-label).

- Wheat (representative for cereals): foliar application of 0.13 and 0.15 kg as/ha. Sampling of forage hay, mature grain and straw.
- Soybean (representative for pulses and oilseeds): three foliar applications of 0.06 kg as/ha. Sampling of forage, hay, seed and straw.

In wheat, after application of the pyrazol labelled bixafen, at harvest the TRR was 0.16 mg eq/kg and 24 mg eq/kg in the grain and straw, respectively. In the dichlorphenyl-label study, comparable TRR values were measured (0.23 mg eq/kg for grain and 23 mg eq/kg in straw). On characterisation of the extractable radioactivity one major component was identified in the grain and straw at harvest as parent bixafen, which accounted for 90-93% of the TRR. Desmethyl-bixafen was the only metabolite identified. This metabolite did not represent more than 3% (0.004 mg/kg) and 2% (0.43 mg/kg) of the total radioactivity in the grain and straw, respectively. In forage and hay, the ratio of bixafen and desmethyl-bixafen was comparable to the results in grain and straw. The remaining unextractable radioactivity in grain and straw accounted for less than or equal to 6% of the total radioactivity; in forage and hay the percentage was comparable.

In soybeans, the TRR measured in seed and straw was 0.02 mg eq/kg and 13 mg eq/kg in the pyrazole study. In the dichlorophenyl-study the TRR was <0.01 mg eq/kg and 9.5 mg eq/kg. In straw more than 90% of the applied radioactivity was extractable with acetonitrile/water. In soybean seed, the extractability was significant lower: in the pyrazole study, after microwave extraction, 78% of the TRR was extractable, whereas in the dichlorophenyl-study, using conventional extraction technique, only 53% of the TRR was extractable.

The major component identified in seed and straw at harvest was parent bixafen, which accounted for 30% and 90% of the TRR respectively. The metabolites identified in seed was desmethyl-pyrazole-4-carboxylic acid (19% of the TRR, <0.01 mg/kg) and pyrazole-4-carboxylic acid (12% of TRR, <0.01 mg/kg). In straw only desmethyl bixafen was identified and quantified (0.5% of TRR, 0.06 mg/kg). In addition, several other compounds which could not be identified were observed in soybeans, none of the represented more than 20% TRR (<0.1 mg/kg) and 1% TRR (0.06 mg/kg) in seed and straw respectively.

Based on the plant metabolism data submitted for wheat and soybean, the EMS concluded that for cereals the following residue definitions should be applied:

Residue definition for risk assessment: sum of bixafen and its metabolite desmethyl-bixafen, expressed as bixafen;

Residue definition for enforcement: bixafen

EFSA agrees with this provisional residue definition proposed by the EMS which will be discussed with experts in the framework of the peer review under Directive 91/414/EEC. However, the MRL proposals and the risk assessment need to be reconsidered if in the peer review different residue definitions are derived.

3.1.1.2. Magnitude of residues

In support of the MRL request, the applicant submitted in total 20 supervised field trials on wheat and 19 trials on barley. In some of the trials the PHI deviated by more that 25% from the PHI defined in the GAP. EFSA therefore did not include these trials in the assessment. The trials representing northern conditions were performed in northern France, Germany, United Kingdom, Sweden and Belgium in 2006 and 2007. Trials reflecting the southern conditions were performed in Greece, Italy, southern France, Spain and Portugal. The results were reported for the residue definition for risk assessment and the residue definition enforcement separately.

The summarised results of the trials are presented in table 3-1.

The trials are sufficient to conclude on the residue behaviour in wheat in NEU and SEU and to derive an MRL proposal. The proposed MRL of 0.05 mg/kg for wheat can be extrapolated to rye (European Commission, 2008). EFSA also calculated an indicative MRL proposal for wheat straw (20 mg/kg) in case MRLs will be established for feed in the future. For barley, sufficient trials are available representing the residue behaviour in SEU. However, for the NEU only 5 trials were matching with the proposed GAP. Thus, three additional trials are required to fulfil the data requirements established in the EC guidance documents (European Commission, 2008). The MRL proposal for barley grain is supporting the proposed GAP in SEU only. The proposed MRL for barley can also be extrapolated to oats, grown in SEU. The residues on barley straw are slightly below the residues observed on wheat straw. An indicative MRL proposal is calculated also for barley straw (15 mg/kg).

The samples derived from the supervised field trials were microwave extracted with acetonitrile/water and the resulting extracts filtered and analysed by LC/MS/MS, using a C18 column and isotopically labelled internal standards. The method was sufficiently validated for bixafen and its metabolite desmethyl-bixafen in wheat (grain, straw, and foliage), lettuce, turnip roots. For each analyte a LOQ of 0.01 mg/kg was achievable. The results for desmethyl-bixafen were not re-calculated to bixafen, but as the difference in molecular weight of the parent bixafen and desmethyl-bixafen is negligible (less than 4%), a correction would not alter the results significantly.

The storage of samples prior to analysis did not exceed 8 months. Storage stability was demonstrated for bixafen and its metabolite desmethyl-bixafen for up to 12 months in lettuce, potato, rape seed and wheat (foliage, grain and straw).

It is concluded that the supervised field trials provided are valid regarding the storage stability and the analytical methodology applied.

Table 3-1. Overview of the available residues trials data

Commodity	Region [a]	Outdoor /Indoor	Individual trial results (mg/kg)		STMR (mg/kg) [b]	HR (mg/kg) [c]	MRL proposal (mg/kg)	Median CF [d]	Comments Calculated R_{ber} and R_{max} [e]
			Residue definition: Enforcement (bixafen)	Residue definition: Risk assessment (sum of bixafen and desmethyl-bixafen)					
Wheat → rye, triticale	NEU	Outdoor	3*<0.01; 2*0.01; 2*0.03	3*<0.02; 2*0.02; 2*0.04	0.01	0.03	0.05	2	Although only 7 trials instead of 8 are available representative for the intended GAP, the data are acceptable for deriving an MRL proposal because all results are in the same order of magnitude. R_{ber}= 0.06 R_{max}= 0.049
Wheat → rye, triticale	SEU	Outdoor	5*<0.01; 0.01; 0.02; 0.03	5*<0.02; 0.02; 0.03; 0.04	0.01	0.03	**0.05**	2	R_{ber}= 0.03 R_{max}= 0.037
Barley → oat	NEU	Outdoor	0.04; 0.07; 2*0.09; 0.1	0.05; 0.08; 2*0.1; 0.11	0.09	0.1		1.11	The number of trials is not sufficient to derive an MRL proposal for NEU. Three additional trials are required to complete the dataset.
Barley → oat	SEU	Outdoor	0.03; 0.04; 0.06; 0.08; 0.1; 0.14; 0.25; 0.34	0.04; 0.05; 0.08; 0.1; 0.11; 0.16; 0.3; 0.38	0.09	0.34	**0.5**	1.23	R_{ber}= 0.45 R_{max}= 0.48
Wheat straw	NEU	Outdoor	0.95; 1.3; 1.8; 3.6; 4.1; 8.4; 10	1.3; 1.5; 2.1; 3.8; 4.4; 9.7; 11	3.6	10	**20**	1.15	Indicative MRL proposal R_{ber}= 16.8 R_{max}= 16.4
Wheat straw	SEU	Outdoor	0.79; 1.4; 1.7;1.8; 3.2; 3.6; 5.4; 5.7;	1.2; 2*1.9; 2.2; 3.7; 4.1; 6.0; 6.2	2.5	5.7	10	1.15	Indicative MRL proposal R_{ber}= 9.9 R_{max}= 8.9

Commodity	Region (a)	Outdoor /Indoor	Individual trial results (mg/kg)		STMR (mg/kg) (b)	HR (mg/kg) (c)	MRL proposal (mg/kg)	Median CF (d)	Comments Calculated R_{ber} and R_{max} (e)
			Residue definition: Enforcement (bixafen)	Residue definition: Risk assessment (sum of bixafen and desmethyl-bixafen)					
Barley straw	NEU	Outdoor	0.7; 0.86; 4.8; 5.4; 10	0.74; 1.0; 5.2; 5.6; 12	4.8	10	15	1.08	Indicative MRL proposal R_{ber}= 15.4 R_{max}= 20.4
Barley straw	SEU	Outdoor	0.46; 0.75; 1.5; 3.1; 3.7; 5.2; 5.7; 6.2	0.5; 1.0; 1.7; 3.3; 4.1; 5.6; 6.2; 6.7	3.4	6.7	**15**	1.09	Indicative MRL proposal R_{ber}= 11.2 R_{max}= 10.5

(a): NEU, SEU, EU or Import (country code). In the case of indoor uses there is no necessity to differentiate between NEU and SEU.
(b): Median value of the individual trial results according to the enforcement residue definition.
(c): Highest value of the individual trial results according to the enforcement residue definition.
(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residues trial.
(e): Calculation of R_{ber} and R_{max} according to Guidance document 7039/VI/95- Calculation of maximum residue levels and safety intervals (European Commission, 1997g)
(*): Indicates that the MRL is set at the limit of analytical quantification.

3.1.1.3. Effect of industrial processing and/or household preparation

A hydrolysis study simulating conditions of pasteurisation baking/brewing/boiling and sterilisation was evaluated by the EMS as described in the relevant European guidance document (European Commission, 1997d). Under the conditions tested (20 min at 90°C at pH 4, 60 min at 100°C at pH 5 and 20 min at 120°C at pH 6) no degradation occurred. Thus, it is concluded that the active substance is hydrolytically stable at elevated temperatures and at pH values between 4 and 7.

Wheat: No specific processing studies were submitted for wheat. But since the residues in wheat grain are not exceeding 0.05 mg/kg and the consumer intake is below 10% of the ADI, no processing studies are necessary for wheat (European Commission, 1997d).

Barley: Four processing studies with barley grain are available. Barley treated with the two fold dose rate compared with the intended GAP contained residues between 0.04 mg/kg and 0.26 mg/kg. Barley grain was processed to pearl barley, pearl barley rub off, malted culms, brewer's malt, brewer's grain, hops draff, brewers yeast and beer. No details about the processing conditions were reported by the EMS (e.g. amount of malt used in brewing process, kilning temperature and time, temperature regimes). The final products were analysed for bixafen and desmethyl-bixafen. In general, in all processed samples the residues had decreased or not altered, with the exception of pearl barley rub off where an increase by a factor of 4 was observed. This provisional processing factor of 4 was used in the calculation of the dietary intake of livestock to estimate the residue concentration in wheat and rye bran instead of the default processing factor of 8. In Table 3-2 the enforcement processing factors for food commodities which are likely to be in trade are summarised. Since the residue definition for risk assessment is different, a conversion factor has been derived which has to be taken into account in case of a risk assessment for processed commodities.

The processing factors should be considered as provisional as the residue definitions are not yet agreed by the peer review. Thus, EFSA does not recommend to include them in Annex VI of Regulation 396/2005.

Table 3-2. Overview of the available processing studies

Processed commodity	Number of studies	Median PF [(a)]	Median CF [(b)]	Comments
Enforcement residue definition: bixafen				
Pearl barley	4	0.22	1.29	Provisional processing factor
Brewers malt	4	0.86	1.25	
Brewers yeast	4	0.19	1.25	
Beer	4	0.06	2	
Pear barley rub off	4	4	1.08	

(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
(b): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

3.1.2. Rotational crops

3.1.2.1. Preliminary considerations

Since the intended GAP refers to a use in crops that are grown in crop rotation, the possibility of residues in succeeding crops has to be assessed.

3.1.2.2. Nature of residues

The metabolism and distribution of bixafen in rotational crops was investigated in wheat, turnips and Swiss chard. The crops were grown in soil that had been treated with pyrazole and dichlorophenyl-ring labelled [C^{14}] bixafen, at a rate of 0.79 to 0.85 kg as/ha (3.1 to 3.4 N). Crops were planted 30, 138 and 285 days after application.

At harvest the TRR in Swiss chard (expressed as parent equivalent) was less than or equal to 0.06 mg/kg. The parent compound accounted for 26 to 35% of the TRR in the pyrazole study and between 52 and 71% in the dichlorophenyl-study.

In wheat grain no radioactivity above the LOQ of 0.01 mg/kg was detectable. In wheat straw, the TRR ranged between 0.49 mg eq/kg at the shorter pre-planting interval and 0.22 mg eq/kg after 285 days pre-planting interval. Parent bixafen accounted for 14 to 23% in the pyrazole study and 14 to 37% in the dichlorphenyl-study.

In turnip roots, the TRR was in the range of 0.01 mg eq/kg to 0.05 mg eq/kg. Significant concentrations of parent bixafen above the LOQ were only found in the sample derived from the shortest pre-planting interval (0.03 mg/kg). In turnip tops the TRR was between the LOQ and 0.08 mg eq/kg. Again, parent compound was quantifiable only in samples grown after 30 days pre-planting interval.

In all samples several metabolites were identified in different percentages of the TRR. In wheat straw the most predominant metabolite was desmethyl-bixafen. None of the other metabolites identified exceeded a concentration of 0.01 mg/kg. From the nature of the identified metabolites it was concluded that the bridge between the pyrazole ring and the dichlorophenyl ring had been broken and lead to metabolites such as pyrazolone-4-carboxylic acid with no corresponding dichlorophenyl ring metabolite being identified in the dichlorophenyl study.

EFSA agrees with the RMS conclusion that for rotational crops the same residue definition as for the primary crops should be applicable.

3.1.2.3. Magnitude of residues

Four residue trials were conducted to investigate the magnitude of residues in succeeding or rotational crops. Winter/spring wheat, lettuce, and turnip/carrots were grown in soil which had been treated at an application rate of 0.28 kg as/ha. (1.1N) and aged for 30 days and in soil which had been previously used to grow barley (treated with 2 foliar applications of bixafen at a combined rate of 0.28 as/ha (1.1N)). The barley crop was harvested at maturity 52 to 73 days after the last application and the soil cultivated ready for planting following crops. Rotational crops were planted into the soil at 60 to 70 and 298 to 331 days after the last application to simulate winter and spring rotations. Rotational crop samples were taken at set intervals up to maturity and analysed for bixafen and desmethyl-bixafen. In all samples bixafen and desmethyl-bixafen residues were below the LOQ of 0.01 mg/kg, with the exception of one sample of lettuce (sampled at an immature growth stage) which contained 0.05 mg/kg of bixafen and one sample of wheat straw in which desmethyl-bixafen residues were found at a concentration of 0.02 mg/kg.

On the basis of the studies presented in the evaluation report, EFSA concludes that the probability of bixafen related residues in succeeding crops is low. However, Member States intending to grant an authorisation for bixafen containing plant protection products should consider the need to define specific restrictions, e.g. plant back intervals, in order to avoid contamination of succeeding crops.

3.2. Nature and magnitude of residues in livestock

3.2.1. Dietary burden of livestock

The use of bixafen results in significant residues in cereal grain and straw. Since these commodities are usually used as livestock feed for ruminants, poultry and pigs, an assessment of the possible carry-over of residues in food of animal origin has to be performed. EFSA calculated the median and maximum dietary burdens for the different types of livestock using the agreed European methodology (European Commission, 1997g). The input values for the relevant commodities have been selected according to the recommendations of the 2004 JMPR meeting (WHO/FAO, 2005) and are summarised in Table 3-3.

Table 3-3. Input values for the dietary burden calculation

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: sum of bixafen and desmethyl-bixafen				
Wheat grain	0.02	STMR*CF	0.02	STMR*CF
Barley grain	0.11	STMR (SEU)*CF	0.11	STMR (SEU)*CF
Rye grain	0.02	STMR (Wheat)*CF	0.02	STMR (Wheat)*CF
Oats grain	0.11	STMR (barley, SEU)*CF	0.11	STMR (barley, SEU)*CF
Wheat bran	0.08	STMR *CF*PF (4, see 3.1.1.3)	0.08	STMR *CF*PF (4, see 3.1.1.3)
Rye bran	0.44	STMR (SEU)*CF*PF (4, see 3.1.1.3)	0.44	STMR (SEU)*CF*PF (4, see 3.1.1.3)
Wheat straw	4.14	STMR (NEU)*CF	11.50	HR*CF
Barley straw	3.71	STMR (SEU)*CF	7.30	HR*CF
Rye straw	4.14	STMR (wheat. NEU)*CF	11.50	HR*CF
Oats straw	3.71	STMR (barley, SEU)*CF	7.30	HR*CF

The results of the dietary burden calculation reported in Table 3-4 indicate that a significant intake at or above the trigger value of 0.1 mg/kg feed (dry matter) is expected for dairy and meat ruminants and for pigs. For poultry, no significant intake is expected.

Table 3-4. Results of the dietary burden calculation

	Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Max dietary burden (mg/kg DM)	Trigger exceeded?
Risk assessment residue definition: sum of bixafen and desmethyl-bixafen						
Dairy ruminants	0.100870	0.038629	Wheat straw	2.774	1.062	Yes

	Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Max dietary burden (mg/kg DM)	Trigger exceeded?
Meat ruminants	0.289303	0.105914	Wheat straw	6.741	2.468	Yes
Poultry	0.005691	0.005691	Barley grain	0.090	0.09	No
Pigs	0.004119	0.004119	Barley grain	0.103	0.103	Yes

3.2.2. Nature of residues

Livestock metabolism studies on lactating goats and laying hens have been assessed by the EMS. Goat: The metabolism and distribution of bixafen was investigated in lactating goats using pyrazole and dichlorophenyl ring labelled [14C]bixafen. The goats were dosed at a rate of 35-46 mg/kg feed (corresponding to *ca.* 6N for meat ruminants and 15N for dairy ruminants). The overall recovery of radioactivity was 75 to 89%, the bulk of the radioactivity was excreted (74-88%).

Less than 0.3% of the TRR was detected in the milk and less than 1.1% in the tissues. The plateau of the total radioactivity in milk was reached after 2 days. On characterisation of the extractable radioactivity two major components were identified in the milk as bixafen and its metabolite desmethyl bixafen, which represented 91 and 93% of the total radioactivity in the milk in the pyrazole and the dichlorophenyl studies respectively. Two other metabolites were identified, plus several unknowns which individually were present at levels of less than 0.01 mg/kg. The remaining unextractable radioactivity accounted for less than 0.4% (<0.01 mg/kg) of the total radioactivity in the milk.

In muscle and fat, bixafen and desmethyl bixafen represented 99% (pyrazole study) and 100 % of the total radioactivity (dichlorophenyl study), respectively. In muscle, less than 2% (<0.01 mg/kg) were unextractable; in fat the percentage was less than 1%.

For liver, parent bixafen and its metabolite desmethyl bixafen represented 51 and 65% of the TRR in the pyrazole and the dichlorophenyl studies, respectively. Several other metabolites were identified, none of them accounted for more than 10% of the TRR. Several compounds could not be identified, but they did not exceed a level of 0.04 mg/kg (expressed as bixafen equivalent). The unextractable radioactivity was less than 9% (0.06 mg eq/kg).

In kidney, the amount of bixafen and desmethyl bixafen accounted for ca. 82% of the TRR in both studies with different labels. Two other metabolites were identified which individually were present at levels of less than 0.03 mg/kg. The remaining unextractable residues accounted for less than 4% (<0.01 mg eq/kg).

Poultry:

Hens were dosed at rate of 26 to 32 mg/kg feed (DM) which is the 300-fold concentration of the expected dietary burden. The overall recovered radioactivity was 90 to 94%, the major part of it was excreted (88 to 93%) with less than 1.2% in eggs and less than 0.3% in the tissues. Total ^{14}C residues in the tissues (expressed as parent equivalent) were 0.03 and 0.04 mg/kg for muscle; 0.23 and 0.38 mg/kg for fat and 0.64 and 0.81 mg/kg for liver in the pyrazole and dichlorophenyl studies respectively.

On characterisation of the extractable radioactivity two major components were identified in eggs as parent bixafen and its metabolite desmethyl bixafen, which represented 91% and 90% of the total radioactivity in the eggs in the pyrazole and dichlorophenyl studies, respectively.

In fat, parent bixafen and its metabolite desmethyl bixafen represented 55% and 99% of the TRR in the studies with the pyrazole and the dichlorophenyl label. For liver, parent bixafen and its metabolite accounted for 47 and 53 % of the TRR. Including the conjugate of bixafen, the TRR represented 64% and 79% of the TRR. In muscle bixafen and desmethyl bixafen accounted for 58% and 92% of the TRR.

Several other metabolites were identified in the tissues investigated, bixafen conjugate being the only metabolite which accounted for more that 10% of the TRR in liver, but the absolute concentrations were low (0.11 and 0.22 mg/kg in the pyrazole and dichlorophenyl studies).

The RMS noted that all of the animal metabolites identified in the edible parts of ruminants and poultry were also identified in the rat metabolism. Based on the studies, the RMS concluded that the residue definition for food commodities of animal origin should be defined as follows:

Residue definition for animal products (monitoring and risk assessment): sum of bixafen and its metabolite desmethyl bixafen expressed as bixafen.

3.2.3. Magnitude of residues

The applicant provided feeding studies in cows and poultry investigating the magnitude of residues in livestock. Since the dietary burden trigger value of 0.1 mg/kg DM was only exceeded for ruminants, the poultry study is not further discussed in this assessment.

Feeding study in cows: Twelve lactating cows (three per dose group) each received twenty nine daily doses of bixafen, at rates of 4 (1.3N for dairy cattle and 0.6N for beef cattle), 12 (4N for dairy cattle and 1.7N for beef cattle) and 40 (13N for dairy cattle and 6N for beef cattle) mg/kg in feed (dry matter). The cows were sacrificed 17 to 19 hours after the last dose. The cows in the depuration study received 40 mg/kg DM for 29 days; milk samples were taken between 7 to 21 days after the last dosing. 7, 14 and 21 days after cessation of the dosing the cows of the depuration study were sacrificed.

On analysis of the samples, residues of total bixafen (bixafen plus desmethyl-bixafen) in milk reached a plateau after 4 days of 0.03, 0.07, and 0.22 mg/kg in the 4, 12 and 40 mg/kg (DM) dose groups.

The residue concentration measured in the different tissues derived after 29 days of dosing are summarised in Table 3-5.

After cessation of feeding bixafen, residues in milk decreased rapidly to the LOQ within 5 days. In muscle and kidney derived from the depuration study no residues above the LOQ were determined after 7 days. In fat, the residues dropped below the LOQ after 14 days. In liver, residues of 0.08 mg/kg were still determined after 21 days after the dosing with bixafen was stopped.

The study was sufficient to derive MRL proposals for bixafen according to the proposed residue definition for food products derived from cattle.

Assuming a similar exposure and residue behaviour for other ruminants, the derived MRL proposals may be extrapolated to sheep and goats. The cattle feeding study may also be used to establish MRLs for pigs (OECD, 2007). However, in this case the significant lower dietary burden has to be considered. Thus, extrapolating the results from the cattle feeding study to the expected dietary for swine, no residues above the LOQ are expected and therefore the MRLs are proposed at LOQ of 0.02 mg/kg. For horses the dietary intake pattern may be different, but no detailed data are available to estimate the dietary burden. Therefore EFSA is not in a position to give a MRL recommendation for horse meat, fat, liver, kidney and milk.

Table 3-5. Overview of the values derived from the livestock feeding studies

Commodity	Dietary burden		Results of the livestock feeding study						STMR (mg/kg)	HR (mg/kg)	MRL proposal (mg/kg)	CF for RA
	Med. (mg/kg feed, DM)	Max. (mg/kg feed, DM)	Dose Level (mg/kg feed, DM)	n	Result for enforcement		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
Residue definition (enforcement and risk assessment): sum of bixafen and desmethyl bixafen, expressed as bixafen												
Ruminant meat	2.468	6.741	4	3	0.05	0.07	0.05	0.07	0.029	0.135	0.15	1
			12	3	0.16	0.26	0.16	0.26				
			40	3	0.82	1.0	0.82	1.0				
Ruminant fat	2.468	6.741	4	3	0.15	0.21	0.15	0.21	0.137	0.303	0.4	1
			12	3	0.22	0.48	0.22	0.48				
			40	3	1.2	1.9	1.2	1.9				
Ruminant liver	2.468	6.741	4	3	0.57	0.69	0.57	0.69	0.411	1.036	1.5	1
			12	3	1.4	1.7	1.4	1.7				
			40	3	5.0	5.4	5.0	5.4				
Ruminant kidney	2.468	6.741	4	3	0.14	0.15	0.14	0.15	0.1	0.225	0.3	1
			12	3	0.35	0.37	0.35	0.37				
			40	3	1.2	1.3	1.2	1.3				
Milk	1.062	2.774	4	3	0.03	0.05	0.03	0.05	0.015	0.039	0.04	1
			12	3	0.07	0.12	0.07	0.12				
			40	3	0.22	0.36	0.22	0.36				
Ruminant meat → swine meat	0.103	0.103	4	3	0.05	0.07	0.05	0.07	<0.02	<0.02	0.02(*)	1
Ruminant fat →	0.103	0.103	4	3	0.15	0.21	0.15	0.21	<0.02	<0.02	0.02(*)	1

Commodity	Dietary burden		Results of the livestock feeding study						STMR (mg/kg)	HR (mg/kg)	MRL proposal (mg/kg)	CF for RA
	Med. (mg/kg feed, DM)	Max. (mg/kg feed, DM)	Dose Level (mg/kg feed, DM)	n	Result for enforcement		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
swine fat												
Ruminant liver → swine liver	0.103	0.103	4	3	0.57	0.69	0.57	0.69	<0.02	<0.02	0.02(*)	1
Ruminant kidney → swine liver	0.103	0.103	4	3	0.14	0.15	0.14	0.15	<0.02	<0.02	0.02(*)	1

(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.
→ Trials on one crop or animal species are extrapolated to another crop or animal species

4. Consumer risk assessment

The consumer intake calculation was performed with revision 2 of the EFSA PRIMo (Pesticide Residue Intake Model, EFSA, 2007), using the STMR and HR values as derived from the supervised field trials and the feeding study on ruminants. Swine products are not included because no significant residues are expected. The input parameters are summarised in Table 4-1.

Table 4-1. Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: sum of bixafen and desmethyl-bixafen				
Wheat (including triticale)	0.02	STMR*CF	0.02	STMR*CF
Rye	0.02	STMR*CF	0.02	STMR*CF
Barley	0.11	STMR (SEU)*CF	0.11	STMR (SEU)*CF
Oats	0.11	STMR (SEU)*CF	0.11	STMR (SEU)*CF
Bovine, sheep and goat meat	0.029	STMR	0.135	HR
Bovine, sheep and goat fat	0.137	STMR	0.303	HR
Bovine, sheep and goat liver	0.411	STMR	1.036	HR
Bovine, sheep and goat kidney	0.1	STMR	0.225	HR
Milk of cows, sheep and goat	0.015	STMR	0.015	STMR

The results of the consumer risk assessment are attached in Appendix B. The calculations demonstrate that no chronic consumer health risk is expected from the crops treated according to the intended GAPs including the residues that may result in food of animal origin. In all diets included in the EFSA PRIMo, the long-term dietary intake accounted for less than 4% of the ADI. The highest individual contributors are milk (max. 3.5% of the ADI for UK infants), wheat (0.9% of the ADI in the WHO cluster diet B) and barley (0.7% of the ADI for Irish adults). As regards the short-term intake, for all food commodities the expected exposure was well below the ARfD considering the critical European consumer, i.e. the consumer for which the highest intake was identified among the diets included in the EFSA PRIMo. The highest intakes were calculated for bovine liver (4.2% of the ARfD for the UK infant), milk (0.9% of the ARfD for UK infants), bovine meat (0.9% of the ARfD for DE child) and sheep meat (0.7%.of the ARfD for DE child). For all other commodities the exposure was calculated to be below 0.5% of the ARfD.

EFSA concludes that the intended uses of bixafen on cereals (wheat, rye, barley and oats) are acceptable from a consumer safety point of view; the residues expected after treatment of the crops according to the intended GAP will not lead to an exceedance of the toxicological reference values.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The toxicological profile of bixafen was assessed by the RMS in the framework of the preparation of the Draft Assessment Report. The data were sufficient to conclude on an ADI value of 0.02 mg/kg and an ARfD of 0.2 mg/kg. Since the peer review is not yet finalised for this active substance, the toxicological reference values should be considered as provisional only.

The metabolism of bixafen was investigated in primary and rotational crops. In addition, livestock metabolism studies were performed with lactating goats and laying hens which were exposed to bixafen residues via feed. Based on the results of these studies the following residue definitions were derived:

Commodities	**Residue definition risk assessment**	**Residue definition enforcement**
Cereals, pulses and oilseeds	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen	Bixafen
Animal commodities	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen	Sum of bixafen and its metabolite desmethyl bixafen, expressed as bixafen

Analytical methods are available which can be used for enforcement of MRLs according to the proposed residue definitions. For plant matrices, validation data demonstrated that an LOQ of 0.01 mg/kg is achievable. For animal matrices the validated LOQ is 0.02 mg/kg (for the proposed residue definition sum of bixafen and desmethyl bixafen, expressed as bixafen).

The supervised field trials submitted in support of the intended uses in wheat and barley were sufficient to derive MRL proposals for these crops. However, it is noted that for the NEU GAP for barley the data package was not complete and 3 additional trials have to be provided. It is concluded that for wheat an MRL of 0.05 mg/kg would be required to accommodate for the intended use, for barley (SEU GAP) an MRL proposal of 0.5 mg/kg could be derived. According to the EC guidance documents, these MRLs can be extrapolated to rye and oats, respectively. Under processing conditions simulating pasteurisation, baking/brewing/boiling and sterilisation bixafen residues are stable. Specific processing studies were performed with barley treated with the two-fold application rate compared with the intended GAP. The processed products derived from barley and by-products from the brewing process (pearl barley, brewer's malt, beer and brewer's yeast) all contained significantly lower residues compared with unprocessed barley, except pearl barley rub off in which the residues increased by a factor of *ca.* 4.

The rotational crop studies demonstrated that the occurrence of bixafen related residues in rotational crops grown in crop rotation after primary crops treated with bixafen in accordance with the intended GAP is low.

The calculation of the expected dietary burden for ruminants, poultry and pigs, taking into account the residues of bixafen on cereals grain, straw or bran, revealed that for ruminants and pigs a significant intake is expected. Thus, feeding studies with cows which received bixafen residues via feed were

used to estimate the residue concentrations in animal tissues and milk. These studies were adequate to derive MRL proposals for these commodities.

The consumer exposure assessment was performed with revision 2 of the EFSA PRIMo (Pesticide Residue Intake Model), taking into account the residues in wheat, rye, barley, oats and the animal commodities for which MRL proposals were derived. The long-term dietary intake for all diets included in the EFSA PRIMo was low (below 4% of the ADI). The highest contributors were milk (2.9%), wheat (0.9%) and barley (0.7%). Regarding the short term dietary intake, the expected exposure was well below the ARfD for all food commodities concerned. The highest intake were calculated for bovine liver (4.2% of the ARfD for the UK infant), milk (0.9% of the ARfD for UK infants), bovine meat (0.9% of the ARfD) and sheep meat (0.7% of the ARfD)). For all other commodities the exposure was calculated to be below 0.5% of the ARfD.

EFSA concludes that the intended uses of bixafen on cereals (wheat, rye, barley and oats) are acceptable from a consumer safety point of view, since the residues expected after treatment of the crops according to the intended GAP will not lead to an unacceptable consumer exposure.

RECOMMENDATIONS

The following temporary MRLs are proposed for the intended uses assessed in this reasoned opinion which are recommended to be included in Annex III of Regulation 396/2005:

Code number	Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Justification for the proposal
	Bixafen			
0500010	Barley	Currently the default MRL of 0.01 mg/kg is applicable (Art. 18(1) (b)).	0.5	The proposed MRLs are sufficiently supported by data. The dietary risk assessment did not reveal a potential consumer health concern. The proposed MRL for barley and oats represent the SEU GAP only. For the NEU GAP, three additional supervised field trials are required to complete the data set as required in the EC guidance document.
0500050	Oats		0.5	
0500070	Rye		0.05	
0500090	Wheat		0.05	
	Sum of bixafen and desmethyl bixafen, expressed as bixafen			
1011010	Swine meat	Currently the default MRL of 0.01 mg/kg is applicable (Art. 18(1) (b)).	0.02 (*)	The proposed MRLs are sufficiently supported by data. No consumer health risk was identified.
1011020	Swine fat		0.02 (*)	
1011030	Swine liver		0.02 (*)	
1011040	Swine kidney		0.02 (*)	
1012010	Bovine meat		0.15	
1012020	Bovine fat		0.4	
1012030	Bovine liver		1.5	
1012040	Bovine kidney		0.3	
1013010	Sheep meat		0.15	
1013020	Sheep fat		0.4	
1013030	Sheep liver		1.5	

Code number	Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Justification for the proposal
1013040	Sheep kidney		0.3	
1014010	Goat meat		0.15	
1014020	Goat fat		0.4	
1014030	Goat liver		1.5	
1014040	Goat kidney		0.3	
1020010	Cattle milk		0.04	
1020020	Sheep milk		0.04	
1020030	Goat milk		0.04	
Not yet allocated	Barley straw	Currently no MRLs are established for feed items	15	In view of future needs to establish MRLs for feed items, EFSA derived MRL proposals for straw.
	Oats straw		15	
	Rye straw		20	
	Wheat straw		20	

(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.

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APPENDIX A – GOOD AGRICULTURAL PRACTICES (GAPS)

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of Pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage and season (j)	number min/ max (k)	interval between applications (min)	g as/hL min-max (l)	water L/ha min - max	g as/ha min – max (l)		
Wheat, Rye, Triticale	France	Bixafen EC 125	F	*Stem and leaf diseases*	EC	125 g/l bixafen	foliar spray	BBCH 25 – 69* Spring	Max 2	refer to growth stage*	41.7 – 125g	100 - 300	125g	35	*timing, number of applications and spray interval may vary according to national conditions
Barley, Oats	France	Bixafen EC 125	F	*Stem and leaf diseases*	EC	125 g/l bixafen	foliar spray	BBCH 25 – 61* Spring	Max 2	refer to growth stage*	41.7 – 125g	100 - 300	125g	35	
Wheat, Rye, Triticale	UK	Bixafen EC 125	F	*Stem and leaf diseases*	EC	125 g/l bixafen	foliar spray	BBCH 25 – 69* Spring	Max 2	refer to growth stage*	41.7 – 125g	100 - 300	125g	35	
Barley, Oats	UK	Bixafen EC 125	F	*Stem and leaf diseases*	EC	125 g/l bixafen	foliar spray	BBCH 25 – 61* Spring	Max 2	refer to growth stage*	41.7 – 125g	100 - 300	125g	35	

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s). (a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure) (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I) (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl). (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

APPENDIX B – PESTICIDE RESIDUES INTAKE MODEL (PRIMO)

Bixafen			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0,01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0,02**	ARfD (mg/kg bw):	**0,2**
Source of ADI:	**UK**	Source of ARfD:	**UK**
Year of evaluation:	**2009**	Year of evaluation:	**2009**

The toxicological reference values as proposed by the EMS should be considered as provisional.
The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment - refined calculations

	TMDI (range) in % of ADI minimum - maximum
	4
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
3,5	UK Infant	2,9	Milk and cream,	0,3	Wheat	0,2	Bovine: Liver	
3,4	FR toddler	3,0	Milk and cream,	0,3	Wheat	0,2	Bovine: Meat	
3,1	NL child	2,2	Milk and cream,	0,5	Wheat	0,2	Bovine: Meat	
2,4	DK child	0,9	Milk and cream,	0,6	Wheat	0,4	Rye	
2,1	FR infant	1,9	Milk and cream,	0,1	Wheat	0,1	Bovine: Meat	
2,0	UK Toddler	1,5	Milk and cream,	0,4	Wheat	0,0	Bovine: Liver	
1,8	IE adult	0,7	Barley	0,5	Sheep: Liver	0,2	Wheat	
1,7	DE child	1,1	Milk and cream,	0,4	Wheat	0,1	Oats	
1,7	WHO Cluster diet B	0,9	Wheat	0,2	Milk and cream,	0,2	Barley	
1,6	ES child	0,9	Milk and cream,	0,4	Wheat	0,2	Bovine: Meat	
1,4	WHO cluster diet D	0,7	Wheat	0,4	Milk and cream,	0,1	Barley	
1,3	WHO cluster diet E	0,4	Barley	0,4	Wheat	0,2	Milk and cream,	
1,3	WHO Cluster diet F	0,4	Wheat	0,3	Barley	0,3	Milk and cream,	
1,3	SE general population 90th percentile	0,9	Milk and cream,	0,3	Wheat	0,0	Rye	
1,1	NL general	0,5	Milk and cream,	0,2	Barley	0,2	Wheat	
1,1	WHO regional European diet	0,4	Milk and cream,	0,3	Wheat	0,2	Barley	
1,0	ES adult	0,4	Milk and cream,	0,3	Barley	0,2	Wheat	
0,9	DK adult	0,4	Milk and cream,	0,2	Wheat	0,1	Bovine: Liver	
0,7	IT kids/toddler	0,7	Wheat	0,0	Barley	0,0	Oats	
0,7	LT adult	0,3	Milk and cream,	0,1	Rye	0,1	Wheat	
0,7	FI adult	0,4	Milk and cream,	0,1	Wheat	0,1	Rye	
0,6	FR all population	0,3	Wheat	0,2	Milk and cream,	0,1	Bovine: Meat	
0,5	UK vegetarian	0,2	Milk and cream,	0,2	Wheat	0,0	Oats	
0,4	UK Adult	0,2	Milk and cream,	0,2	Wheat	0,0	Bovine: Liver	
0,4	PT General population	0,4	Wheat	0,0	Barley	0,0	Oats	
0,4	IT adult	0,4	Wheat	0,0	Barley	0,0	Oats	
	PL general population		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)		FRUIT (FRESH OR FROZEN)	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Bixafen is unlikely to present a public health concern.

Acute risk assessment /children - refined calculations	Acute risk assessment / adults / general population - refined calculations

The acute risk assessment is based on the ARfD.

For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.

In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.

In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.

Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.

Unprocessed commodities

No of commodities for which ARfD/ADI is exceeded (IESTI 1): ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 1):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---		
IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
4,2	Bovine: Liver	1,036 / -	4,2	Bovine: Liver	1,036 / -	1,4	Bovine: Liver	1,036 / -	1,4	Bovine: Liver	1,036 / -
0,9	Milk and milk products:	0,015 / -	0,9	Milk and milk	0,015 / -	0,4	Bovine: Meat	0,135 / -	0,4	Bovine: Meat	0,135 / -
0,9	Bovine: Meat	0,135 / -	0,9	Bovine: Meat	0,135 / -	0,4	Barley	0,1107 / -	0,4	Barley	0,1107 / -
0,7	Sheep: Meat	0,135 / -	0,7	Sheep: Meat	0,135 / -	0,4	Sheep: Liver	1,036 / -	0,4	Sheep: Liver	1,036 / -
0,4	Bovine: Kidney	0,225 / -	0,4	Bovine: Kidney	0,225 / -	0,3	Sheep: Meat	0,135 / -	0,3	Sheep: Meat	0,135 / -
0,3	Bovine: Fat	0,303 / -	0,3	Bovine: Fat	0,303 / -	0,2	Bovine: Kidney	0,225 / -	0,2	Bovine: Kidney	0,225 / -
0,2	Oats	0,1107 / -	0,2	Oats	0,1107 / -	0,1	Milk and milk	0,015 / -	0,1	Milk and milk products: Cattle	0,015 / -
0,2	Milk and milk products:	0,015 / -	0,2	Milk and milk	0,015 / -	0,1	Goat: Meat	0,135 / -	0,1	Goat: Meat	0,135 / -
0,1	Wheat	0,02 / -	0,1	Wheat	0,02 / -	0,1	Bovine: Fat	0,303 / -	0,1	Bovine: Fat	0,303 / -
0,1	Barley	0,1107 / -	0,1	Barley	0,1107 / -	0,1	Oats	0,1107 / -	0,1	Oats	0,1107 / -
0,1	Rye	0,02 / -	0,1	Rye	0,02 / -	0,1	Wheat	0,02 / -	0,1	Wheat	0,02 / -
0,0	Milk and milk products:	0,015 / -									
No of critical MRLs (IESTI 1)		---				**No of critical MRLs (IESTI 2)**		---			

Processed commodities

No of commodities for which ARfD/ADI is exceeded: ---				**No of commodities for which ARfD/ADI is exceeded:** ---			
		*****)**				*****)**	
Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	
0,1	Wheat flour	0,01 / -		0,1	Bread/pizza	0,05 / -	

*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

**) pTMRL: provisional temporary MRL

***) pTMRL: provisional temporary MRL for unprocessed commodity

Conclusion:

For Bixafen IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

For processed commodities, no exceedance of the ARfD/ADI was identified.

APPENDIX C – EXISTING EC MRLS

For bixafen, no specific MRLs have been established in Annex II or III of Regulation (EC) No 396/2005. Thus, according to Article 18(2) the default MRL of 0.1 mg/kg is applicable for all commodities

ABBREVIATIONS

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH scale	A system for a uniform coding of phenologically similar growth stages of all mono- and dicotyledonous plant species elaborated by the "Biologische Bundesanstalt für Land-und Forstwirtschaft, Bundessortenamt und Chemische Industrie"
bw	body weight
CAC	Codex Alimentarius Commission
CAS	Chemical Abstract Service
CF	conversion factor for enforcement residue definition to risk assessment residue definition
CXL	codex maximum residue limit
d	day
DAR	Draft Assessment Report (prepared under Directive 91/414/eec)
DAT	days after treatment
DM	dry matter
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
EC	European Community
EC	emulsifiable concentrate
ECD	electron capture detection
EDI	estimated daily intake
EFSA	European Food Safety Authority
EMS	evaluating Member State
eq	equivalent
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FID	flame ionization detection
GAP	good agricultural practice
GC	gas chromatography
GR	granule
GS	growth stage
ha	hectare
hL	hectolitre

HPLC	high performance liquid chromatography
HR	highest residue
ILV	independent laboratory validation
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOQ	limit of quantification
MRL	maximum residue limit
MS	Member States
NEU	Northern European Union
NOAEL	no observed adverse effect level
PF	processing factor
PHI	pre harvest interval
ppm	parts per million (10^{-6})
PRIMo	Pesticide Residues Intake Model
RMS	rapporteur Member State
SEU	Southern European Union
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
UVD	ultra-violet detection
WHO	World Health Organisation
WP	wettable powder