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Fenoxaprop-P-ethyl

Volume 3 – B.5 (PPP) – Puma S 69 EW

Rapporteur Member State: Austria
Co-Rapporteur Member State: Finland

Version History

When	What
2005/April	Initial DAR
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B.5. METHODS OF ANALYSIS

Comments with respect to the Annex I renewal of approval process

The dossier contains study reports already submitted by Bayer CropScience for the Annex I inclusion of AE F046360 (fenoxaprop-P-ethyl), as well as new data, not yet evaluated at EU level and that was considered by the notifier to be necessary for the renewal of approval of AE F046360. In order to distinguish these, reference to studies in the original dossier are depicted in grey.

For summaries of studies submitted during the frame of the first Annex I inclusion please refer to the corresponding section in the Monograph 2005.

B.5.1. METHODS USED FOR THE GENERATION OF PRE-AUTHORISATION DATA

B.5.1.1. Analysis of the plant protection product

B.5.1.1.1. Methods for the determination of the active substance and/or variant in the plant protection product

Studies already evaluated during the first EU review process for inclusion of AE F046360 on Annex I:

Reference:	**Determination of AE F046360 (fenoxaprop-P-ethyl) in technical grade and pure active ingredient and also determination of AE F046360 (fenoxaprop-P-ethyl) and AE F107892 (mefenpyr-diethyl) in formulations by liquid chromatography (HPLC)**
Author(s), year:	Bogdoll, B.; Eichelmann, C.; Kloeckner, C.; 2003
Report/Doc. number:	C030496 / M-219452-01-1
Guideline(s):	CIPAC: 484/TC/M1-3 + 484/EW/M1-3, Vol. J; EU (=EEC): 91/414/EEC Annex II 4.1, 91/414/EEC Annex III 5.1; USEPA (=EPA): OPPTS 830.1800
GLP:	no

Reference:	**Validation of the analytical method AL 009/94-0 for quantitation of Hoe 107892 and Hoe 046360 in the formulated product Hoe 046360 24 EW08 A802**
Author(s), year:	Mueller, T.; 1994
Report/Doc. number:	A53438 / M-237746-01-1
Guideline(s):	--
GLP:	yes

Reference:	**Analysis of technical and formulated pesticides (Fenoxaprop-ethyl)**
Author(s), year:	Dobrat, W.; Martijn, A.; 2000
Report/Doc. number:	CIPAC 484 / M-211540-01-1
Guideline(s):	CIPAC: 484/EW/M1-3, 484/TC/M/1-3
GLP:	no

Reference:	**Validation of the analytical method AL048/96-2 for the determination of AE F046360 (fenoxaprop-P-ethyl) and AE F122006 in AE F046360 42 EC14 A3 Code: AE F046360 42 EC14 A3**
Author(s), year:	Mueller, T.; 1998
Report/Doc. number:	A67435 / M-147819-01-1
Guideline(s):	EU (=EEC): 91/414/EEC Annex III 5.1; USEPA (=EPA): OPPTS 830.1700
GLP:	yes

Reference:	**Validation of the analytical method AL009/94-3 for the determination of AE F046360 (fenoxaprop-P-ethyl) and AE F107892 (mefenpyr-diethyl) and AL005/91-1 for the determination of AE F066606 (MCPA-isooctyl) in AE F046360 50 EC51 A2F**
Author(s), year:	Mueller, T.; 1998
Report/Doc. number:	C001740 / M-183264-01-1
Guideline(s):	USEPA (=EPA): OPPTS 830.1700
GLP:	yes

Method AM013008FF2

Reference:	**Determination of the sum of (D+)- and (L-)-enantiomers of fenoxaprop-P-ethyl and mefenpyr-diethyl in formulations - Assay HPLC, external standard**
Author(s), year:	Michel, A.; 2009
Report/Doc. number:	AM013008FF2 / M-303825-02-1
Guideline(s):	EU 91/414/EEC Annex III 5.1
GLP:	no

Reference:	**Amendment 2 to the validation report VB2-AM013008FF2 - Validation of HPLC-method AM013008FF2 - Determination of the sum of (D+)- and (L-)-enantiomers of fenoxaprop-p-ethyl and mefenpyr-diethyl in formulations - fenoxaprop-p-ethyl+mefenpyr-diethyl EW 144 (69+75) G**
Author(s), year:	Michel, A.; 2011
Report/Doc. number:	VB2-AM013008FF2 / M-366815-03-1
Guideline(s):	EU 91/414/EEC Annex III 5.1SANCO/3030/99 rev. 4
GLP:	no

Principle of method AM013008FF2

The method is capable to determine sum of both enantiomers (fenoxaprop-P-ethyl and fenoxaprop-M-ethyl), mefenpyr-diethyl and where applicable impurities in formulations.

The separation between AE F046360 and mefenpyr-diethyl and from impurities is performed by HPLC. Separation is achieved by gradient profile HPLC (with 2,2,4-trimethylpentane /1,4-dioxan) on a silica gel stationary phase (Zorbax RX-SIL, particle size 1.8 µm; column: stainless steel, 50 mm x 4.6 mm ID).

Fenoxaprop-ethyl and mefenpyr-diethyl are detected in the eluate by UV absorption at 280 nm. Quantification is carried out by external standard evaluation.

Validation data (VB2-AM013008FF2) are summarised in Table B.5.1.1-1

Table B.5.1.1-1: Summary of validation data

Analyte	Calibration* (linear between) [mg/L]	Levels [% w/w]	Accuracy Recovery [% w/w] n = 6	Levels [% w/w]	Precision Repeatability RSD [%] (n = 6)	Specificity	LOQ	Reference
Fenoxaprop-ethyl sum of R and S enantiomer	10.8 - 540 (n = 18) r = 1.000	3.58 – 10.79	99.74	6.60	0.39 RSDr : 2.02	The UV-spectra of reference items and analyte in the sample show no spectral difference; the retention times are identical. No interference	--	Michel, A.; 2011 VB2-AM013008FF2
Mefenpyr-diethyl	10.0 – 500 (n = 18) r = 1.000	3.84 – 11.0	100.04	7.1	0.35 RSDr : 1.99			

* The data of the linearity were taken from a previous validation study. For the evaluation of the precision and accuracy data within the study VB2-AM013008FF2 new calibration solutions were produced and used during this validation work. Graphs and equations are available.

Conclusion

Method AM013008FF2 is sufficiently validated according to guidance document SANCO 3030/99 rev. 4.

Method AM006205FF3

Reference:	**Determination of the optical purity of fenoxaprop-p-ethyl (AE F046360) in formulations by liquid chromatography (HPLC)**
Author(s), year:	Michel, A.; 2007
Report/Doc. number:	AM006205FF3 / M-287926-01-1
Guideline(s):	EU 91/414/EEC Annex III 5.1
GLP:	no

Reference:	**Validation of HPLC method AM006205FF3 - Determination of the optical purity of fenoxaprop-p-ethyl (AE F046360) in formulations - Fenoxaprop-p-ethyl+mefenpyr-diethyl EW 144 (69+75) G**
Author(s), year:	Michel, A.; 2010
Report/Doc. number:	VB1-AM006205FF3 / M-366805-01-1
Guideline(s):	EU 91/414/EEC Annex III 5.1SANCO/3030/99 rev. 4
GLP:	no

Principle of method AM006205FF3 (previously named LM006205FF1)

The method is capable to determine the optical purity of AE F046360 in formulated products. The isomeric mixture of AE F046360 (R-enantiomer) and fenoxaprop-M-ethyl (S-enatiomer, AE F085791) is separated from formulation components and each other on a chiral phase HPLC column. Separation is achieved by any gradient HPLC system on a silica gel stationary phase (Nucleodex beta-PM, EC particle size 5 µm; column: stainless steel, 200 mm x 4.0 mm).

Both substances are detected in the eluate by UV absorption at 237 nm.

Validation data (VB1-AM006205FF3) are summarised in Table B.5.1.1-2

Table B.5.1.1-2: Summary of validation data

Analyte	Calibration* (linear between) [mg/L]	Levels [% w/w]	Accuracy Recovery [% w/w] n = 6	Levels [% w/w]	Precision Repeatability RSD [%] (n = 6)	Specificity	LOQ	Reference
Fenoxaprop-P-ethyl R enantiomer	1.0 – 72 (n = 15) r = 1.000	97.22	99.95	97.04	0.01 RSDr : 1.35	The UV-spectra of reference items and analyte in the sample show no spectral difference; the retention times are identical. No interference (< 0.3%)	--	Michel, A.; 2010 VB1-AM006205FF3
Fenoxaprop-M-ethyl S enantiomer	1.0 – 72 (n = 15) r = 1.000	2.78	102.02	3.0	0.43 RSDr : 2.28			

* The data of the linearity were taken from a previous validation study (FTA05/017). . Graphs and equations are available.

Conclusion

Method AM006205FF3 is sufficiently validated according to guidance document SANCO 3030/99 rev. 4.

B.5.1.1.2. Methods for determination of relevant impurities identified in the technical material or which may be formed during manufacture of the plant protection product or from degradation of the plant protection product during storage

Fenoxaprop-P-ethyl, the active ingredient in AE F046360 + mefenpyr-diethyl EW 144 (069+075) g/L does not contain any relevant impurities.

B.5.1.1.3. Methods for the determination of relevant co-formulants or components of co-formulants, where required by the national competent authorities

B.5.1.1.4.

With respect to toxicological, eco-toxicological or environmental aspects the product does not contain any relevant formulants. Therefore, a special analytical method and validation is not needed.

B.5.1.2. Methods for the determination of residues

B.5.1.2.1. Methods in soil, water, sediment, air and any additional matrices used in support of environmental fate studies

Please refer to Part CA B.5.

B.5.1.2.2. Methods in soil, water and any additional matrices in support of efficacy studies

Please refer to Part CA B.5.

B.5.1.2.3. Methods in feed, body fluids and tissues, air and any additional matrices used in support of toxicological studies

Please refer to Part CA B.5.

B.5.1.2.4. Methods in body fluids, air, and any additional matrices used in support of operator, worker, resident and bystander exposure studies

Please refer to Volume 3 Part CA B.5.

B.5.1.2.5. Methods in or on plants, plant products, processed food commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies

Please refer to Volume 3 Part CA B.5.

B.5.1.2.6. Methods in soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies

Please refer to Volume 3 Part CA B.5 and Part CP B.9.

B.5.1.2.7. Methods in water, buffer solutions, organic solvents and any additional matrices resulting from the physical and chemical properties tests

Please refer to Volume 3 Part CA B.5.

B.5.2. METHODS FOR POST-APPROVAL CONTROL AND MONITORING PURPOSES

B.5.2.1. Methods for the determination of residues in or on plants, plant products, processed food commodities, food and feed of plant and animal origin

Please refer to Volume 3 Part CA B.5.

B.5.2.2. Methods for the determination of residues in body fluids and tissues

Please refer to Volume 3 Part CA B.5.

B.5.2.3. Methods for the determination of residues in soil

Please refer to Volume 3 Part CA B.5.

B.5.2.4. Methods for the determination of residues in water

Please refer to Volume 3 Part CA B.5.

B.5.2.5. Methods for the determination of residues in air, unless the applicant shows that exposure of operators, workers, residents or bystanders is negligible

Please refer to Volume 3 Part CA B.5.

B.5.2.6. Methods for the determination of residues in body fluids and tissues

Please refer to Volume 3 Part CA B.5.

B.5.3. REFERENCES RELIED ON

Annex point / reference number	Author(s)	Year	Title Source Company name, Report No., Date, GLP status, published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCP Section 5 /01	Michel, A.	2008	Determination of the sum of (D+)- and (L-)-enantiomers of fenoxaprop-P-ethyl and mefenpyr-diethyl in formulations - Assay HPLC, external standard Bayer CropScience, Report No.: AM013008FF2, Edition Number: M-303825-02-1 Date: 2008-07-09 **...Amended: 2009-10-16** GLP/GEP: no, unpublished	N	N		Bayer CropScience
KCP Section 5 /02	Michel, A.	2010	Amendment 2 to the validation report VB2-AM013008FF2 - Validation of HPLC-method AM013008FF2 - Determination of the sum of (D+)- and (L-)-enantiomers of fenoxaprop-p-ethyl and mefenpyr-diethyl in formulations - fenoxaprop-p-ethyl+mefenpyr-diethyl EW 144 (69+75) G Bayer CropScience, Report No.: VB2-AM013008FF2, Edition Number: M-366815-03-1 Date: 2010-04-08 **...Amended: 2011-08-22** GLP/GEP: no, unpublished	N	N		Bayer CropScience
KCP Section 5 /03	Michel, A.	2007	Determination of the optical purity of fenoxaprop-p-ethyl (AE F046360) in formulations by liquid chromatography (HPLC) Bayer CropScience, Report No.: AM006205FF3, Edition Number: M-287926-01-1 Date: 2007-05-16 GLP/GEP: no, unpublished	N	N		Bayer CropScience

Annex point / reference number	Author(s)	Year	Title Source Company name, Report No., Date, GLP status, published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCP Section 5 /04	Michel, A.	2010	Validation of HPLC method AM006205FF3 - Determination of the optical purity of fenoxaprop-p-ethyl (AE F046360) in formulations - Fenoxaprop-p-ethyl+mefenpyr-diethyl EW 144 (69+75) G Bayer CropScience, Report No.: VB1-AM006205FF3, Edition Number: M-366805-01-1 Date: 2010-04-08 GLP/GEP: no, unpublished	N	N		Bayer CropScience
KCP 5.1.1 /01	Bogdoll, B.; Eichelmann, C.; Kloeckner, C.	2003	Determination of AE F046360 (fenoxaprop-P-ethyl) in technical grade and pure active ingredient and also determination of AE F046360 (fenoxaprop-P-ethyl) and AE F107892 (mefenpyr-diethyl) in formulations by liquid chromatography (HPLC) (anal Bayer CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C030496, Edition Number: M-219452-01-1 Date: 2003-03-24 GLP/GEP: no, unpublished	N	N		Bayer CropScience
KCP 5.1.1 /02	Mueller, T.	1994	Validation of the analytical method AL 009/94-0 for quantitation of Hoe 107892 and Hoe 046360 in the formulated product Hoe 046360 24 EW08 A802 Bayer CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A53438, Edition Number: M-237746-01-1 Date: 1994-12-19 GLP/GEP: yes, unpublished	N	N		Bayer CropScience

Annex point / reference number	Author(s)	Year	Title Source Company name, Report No., Date, GLP status, published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCP 5.1.1 /03	Dobrat, W.; Martijn, A.	2000	Analysis of technical and formulated pesticides (Fenoxaprop-ethyl) -public data-, Report No.: CIPAC 484, Edition Number: M-211540-01-1 Date: 2000-01-01 GLP/GEP: no, unpublished	N	N		-public data-