

Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009** as it applies in Great Britain (GB PPP)

Bixlozone (F9600)

Volume 3 – B.2 (AS)

Physical & Chemical Properties

Great Britain

July 2022

Version History

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B.2. PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
B.2.1. MELTING PO	DINT AND BOILING PO	OINT				
Melting, freezing or	EC Method A.1					
solidification point	OECD Method 102					
B.2.1/01	EPA/OPPTS 830.7200	Bixlozone pure Purity: 99.8%	Melting point (onset): 81.5°C		Y	Cowlyn, N. 2017a
	Melting block confirmation by Differential Scanning Calorimetry (DSC)	Batch PL14- 0163		Acceptable.		Study Report No. FP91QY
Boiling point	EC Method A.2					
B.2.1/02	OECD Method 103	Bixlozone pure	The boiling point of bixlozone was not	Acceptable.		Cowlyn, N.
	EPA/OPPTS 830.7220	Purity: 99.8% Batch PL14-	determinable; the test item decomposed before boiling.		Y	2017a Study Report
	Siwoloboff method	0163				No. FP91QY
Decomposition / Sublimation temperature B.2.1/03	OECD Method 103 EPA/OPPTS 830.7220 Siwoloboff method	Bixlozone pure Purity: 99.8% Batch PL14- 0163	In duplicate definitive determinations at a heating rate of 1°C/minute, the onset of decomposition, as indicated by discoloration of the samples, was observed to be approximately 188°C.	Acceptable.	Y	Cowlyn, N. 2017a Study Report No. FP91QY

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Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
B.2.2. VAPOUR PR	ESSURE, VOLATILITY	?				
Vapour pressure B.2.2/01	EC Method A.4 OECD Method 104 EPA OPPTS 830.7950 Vapour pressure balance	Bixlozone pure Purity: 99.9% Batch PL14- 0163		Acceptable. Bixlozone is considered slightly volatile.	Y	Cowlyn N. 2016a Study Report No. BM19FW
Volatility (Henry's Law constant) B.2.2/02	Calculation	Bixlozone pure Purity: 99.9% Batch PL14- 0163	Henry's law constant at 20° C 7.2×10^{-3} Pa. $m^3 \cdot mol^{-1}$	Acceptable.	Y	Cowlyn N. 2016a Study Report No. BM19FW
B.2.3. APPEARANCE	CE (PHYSICAL STATE	, COLOUR)				
Physical state and colour B.2.3/01	EPA/OPPTS 830.302 EPA/OPPTS 830.6303 EPA/OPPTS 830.6304 Visual assessment	Bixlozone pure Purity: 99.8% Batch PL14- 0163	Appearance of pure active ingredient Colour: Munsell system: N9.5/90.0% R (white) Physical state: Solid at 20°C, crystalline with various sized, easily friable, agglomerates. Odour: No discernible odour	Acceptable. Pure and manufactured bixlozone tested.	Y	Cowlyn, N. 2017a Study Report No. FP91QY
Physical state and colour B.2.3/01	EPA/OPPTS 830.302 EPA/OPPTS 830.6303 EPA/OPPTS 830.6304 Visual assessment	Bixlozone technical Purity: 96.0% Batch: PL14- 0049	Appearance of technical material Colour: Pale yellow/brown (2.5Y 9/2 on the Munsell Colour system) Physical state: Solid at 20°C, crystalline with various sized, easily friable, agglomerates. Odour: No discernible odour	Acceptable. Pure and manufactured bixlozone tested.	Y	Cowlyn, N. 2017b Study Report No.: MF50PJ

B.2.4. SPECTRA	UV/VIS, IR, NMR, MS), MOLAR EXTINCTION AT RELEVANT WAVELENGTHS, OPTICAL PURITY
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Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods /	'Results	Comments (Acceptable / Non acceptable)	GLP	Reference
Infrared (IR) B.2.4/02	Infrared (FT-IR) Spectrometer fitted with a diamond single bounce attenuated total reflectance (ATR) accessory	Bixlozone pure Purity: 99.8% Batch PL14- 0163	Wavenumber (cm ⁻¹) 3000 - 3100: 2800 - 3000: 1695: 1200 - 1600: 1000 - 1200: <1000:	Assignment CH (aromatic) stretches C-H (alkyl) stretches C=O stretch C=C (aromatic) stretches C-O stretches C-N stretches N-O stretches CH ₂ , CH ₃ deformations C-H (aromatic) in plane deformations C-Cl skeletal vibrations C-H (aromatic) out of plane deformations	Acceptable. The obtained IR spectra are in agreement with the proposed structure.	Y	Cowlyn, N. 2017c Study Report No. WP36VB
Nuclear magnetic resonance (NMR) B.2.4/03	Bruker 400 MHz Nuclear Magnetic Resonance (NMR) Spectrometer.	Bixlozone pure Purity: 99.8% Batch PL14- 0163	Proton Spectra (CDCl ₃ solvent):	Acceptable. The obtained NMR spectra are in agreement with the proposed structure.	-	Cowlyn, N. 2017c Study Report No. WP36VB

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results			Comments (Acceptable / Non acceptable)	GLP	Reference
			Chemical Shift (ppm)	<u>Obervation</u>	<u>Assignment</u>			
			1.30	Singlet	1			
			4.0	Singlet	2			
			4.8	Singlet	3			
			7.2 - 7.3	Multiple	4,5			
			7.4	Doublet	6			
			Carbon-13 Spec	etra:				
				3 10 8 7 9 6 5 5	DI .			
			Chemical Shift (ppm)	Obervation	Assignment			
			22	Singlet	1			
			43	Singlet	2			
			46	Singlet	3			
			77	Multiple	Solvent			
			79	Singlet	4			
			127 – 134	Series of singlets	5-10			
			175	Singlet	11			
Mass spectra (MS)	Quattro LC Mass	Bixlozone pure	m/z = 274:	protonated molecu	ılar ion	Acceptable.		Cowlyn, N.
B.2.4/04	Spectrometer	Purity: 99.8%	m/z = 159:	loss of C ₅ H ₈ NO ₂		The obtained MS spectra are	-	2017c

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
		Batch PL14- 0163		in agreement with the proposed structure.		Study Report No. WP36VB
Spectra for impurities B.2.4/05 Ultraviolet/visible (UV/VIS)	HPLC- UV	(2,4- dichlorophenyl) methanol FMC-61644	The UV spectrum of the major peak from the HPLC analysis was provided. Absorbance maxima have not been reported and molar extinction values at the maxima in acidic, neutral and basic conditions are also required.	Data for the UV/visible absorption spectra in accordance with OECD 101 are required.	N	Wang, J. 2018 Study report No R-1815
Spectra for impurities B.2.4/05 Infrared (IR)	Infrared (FT-IR) Spectrometer fitted with a diamond single bounce attenuated total reflectance (ATR) accessory	(2,4- dichlorophenyl) methanol FMC-61644	Wavenumber (cm ⁻¹) 3212 – 3299: O-H stretch, alcohol 2861 – 2907: C-H stretch, aliphatic 1442 – 1594: C=C aromatic ring stretch 1354 – 1386: C-H bend, aliphatic 1035 – 1275: C-O stretch 646 – 875: C-H bend, aromatic	Acceptable. The obtained IR spectra are in agreement with the structure.	-	Wang, J. 2018 Study report No R-1815
Spectra for impurities B.2.4/05 Nuclear magnetic resonance (NMR)	Bruker 400 MHz Nuclear Magnetic Resonance (NMR) Spectrometer.	(2,4- dichlorophenyl) methanol FMC-61644	Proton Spectra Chemical Shift (ppm) 7.55-7.57 Multiple b 7.55-7.57 Multiple e 7.43-7.46 Multiple d 4.53-4.54 Multiple g 5.49-5.51 Multiple h	Acceptable. The obtained NMR spectra are in agreement with the structure.	-	Wang, J. 2018 Study report No R-1815

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results			Comments (Acceptable / Non acceptable)	GLP	Reference	
			Carbon-13 S Chemical S (ppm) 132 132. 128. 127. 129. 139. 60.2 * Carbons a separately	Shift Ol	bervation upward upward upward - ownward ose to be in	Assignment a* c* b d e f g ndentified			
Spectra for impurities B.2.4/05 Mass spectra (MS)	GC Mass Spectrometer	(2,4- dichlorophenyl) methanol FMC-61644	m/z = 176	protona	ted molecu	ılar ion	Acceptable. The obtained MS spectra is in agreement with the structure.	-	Wang, J. 2018 Study report No R-1815
B.2.5. SOLUBILITY	IN WATER								
Solubility in water B.2.5/01			The following results were obtained at 20°C:				Acceptable. The water solubility of		
EC Method A.6 OECD Method 105		OECD Method 105 EPA OPPTS 830.7840 Bixlozone pure Purity: 99.9% Batch PL14- 0163	Media Concen (mg/L)			Mean Solubility (mg/L)	bixlozone was not significantly affected by pH. Bixlozone is moderately	. _Y	Cowlyn, N. 2016b
	830 7840 B		Purified water	41.95, 42.45 41.63, 42.04		42.0 ± 0.3 mg/L	soluble.		Study Report No. SD77GL
			pH 4 buffer	44.74, 44.77 40.30, 39.59		42.3 ± 2.2 mg/L	Analysis of samples by HPLC-UV. Method is		

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results					Comments (Acceptable / Non acceptable)	GLP	Reference		
			pH 7 buffer		42.54, 38.93 38.56, 38.22			acceptably validated (See Vol 3 B.5.1.2.7).				
			1 -		48.35, 43.02 40.29, 39.77		.9 ± 1.8 g/L					
B.2.6. SOLUBILITY	'IN ORGANIC SOLVE	NTS										
Solubility in organic solvents								A				
B.2.6/01			Solvent		Solubility (g/L) a	ıt 20 °C	Acceptable. Analysis of methanol, n-				
D.2. 0/01		Bixlozone technical Purity: 96.0% Batch: PL14-	Methanol		120			heptane and n-octanol was		Cowlyn, N.		
	CIPAC MT 181 EC Method A6 OCSPP 830.7840		Acetone Toluene		>250 >250			by the flask method (based on Method A.6) and analysed by HPLC-UV.	Y	2017d.		
			Dichloromethane						1	Study Report		
		0049	Ethyl acetate >250 n-Heptane 14				Method is acceptably validated (See Vol 3 B.5.1.2.7).		No. WT84BM			
			n-Octanol		52		İ			D.3.1.2.7).		
B.2.7. PARTITION	COEFFICIENT N-OCT	ANOL/WATER	ı									
Partition coefficient	EC Method A.8	Bixlozone pure	The following	g result	s were obtai	ned at	20°C:	Acceptable.	Y	Cowlyn, N.		
n-octanol/water	OECD Method 107	Purity: 99.9%						Bixlozone has the potential		2016c		
3	EPA OPPTS 830.7550	Batch PL14- 0163	Compound	Buffe soluti		Pow	Log Pow	to be fat soluble. No pH dependence was observed.		Study Report No. RY85CN		
	Shake flask method			pH 4		2100	3.3	Log Pow <4 hence no potential to bioaccumulate.				
				pH 7		2160	3.3	Analysis of samples by				
				pH 9		2060	3.3	HPLC-UV. Method is				
								acceptably validated (See Vol 3 B.5.1.2.7).				

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference	
			Estimation of log K _{ow} (EPI Suite Pre	diction)			
	KOWWIN v1.68 (EPI Suite v4.11,	N/A	Compound	Log K _{ow} Estimation	The estimated values across the metabolites ranged from		Jackson, S.A. 2018
	US EPA) Software		Bixlozone	3.51	1.97 to 3.03. The predicted		Report No.
	Estimation of K _{ow}		5-hydroxy-bixlozone	1.97	log Kow for the parent compound bixlozone		2018PCP-
			4-hydroxymethyl-bixlozone	2.04	compared well with the		ISX4331
			Bixlozone-3-OH-propanamide	2.20	experimentally determined		
			4-carboxy-bixlozone	2.27	value.		
			Bixlozone-dimethylmalonamide	2.43			
			Bixlozone-hydroxy- isobutyramide	2.51			
			2,4-dichlorobenzoic acid	2.82			
			5'-hydroxy- bixlozone	3.03			
Dissociation constant	ON IN WATER		Not applicable as bixlozone does no groups that are ionisable within an	t contain any		N	Guo, J. 2018
B.2.8/01	-	Scientific justification	groups that are ionisable within an environmentally relevant pH range. Water solubility and partition coefficient determinations at different pH's support this, as no pH dependence of these properties observed		Justification is acceptable		Report No. 2018WHP- ISX4284
B.2.9. FLAMMABIL	ITY AND SHELF-HEA	ATING					
Flammability B.2.9/01	EC Method A.10	Bixlozone technical Purity: 96.0% Batch: PL14-	Bixlozone technical material melted with a yellow sooty flame, which ex immediately after the removal of the Combustion did not propagate along a negative result was obtained in the	tinguished burner flame. the train. As	Acceptable.	Y	Cowlyn, N. 2017e Study Report No. FD69CW

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference		
		0049	test, a definitive burning rate test was not required.					
			Bixlozone technical material was not highly flammable.					
Self-heating				Acceptable.				
B.2.9/02	EC Method A.15	Bixlozone technical Purity: 96.0% Batch: PL14- 0049	The auto-ignition temperature was found to be 382°C.	Bixlozone is a solid hence Method A.16 should be used. However, bixlozone was observed to melt at around 81 °C which resulted in material flowing out of the wire mesh cage, preventing measurement. Test A.15 was used as it employed a glass vessel. The use of test A.15 is considered acceptable.	Y	Cowlyn, N. 2017f Study Report No. CX51MQ		
B.2.10. FLASH POI	NT							
Flash point B.2.10/01	-	-	-	Not applicable as bixlozone melting point is > 40°C.	-	-		
B.2.11. EXPLOSIVE PROPERTIES								
Explosive properties B.2.11/01	EC Method A.14 EPA OPPTS 830.6316	Bixlozone technical Purity: 96.0% Batch: PL14- 0049	- No shock sensitivity No reaction observed in six tests using BAM drop hammer (mass 10 kg, drop height 40 cm).	Acceptable. No explosive properties.	Y	Cowlyn, N. 2017g Study Report No. MV81XS		

Test or Study Annex Point	nurity and		Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference		
			- No friction sensitivity					
			No reaction observed in six tests using BAM friction apparatus with a force of 360 N.					
			- No thermal sensitivity					
			No reaction observed in the range 135-285 °C in a 6 mm or 2 mm orifice.					
			Technical bixlozone does not show a danger of explosion.					
B.2.12. SURFACE T	ENSION							
Surface tension		Bixlozone pure		Acceptable.		Cowlyn, N.		
B.2.12/01	EC Method A.5	Purity: 99.8%	90% saturated aqueous solution at 20°C:	The substance is not considered surface active.	Y	2017a		
	OECD Method 115	Batch PL14- 0163	66.5mN/m			Study Report No. FP91QY		
B.2.13. OXIDISING PROPERTIES								
Oxidizing properties B.2.13/01		Bixlozone technical	Mixtures of 2:1, 1:1 or 1:2 bixlozone /cellulose only burned slowly and did not burn to			Cowlyn, N. 2017h		
	EC Method A.17	Purity: 96.0%	completion.	Acceptable.	Y	Study Report		
		Batch: PL14- 0049	Bixlozone technical has no oxidising properties.			No.VK89JJ		

A may Point Guideline and pu		Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
B.2.14. OTHER STU	DIES					
Relative Density B.2.14/01	EC Method A.3 OECD Method 109 EPA OPPTS 830.7300	Bixlozone pure Purity: 99.8% Batch PL14- 0163	The relative density (D_4^{20}) of bixlozone was found to be 1.37.	Acceptable.	Y	Cowlyn,N. 2017i Study Report No. WS55DS

Summary of physical and chemical properties of the active substance

Bixlozone (pure) is a white, crystalline solid with a melting range of $81.5-83.5^{\circ}$ C. It has a vapour pressure of 1.1×10^{-3} Pa at 20° C and a moderate water solubility of 42.0 mg/L. It is readily soluble in organic solvents and has a Log P_{ow} of 3.3, indicating there is a possibility for bioaccumulation, It is not considered surface active. Bixlozone has a self-ignition temperature of 382° C and does not possess explosive or oxidising properties. There are no implications for classification on the basis of the physicochemical properties.

Data to address the UV/visible absorption spectra of the relevant impurity (2,4-dichlorophenyl)methanol (FMC 61644; 2,4-dichlorobenzyl alcohol) are required.

B.2.15. REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCA 2.1/01- 03 KCA 2.3/01 KCA 2.12/01	Cowlyn, N.	2017a	Title: F9600: Physicochemical Properties Study Report No.: FP91QY FMC Report No.: 2016PCP-ISX3022 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.2/01- 02	Cowlyn, N.	2016a	Title: F9600: Vapour Pressure Study Report No.: BM19FW FMC Report No.: 2015PCP-ISX2327 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.3/01	Cowlyn, N.	2017b	F9600 Technical: Appearance Study Report No.: MF50PJ FMC Report No.: 2016PCP-ISX3021 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.4/01- 04	Cowlyn, N.	2017c	Title: F9600: Spectra (UV/Vis, IR, NMR and MS) Report No.: WP36VB FMC Report No.: 2016PCP-ISX3019 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.4/05	Wang, J.	2018	Identification of FMC-61644 (CAS No. 1777-82-8), Reference No. G384:12-1 FMC (Shanghai) CTC Study No. R-1815	N	N	Not applicable	FMC	None (new active)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
			Non-GLP					
			Unpublished					
KCA 2.5/01	Cowlyn, N.	2016b	Title: F9600: Water Solubility Study Report No.: SD77GL FMC Report No.: 2015PCP-ISX2325 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.6/01	Cowlyn, N.	2017d	Title: F9600: Organic Solvent Solubility Study Report No.: WT84BM FMC Report No.: 2016PCP-ISX3018 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.7/01	Cowlyn, N.	2016c	Title: F9600: Partition Coefficient(n-octanol/water) Study Report No.: RY85CN FMC Report No.: 2015PCP-ISX2326 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.7/02	S. A. Jackson	2018	Title: F9600: Partition Coefficient (log K _{ow}) for Metabolites of F9600 FMC Report No.: 2018PCP-ISX4331 Non-GLP Unpublished	N	N	Not applicable	FMC	None (new active)
KCA 2.8/01	Guo, J.	2018	F9600: Waiver Request for Study on Dissociation Constants in Water FMC Report No: 2018WHP-ISX4284 Non-GLP, Unpublished	N	N	Not applicable	FMC	None (new active)
KCA	Cowlyn, N.	2017e	Title: F9600: Flammability (solids)	N	Y	Study to support new active	FMC	None

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
2.9/01			Study Report No.: FD69CW FMC Report No.: 2016PCP-ISX3017 GLP Unpublished			approval in GB		(new active)
KCA 2.9/02	Cowlyn, N.	2017f	Title: F9600: Auto-Ignition Temperature Study Report No.: CX51MQ FMC Report No.: 2017PCP-ISX3136 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.11/01	Cowlyn, N.	2017g	Title: F9600: Explosive Properties Study Report No.: MV81XS FMC Report No.: 2016PCP-ISX3014 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.13/01	Cowlyn, N.	2017h	Title: F9600: Oxidising Properties Study Report No.: VK89JJ 2016PCP-ISX3015 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)
KCA 2.14/01	Cowlyn, N.	2017i	Title: F9600: Relative Density Study Report No.: WS55DS 2016PCP-ISX3020 GLP Unpublished	N	Y	Study to support new active approval in GB	FMC	None (new active)