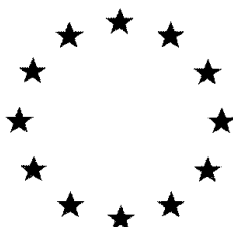


# **European Commission**



**VOLUME 3 – Annex B (AS)**

**- *Flutolanil* -**

**B.2 Physical and chemical properties**

**Rapporteur Member State: The Netherlands**

**June 2018**

**Draft Assessment Report and Proposed decision of the Netherlands prepared  
in the context of the possible approval of flutolanil under Regulation (EC)**

**1107/2009**

## Version history page

Date	Version history
June 2018	Initial RAR

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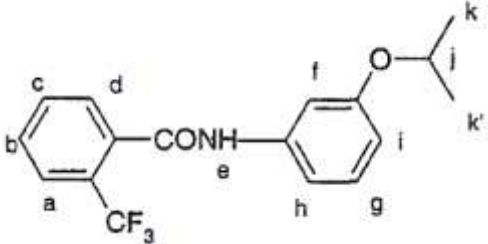
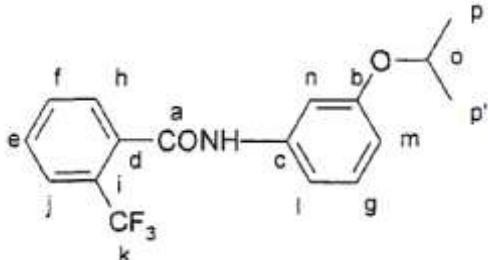
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## B.2 Physical and chemical properties of the active substance

Data that are relied upon that have previously been evaluated to uniform principles are shown in grey.

Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference
<b>B.2.1</b> Melting point and boiling point	Dir 92/69/EEC Method A1	Pure flutolanil Purity: 99.8% Batch: BESS288	Melting point: 103.9 – 105.2°C	Acceptable	Y	CA 2.1/01*: Ristorcelli (2001a) (PC-3022)
	Dir 92/69/EEC Method A2		Boiling starts at 300°C and is accompanied by decomposition.	Acceptable	Y	
<b>B.2.2</b> Vapour pressure, volatility	OECD method 104 (Knudsen Effusion method)	Pure flutolanil Purity: 99.8% Batch: BESS288	Vapour pressure: $4.1 \times 10^{-7}$ Pa at 20°C & $1.0 \times 10^{-6}$ Pa at 25°C	Acceptable	Y	CA 2.2/01*: Ristorcelli (2001b) (PC-3021)
	Quotient of vapour pressure and water solubility	Not applicable - calculation	Volatility, Henry's law constant: $1.65 \times 10^{-5}$ Pa.m <sup>3</sup> .mol <sup>-1</sup> at 20°C (Values used – water solubility: 8.01 mg/L at 20°C and vapour pressure: $4.1 \times 10^{-7}$ Pa at 20°C)	Acceptable	N/A	CA 2.2/02*: Morrissey, MA (1997a) (PC-3017)

Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference										
<b>B.2.3</b> Appearance (Physical state, colour)	OPPTS 830.6302 (colour); OPPTS 830.6303 (appearance) & OPPTS 830.6304 (odour)	Pure flutolanil Purity: 99.8% Batch: BESS288	Appearance: White powder Odour: Slightly chemical	Acceptable	Y	CA 2.3/01* Ristorcelli (2001a) (PC-3022)										
		Flutolanil as manufactured Purity: 99.3% Batch: 950026	Appearance: White solid Odour: Slightly chemical													
<b>B.2.4</b> Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant wavelengths, optical purity	OECD 101	Pure flutolanil Purity: 99.8% Batch: EA530SD4	<u>UV/Vis</u> The UV/Vis absorption spectrum of flutolanil was measured in neutral and acidic methanolic solutions.  <u>Neutral solution</u> $\lambda_{\text{max}} = 208.5 \text{ nm}$ ; $\epsilon = 11709 \text{ l mol}^{-1} \text{ cm}^{-1}$ $\lambda_{\text{max}} = 292.0 \text{ nm}$ ; $\epsilon = 33109 \text{ l mol}^{-1} \text{ cm}^{-1}$ <u>Acidic solution</u> $\lambda_{\text{max}} = 248.0 \text{ nm}$ ; $\epsilon = 10739 \text{ l mol}^{-1} \text{ cm}^{-1}$ $\lambda_{\text{max}} = 212.5 \text{ nm}$ ; $\epsilon = 32126 \text{ l mol}^{-1} \text{ cm}^{-1}$  No absorption above 317.5 nm was observed in neutral solution.  <u>IR</u> The IR absorption spectrum of flutolanil was measured between $4000 \text{ cm}^{-1}$ and $400 \text{ cm}^{-1}$ (KBr disc). <table><tr><th>Wavenumber / <math>\text{cm}^{-1}</math></th><th>Assignment</th></tr><tr><td>3253</td><td>N-H stretching</td></tr><tr><td>1658</td><td>C=O stretching</td></tr><tr><td>1549</td><td>N-H bending</td></tr><tr><td>1317 &amp; 1130</td><td>CF<sub>3</sub> stretching</td></tr></table>	Wavenumber / $\text{cm}^{-1}$	Assignment	3253	N-H stretching	1658	C=O stretching	1549	N-H bending	1317 & 1130	CF <sub>3</sub> stretching	Acceptable	Y	CA 2.4/01* Guesnet (2000) (PC-3015)
Wavenumber / $\text{cm}^{-1}$	Assignment															
3253	N-H stretching															
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Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference																											
			<p><u><sup>1</sup>H NMR</u></p> <div></div> <table><thead><tr><th>Chemical shift / ppm</th><th>Multiplicity</th><th>Assignment</th></tr></thead><tbody><tr><td>7.71</td><td>Doublet</td><td>a</td></tr><tr><td>7.65-7.50</td><td>Multiplet</td><td>b, c, d, e</td></tr><tr><td>7.31</td><td>Singlet</td><td>f</td></tr><tr><td>7.22</td><td>Triplet</td><td>g</td></tr><tr><td>7.02</td><td>Doublet</td><td>h</td></tr><tr><td>6.70</td><td>Doublet</td><td>i</td></tr><tr><td>4.56</td><td>Multiplet</td><td>j</td></tr><tr><td>1.33</td><td>Triplet</td><td>k and k'</td></tr></tbody></table> <p><u><sup>13</sup>C NMR</u></p> <div></div>	Chemical shift / ppm	Multiplicity	Assignment	7.71	Doublet	a	7.65-7.50	Multiplet	b, c, d, e	7.31	Singlet	f	7.22	Triplet	g	7.02	Doublet	h	6.70	Doublet	i	4.56	Multiplet	j	1.33	Triplet	k and k'			
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Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference																		
			<div>MS (ACPI, negative ion mode):<table><tr><th>M/Z</th><th>Assignment</th></tr><tr><td>322</td><td>[M – H]<sup>-</sup></td></tr><tr><td>281</td><td>(M – [C<sub>3</sub>H<sub>7</sub> – H])<sup>-</sup></td></tr></table></div>	M/Z	Assignment	322	[M – H] <sup>-</sup>	281	(M – [C <sub>3</sub> H <sub>7</sub> – H]) <sup>-</sup>															
M/Z	Assignment																							
322	[M – H] <sup>-</sup>																							
281	(M – [C <sub>3</sub> H <sub>7</sub> – H]) <sup>-</sup>																							
B.2.5 Solubility in water	Dir 92/69/EEC Method A6	Pure flutolanil Purity: 99.8% Batch: EA530SD4	Solubility in water at 20°C: 8.01 mg/L Since flutolanil does not form ions, the water solubility was determined in neutral water only.	Acceptable	Y	CA 2.5/01* Morrissey (1997a) (PC-3017)																		
B.2.6 Solubility in organic solvents	OECD 105	Flutolanil as manufactured Purity: 99.3% Batch: 950026	<div>Solubility in organic solvents at 20°C:<table><tr><th>Solvent</th><th>Solubility / g/L</th></tr><tr><td>Acetone</td><td>606</td></tr><tr><td>Acetonitrile</td><td>334</td></tr><tr><td>Dichloromethane</td><td>378</td></tr><tr><td>Ethyl acetate</td><td>365</td></tr><tr><td>n-hexane</td><td>0.39</td></tr><tr><td>Methanol</td><td>322</td></tr><tr><td>n-octanol</td><td>42</td></tr><tr><td>Toluene</td><td>35</td></tr></table></div>	Solvent	Solubility / g/L	Acetone	606	Acetonitrile	334	Dichloromethane	378	Ethyl acetate	365	n-hexane	0.39	Methanol	322	n-octanol	42	Toluene	35	Acceptable	Y	CA 2.6/01* Ristorcelli (2001c) (PC-3023)
Solvent	Solubility / g/L																							
Acetone	606																							
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B.2.7 Partition co-efficient n-octanol/ water	Dir 92/69/EEC Method A8	<div>Pure flutolanil Purity: 100% Batch: 5AE0005P</div> <div>Components of the risk assessment residue definition</div>	<div>Partition coefficient Log P<sub>OW</sub> at 21°C, unbuffered water: 3.17</div> <div>Theoretical Log P<sub>OW</sub> values can be calculated computationally if required once the risk assessment residue definitions have been agreed.</div>	Acceptable	Y	CA 2.7/01* Morrissey (1997b) (PC-3018)																		



Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference
<b>B.2.8</b> Dissociation in water	Expert statement	Not applicable	An examination of the chemical structure of flutolanil indicates that there are no acidic, basic or other functionalities in the molecule that could be dissociated in acidic, neutral or basic water. This was confirmed by a computational estimation of the pKa for flutolanil using ACD Lab pKa module® (version 4. 06). This indicated two theoretical acidic dissociation equilibria – firstly the loss of a proton from the protonated form of the amide nitrogen with an estimated pKa <sub>1</sub> of -2.52; secondly deprotonation of the amide nitrogen in its neutral state to form N <sup>-</sup> with an estimated pKa <sub>2</sub> of 12.44. It was determined that these dissociation constants could not be measured since the required pKas that would needed to be reached are outside of the pH range achievable in aqueous solution.	<b>Acceptable</b>	N	CA 2.8/01* Bascou (2002) (PC-3029)
<b>B.2.9</b> Flammability and self-heating	Flammability of solids: Dir 92/69/EEC Method A10  Self-ignition temperature of solids: Dir 92/69/EEC Method A16	Pure flutolanil Purity: 99.3% Batch: 9950026	Flammability: Flutolanil is not classified for flammability  Self-ignition: Flutolanil did not self-ignite prior to melting	<b>Acceptable</b>	Y	CA 2.9/01* Francois (2000) (PC-3020)
<b>B.2.10</b> Flash point			Not applicable – this test is not required for solid substances			
<b>B.2.11</b> Explosive properties	Dir 92/69/EEC Method A14	Pure flutolanil Purity: 99.3% Batch: 9950026	Flutolanil is not classified as explosive (shock, friction, thermal sensitivity)	<b>Acceptable</b>	Y	CA 2.11/01* Francois (2000) (PC-3020)

Data Point	Guideline and method	Test material purity and specification	Results	Comment	GLP Y/N	Reference
<b>B.2.12</b> Surface Tension	OECD 115	Pure flutolanil Purity: 99.8% Batch: BESS288	Surface tension of a 90% saturated aq. solution at 20°C: 71.3 mN/m. Flutolanil is not a surface active substance	<b>Acceptable</b>	Y	CA 2.12/01* Ristorcelli (2001a) (PC-3022)
<b>B.2.13</b> Oxidising properties	Dir 92/69/EEC Method A17	Pure flutolanil Purity: 99.3% Batch: 9950026	Flutolanil is not classified as oxidising	<b>Acceptable</b>	Y	CA 2.13/01* Francois (2000) (PC-3020)
<b>B.2.14</b> Other studies	OECD 109	Pure flutolanil Purity: 99.8% Batch: BESS288	Relative density at 20°C: 1.321	<b>Acceptable</b>	Y	CA 2.14/01* Ristorcelli (2001a) (PC-3022)

\* These studies were evaluated under Uniform Principles for the first approval of flutolanil and are considered acceptable for the renewal of approval.

### 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
CA 2.1/01	Ristorcelli, D.	2001a	Flutolanil: Physical Characteristics Covance Laboratories Ltd PC-3022 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.2/01	Ristorcelli, D.	2001b	Flutolanil -Vapour Pressure Covance Laboratories Ltd PC-3021 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.2/02	Morrissey M. A.	1997a	FLUTOLANIL: Determination of water solubility Covance Laboratories Inc. PC-3017 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.3/01	Ristorcelli, D.	2001a	Flutolanil: Physical Characteristics Covance Laboratories Ltd PC-3022 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.4/01	Guesnet, J. L.	2000	Flutolanil NMR, IR, MS and UV-visible spectra Aventis CropScience PC-3015 GLP: Yes Published: No	N	N	-	Nihon Nohyaku
CA	Morrissey M.	1997a	FLUTOLANIL: Determination of water solubility	N	N	-	Nihon Nohyaku

2.5/01	A.		Covance Laboratories Inc. PC-3017 GLP: Yes Published: No				Co. Ltd
CA 2.6/01	Ristorcelli, D.	2001c	Flutolanil - Solvent Solubility Covance Laboratories Ltd PC-3023 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.7/01	Morrissey, M. A.	1997b	Flutolanil: Determination of Octanol/Water Partition Coefficient Covance Laboratories Inc. PC-3018 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.8/01	Bascou, J. P.	2002	Flutolanil Assessment on the dissociation constant Aventis CropScience PC-3029 GLP: No Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.9/01	Francois, J. M.	2000	Flutolanil - Determination of the explosion properties, flammability, ability for self heating and oxidising properties Rhodia Rhoditech PC-3020 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.11/01	Francois, J. M.	2000	Flutolanil - Determination of the explosion properties, flammability, ability for self heating and oxidising properties Rhodia Rhoditech PC-3020 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.12/01	Ristorcelli, D.	2001a	Flutolanil: Physical Characteristics Covance Laboratories Ltd PC-3022 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd

CA 2.13/01	Francois, J. M.	2000	Flutolanil - Determination of the explosion properties, flammability, ability for self heating and oxidising properties Rhodia Rhoditech PC-3020 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd
CA 2.14/01	Ristorcelli, D.	2001a	Flutolanil: Physical Characteristics Covance Laboratories Ltd PC-3022 GLP: Yes Published: No	N	N	-	Nihon Nohyaku Co. Ltd