European Commission

Draft Assessment Report prepared according to the Commission Regulation (EU) N° 1107/2009

Napropamide-M

Volume 3 – B.2 (AS)

Rapporteur Member State: United Kingdom

Version History

When	What
June 2017	Initial DAR

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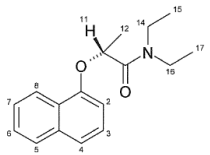
B.2. PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE – NAPROPAMIDE-M

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 POINT AND BOILING POINT						
Melting, freezing or solidification point **B.2.1/01**	Method EEC A1 (DSC)	napropamide-M Batch No: UPH-08/DNE-263/PURE/20121222, Purity: 99.85% (total D- + L-isomer) Napropamide reference standard (racemate) – batch No – UPH-08/NE-261/STD/20121227, Purity: 99.82% (total D- + L-isomer)	Melting Point (ºC) [tested at atmospheric pressure = 101 kPa] Napropamide-M : 92.2 Napropamide (racemate) : 71.2	Acceptable.	Yes	Bates, G. (2014), J19544
Boiling point **B.2.1/02**	Method EEC A2 (DSC)	Napropamide-M Purity: 99.85% (total D- + L-isomer) (Batch No: UPH-08/DNE-263/PURE/20121222) Napropamide (racemate) Purity: 99.82% (total D- + L-isomer) (Batch No – UPH-08/NE-261/STD/20121227)	Boiling Point (ºC) [tested at atmospheric pressure = 101 kPa] Napropamide-M : 319.4 Napropamide (racemate) : 319.3	Acceptable	Yes	Bates, G. (2014), J19544
Decomposition / Sublimation temperature **B.2.1/03**	Method EEC A2	Napropamide-M Purity: 99.85% (total D- + L-isomer) Batch No: UPH-08/DNE-263/PURE/20121222,	See B.2.01 above, the boiling point was determined by DSC using method EEC A2, and the temperature of decomposition was not ascertained.	Acceptable	Yes	Bates, G. (2014), J19544

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td colspan="7">B.2.2. VAPOUR PRESSURE, VOLATILITY</td></tr>
<tr><td>Vapour pressure
B.2.2/01</td><td>OECD 104,
EEC A4
(Effusion Method)</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)</td><td>The vapour pressure was measured at a higher temperature (50-60°C) and the vapour pressure at 25°C was determined by calculation as 3.80 x 10^{-6} Pa.</td><td>Acceptable</td><td>Yes</td><td>Patel, A.H (2013), 207-2-11-6176</td></tr>
<tr><td>Volatility (Henry’s Law constant)
B.2.2/02</td><td>Calculation</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)</td><td>The Henry’s law constant for napropamide-M was calculated from experimentally determined values of vapour pressure and water solubility.
<table><tr><th>Henry’s law constant</th><th>Units</th></tr><tr><td>2.644 x 10^{-5}</td><td>Pa m^3 mol^{-1}</td></tr><tr><td>1.076 x 10^{-8}</td><td>dimensionless</td></tr></table>The Henry’s law constant is <b>2.644 x 10-5 Pa m^{3}mol^{-1}</td><td>Acceptable</td><td>N</td><td>Peatman, M.H (2014), UPL/16/01-HLC1</td></tr>
<tr><td colspan="7">B.2.3. APPEARANCE (PHYSICAL STATE, COLOUR)</td></tr>
<tr><td>Physical state and colour
B.2.3/01</td><td>Visual assessment</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)
Napropamide-M technical Batch No: UPH-08/DNE-263/TECH/20121226
Purity: 97.26% (total D- + L-isomer)</td><td>Napropamide-M purified: Beige crystalline solid with no discernible odour.
Napropamide-M technical: Beige, crystalline, solid with minty, phenolic, type odour.</td><td>Noted</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
</table>

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td colspan="7">B.2.4. SPECTRA (UV/VIS, IR, NMR, MS), MOLAR EXTINCTION AT RELEVANT WAVELENGTHS, OPTICAL PURITY</td></tr>
<tr><td>Ultraviolet/visible (UV/VIS)
B.2.4/01</td><td>OECD 101
(UV/Vis)</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)</td><td>The test material was diluted in ethanol and aliquots of this solution were added to solutions of: 1. water (pH 1.98 – acid medium), 2. water (pH 10.14 – alkaline medium) and 3. water (pH 7.10 – neutral medium)
<u>Acidic media:</u>
<table><tr><td>λ max (nm)</td><td>ε (L.mol^{-1}.cm^{-1})</td></tr><tr><td>217</td><td>4.8139 x 10^4</td></tr><tr><td>289</td><td>4.987 x 10^3</td></tr></table><u>Neutral media:</u>
<table><tr><td>λ max (nm)</td><td>ε (L.mol^{-1}.cm^{-1})</td></tr><tr><td>217</td><td>5.2385 x 10^4</td></tr><tr><td>290</td><td>5.579 x 10^3</td></tr></table><u>Basic/ alkali media:</u>
<table><tr><td>λ max (nm)</td><td>ε (L.mol^{-1}.cm^{-1})</td></tr><tr><td>217</td><td>1.3123 x 10^5</td></tr><tr><td>291</td><td>2.271 x 10^3</td></tr></table></td><td>Data generated between 190 – 750 nm.
Acceptable.</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
<tr><td>Infrared (IR)
B.2.4/02</td><td>FTIR</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)</td><td>The active substance was examined by Fourier Transform Infra red (FTIR) Spectroscopy. The sample was examined by preparing IR disc consisting of nampropamide-M (purified material) and a previously dried FTIR grade Potassium Bromide
<table><tr><th>Wavenumber (cm^{-1})</th><th>Signal type</th></tr><tr><td>3000-3100</td><td>Alkene (C-H)</td></tr><tr><td>1625 - 1650</td><td>Alkene (C=C)</td></tr><tr><td>3000 - 3100</td><td>Aromatic (C-H)</td></tr><tr><td>1570 – 1625, 1475 – 1525</td><td>Aromatic (C=C)</td></tr><tr><td>2800 - 3000</td><td>Alkane (C-H)</td></tr></table></td><td>The observed spectrum was consistent with the structure for a match with napropamide-M.
Acceptable.</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
</table>

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>1625 - 1700</td><td>Amide (C=O)</td></tr>
<tr><td>1100 - 1200</td><td>Amide (C-O)</td></tr>
<tr><td>2900 – 3000, 2840 – 2920, 1425 -1475, 1350 - 1400</td><td>Alkane (CH_3-CH)</td></tr>
<tr><td>2910 – 3000, 2875 – 2960, 2820 – 2890, 1425 – 1475, 1350 – 1400, 840 – 900, 750 - 800</td><td>Alkane (Ethyl)</td></tr>
<tr><td>3050 – 3110, 2910 – 3055, 1700 – 1800, 1390 – 1450, 1060 – 1120, 875 – 925, 525 - 700</td><td>Alkane (R-CH=CH_2)</td></tr>
<tr><td>1310 – 1400, 1160 – 1290</td><td>Aromatic (Aromatic)</td></tr>
<tr><td colspan="2">Molecule assignments</td></tr>
<tr><td>1575 - 1700</td><td>C=C Stretch</td></tr>
<tr><td>1300 - 1475</td><td>CH Bend</td></tr>
<tr><td>900 - 1300</td><td>C-O Stretch</td></tr>
<tr><td>900 - 1300</td><td>C-N Stretch</td></tr>
<tr><td>800 - 1200</td><td>C-C Stretch</td></tr>
<tr><td>600 - 900</td><td>C-H Rock</td></tr>
</table>
</td><td></td><td></td><td></td></tr>
<tr><td>Nuclear magnetic resonance (NMR)
B.2.4/03</td><td>^{1}H-NMR</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/D-STD/20121221
Purity: 99.91% (total D- + L-isomer)
(D-isomer or ‘R’ isomer - 100%
L-isomer or ‘S’ isomer– 0%)</td><td>

<table>
<tr><td rowspan="2">Solvent: $CDCl_3$</td><td colspan="3">^{1}H, Test item</td></tr>
<tr><td>Shift</td><td>Mult.</td><td>H’s</td></tr>
<tr><td>2</td><td>6.85</td><td>d</td><td>1</td></tr>
<tr><td>3</td><td>7.36</td><td>t</td><td>1</td></tr>
<tr><td>4</td><td>7.47</td><td>d</td><td>1</td></tr>
<tr><td>5</td><td>7.82</td><td>m</td><td>1</td></tr>
<tr><td>6, 7</td><td>7.51</td><td>m</td><td>2</td></tr>
</table>
</td><td>1H-NMR produced data consistent with the proposed structure of napropamide-M. Acceptable.</td><td>Yes</td><td>Marshall, I. (2013), SEL/7234/1</td></tr>
</table>

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>8</td><td>8.82</td><td>m</td><td>1</td></tr>
<tr><td>11</td><td>5.15</td><td>q</td><td>1</td></tr>
<tr><td>12</td><td>1.76</td><td>d</td><td>3</td></tr>
<tr><td>14, 16</td><td>3.41, 3.47, 3.59#</td><td>3 * m</td><td>4</td></tr>
<tr><td>15, 17</td><td>1.02, 1.13#</td><td>2 * t</td><td>6</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td>solvent</td><td>1.67, 7.28</td><td>bs, s</td><td>-</td></tr>
</table>
- signals are complex due to restricted rotation about amide bond.
</td><td></td><td></td><td></td></tr>
<tr><td>Mass spectra (MS)
B.2.4/04</td><td>GC-MS</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222,
Purity: 99.85% (total D- + L-isomer)</td><td>The retention time of the napropamide-M reference standard and active substance have identical retention time of 10.732 min.
Acquisition range – m/z 50 - 300
Molecular ion – m/z 271, Typical fragmentations: strong base ion at m/z 72, other major ions and associated clusters – m/z 171, 128, 115, 100, 57.</td><td>The observed spectrum was consistent with the structure for a match with napropamide-M.
Acceptable.</td><td>Yes</td><td>Bates, G. (2014), J19544</td></tr>
<tr><td>Optical Purity
B.2.4/05</td><td>Chiral HPLC-UV</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/D-STD/20121221
Purity: 99.91% (total D- + L-isomer)
(D-isomer or ‘R’ isomer - 100%
L-isomer or ‘S’ isomer– 0%)
Napropamide (racemate) Reference standard.
UPH-08/NE-261/SRD/20121227
Purity: 99.82% (total D- + L-isomer)
(D-isomer or ‘R’ isomer - 49.745%, L-isomer or ‘S’ isomer – 50.255%)</td><td>The test item sample of napropamide-M was shown to consist entirely of the D-isomer (or ‘R’ isomer) by HPLC chiral analysis. Comparison with the sample of napropamide racemate standard allowed confirmation of elution time for the D (‘R’) and L (‘S’) isomers.

Method validation data were not provided, however the applicant noted that this was a chemical properties spectral test to provide ‘qualitative’ NMR data on the provided (certified) napropamide-M test item. The determination of the chiral ratio (optical purity) using chiral HPLC conditions was conducted to demonstrate qualitatively that it was 100% optically pure D isomer, i.e. napropamide-M.</td><td>Acceptable (see separate data on determination of chiral ratio/optical purity in vol 4 and section B5).</td><td>Yes</td><td>Marshall, I. (2013), SEL/7234/1</td></tr>
<tr><td>Spectra for</td><td></td><td></td><td>No data has been provided.</td><td></td><td></td><td></td></tr>
</table>

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
impurities **B.2.4/06**						
B.2.5. SOLUBILITY IN WATER						
Solubility in water **B.2.5/01**	EEC A6 (Flask method) HPLC Method M798	Napropamide-M Batch No: UPH-08/DNE-263/PURE/20121222 Purity: 99.85% (total D- + L-isomer)	The solubility of napropamide-M in water is approximately 0.039g/L or 39 mg/L at 20ºC The solubility of napropamide-M in water is very low. GC Laboratories HPLC Method M798 was used to determine content of napropamide-M in water. This method (M798) was fully validated in accordance with SANCO3029/99/rev.4 The solubility was assessed at 'neutral' pH. [The report noted how the water was assessed as too acidic (pH of 5.8) and so an adjustment was made by adding a few drops of 0.1 M NaOH. The final pH of the test solution was not reported]	It is noted in the data requirements (EU) 283/2013 that 'If the active substance has a pKa value between 2 and 12 water solubility shall also be determined in acidic range (pH 4-5) and the alkaline range (pH9 to 10)'. The dissociation constant (pKa) of napropamide-M pure has not been determined as Napropamide-M is neither acid nor base and dissociation is not expected to occur. As such the water solubility has only been determined at a neutral pH only. This is acceptable.	Y	Bates, G. (2014), J19544
B.2.6. SOLUBILITY IN ORGANIC SOLVENTS						

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td>Solubility in organic solvents
B.2.6/01</td><td>CIPAC Method MT181</td><td>Napropamide-M technical
Batch No: UPH-08/DNE-263/TECH/20121226

Purity: 97.26 % (total D- + L-isomer)</td><td>Test was repeated to improve accuracy of reported results (preliminary results had not given reasonable agreement with published values). The following results were then obtained (rest temperature 21°C):
<table><tr><th>Solvent Class</th><th>Solvent</th><th>Solubility (g/L)
Av</th></tr><tr><td>Aliphatic hydrocarbon</td><td>n-Heptane</td><td>< 10</td></tr><tr><td>Aaromatic hydrocarbon</td><td>p-Xylene</td><td>> 200</td></tr><tr><td>Halogenated hydrocarbon</td><td>1,2 - Dichloroethane</td><td>> 250</td></tr><tr><td>Alcohol</td><td>Methanol</td><td>> 250</td></tr><tr><td>Ketone</td><td>Acetone</td><td>> 250</td></tr><tr><td>Ester</td><td>Ethyl acetate</td><td>> 200</td></tr></table></td><td>MT 181 is not specifically tailored to determine the solubility of materials with solubility lower than 10 g/L, therefore the solubility in n-Heptane has not specifically been determined.

In view of the results the solubility in solvents has only been approximately determined for all of the solvents tested, however the data requirements (Regulation 283/2013) request that solubility in organic solvents should be determined and reported if less than 250 g/L

Acceptable</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
<tr><td colspan="7">B.2.7. PARTITION COEFFICIENT N-OCTANOL/WATER</td></tr>
<tr><td>Partition coefficient n-octanol/water
B.2.7/01</td><td>EEC A8, OECD 107 (HPLC Method M789)</td><td>Napropamide-M
Batch No: UPH-08/DNE-263/PURE/20121222
Purity: 99.85% (total D- + L-isomer)</td><td>Shake flask method used.
The value of Log Pow obtained for napropamide-M at 22ºC and pH 7 was 3.27

GC Laboratories HPLC Method M798 was used to determine partition coefficient. The method M798 was fully validated in accordance with SANCO3029/99/rev.4.</td><td>It is noted in the data requirements (EU) 283/2013 that ‘The effect of pH (4 to 10) shall be investigated when the active substance has a pKa value between 2 and 12’. The dissociation constant (pKa) of napropamide-M pure has not been determined as</td><td>Yes</td><td>Bates, G. (2014), J19544</td></tr>
</table>

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
				Napropamide-M is neither acid nor base and dissociation is not expected to occur. As such the partition coefficient has only been determined at a neutral pH. This is acceptable.		
Partition coefficient n-octanol/water B.2.7/02	OECD 107 (shake-flask method) and EPI SUITE data (KOWWIN version 1.68) calculation method	2-(1-naphthyloxy) propanoic acid [NOPA] Batch No. UPH-08/DNE-263/NOPA/216-14 Purity: 99.15 %	Log Pow: 4.23 (see comment) Determined at pH 7.30 and 23ºC GC Laboratories HPLC Method M844 was used to determine partition coefficient Method M844 was not fully validated in accordance with SANCO3029/99/rev.4 for NOPA, and the determination is not considered that reliable for the levels of NOPA determined in the aqueous phase. See section B.5 for further details. EPI SUITE data for comparison (KOWWIN version 1.68) Log Pow: 2.92 (see comment)	The method of analysis (M844) was not appropriately validated and the evaluator of the methods of analysis concluded that the determination of this analyte in the aqueous phase was not reliable, as such these experimentally derived data for NOPA should not be relied upon. The EPI suite data (calculated estimates) are also presented (it is difficult to know how reliable these theoretical estimates/calculated values are).	Y	Bates, G. (2015) J20145
Partition coefficient n-octanol/water B.2.7/03	OECD 107 (shake-flask method) and EPI SUITE data (KOWWIN version 1.68) calculation method	Naphthalen-1-ol [alpha-naphthol] Batch No. SZB8325XV Purity: 99.90%	Log Pow: 2.83 Determined at pH 7.30 and 21.5ºC GC Laboratories HPLC Method M844 was used to determine partition coefficient. For alpha-napththol, Method M844 was regarded as adequately validated. See section B.5 for further details. EPI SUITE data for comparison (KOWWIN version 1.68)	Acceptable- there is reasonably good agreement between the experimentally derived and calculated (EPI suite data) values.	Y	Bates, G. (2015) J20145

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
			Log Pow: 2.69			
Partition coefficient n-octanol/water B.2.7/04	OECD 107 (shake-flask method) and EPI SUITE data (KOWWIN version 1.68) calculation method	N,N-diethyl-2-(4-hydroxy-1-naphthyl)propanamide [napropamide Isomer I] BatchNo: UPH-08/DNE-263/ISM-I/271 Purity: 96.98%	Log Pow: 3.08 Determined at pH 7.30 and 21.0ºC GC Laboratories HPLC Method M844 was used to determine partition coefficient For isomer-I, Method M844 was regarded as adequately validated. See section B.5 for further details. EPI SUITE data for comparison (KOWWIN version 1.68) Log Pow: 3.32	Acceptable- there is reasonably good agreement between the experimentally derived and calculated (EPI suite data) values.	Y	Bates, G. (2015) J20145
Partition coefficient n-octanol/water B.2.7/05	OECD 107 (shake-flask method) and EPI SUITE data (KOWWIN version 1.68) calculation method	N,N-diethyl-2-(1-hydroxy-2-naphthyl)propamide [Napropamide Isomer II] Batch No: UPH-08/DNE-263/ISM-II/271-14 Purity: 96.80%	Log Pow: 2.52 (see comment) Determined at pH 7.30 and 22.5ºC GC Laboratories HPLC Method M844 was used to determine partition coefficient Method M844 was not fully validated for Isomer II in accordance with SANCO3029/99/rev.4. See section B.5 for further details. EPI SUITE data for comparison (KOWWIN version 1.68) Log Pow: 3.32 (see comment)	Method M844 was not fully validated in accordance with SANCO3029/99/rev.4 for Isomer II, and the determination of Isomer II in this test was not regarded as reliable. . Calculated values are also presented, it is difficult to know how reliable these theoretical/calculated values are.	Y	Bates, G. (2015) J20145
B.2.8. DISSOCIATION IN WATER						
Dissociation constant **B.2.8/01**	OECD 112 (Titrimetric Method)	Napropamide-M Batch No: UPH-08/DNE-263/PURE/20121222 Purity: 99.85% (total D- + L-isomer)	The napropamide-M purified material has no measurable dissociation constant (tested at 20°C).	Under test conditions, the active substance has been shown to not dissociate.	Y	Bates, G. (2014), J19544

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td colspan="7">B.2.9. FLAMMABILITY AND SHELF-HEATING</td></tr>
<tr><td>Flammability
B.2.9/01</td><td>EEC A10</td><td>Napropamide-M technical
Batch No: UPH-08/DNE-263/TECH/20121226
Purity: 97.26 % (total D- + L-isomer)</td><td>The attempts at igniting the sample of technical material failed. The flame was applied for 2 minutes. The sample melted within second and pooled into an oily liquid. Sample did not ignite and flame did not propagate any distance.

The test item is considered as not highly flammable.</td><td>Acceptable</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
<tr><td>Self-heating
B.2.9/02</td><td>EEC A16</td><td>Napropamide-M technical
Batch No: UPH-08/DNE-263/TECH/20121226
Purity: 97.26% (total D- + L-isomer)</td><td>No exothermic activity observed (the test item does not self ignite). Test conducted up to 400°C.</td><td>Acceptable</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
<tr><td colspan="7">B.2.10. FLASH POINT</td></tr>
<tr><td>Flash point
B.2.10/01</td><td>EEC A9</td><td>-</td><td>-</td><td>The flash point was not determined as the melting point of the active substance is above 40ºC. Acceptable.</td><td>-</td><td>-</td></tr>
<tr><td colspan="7">B.2.11. EXPLOSIVE PROPERTIES</td></tr>
<tr><td>Explosive properties
B.2.11/01</td><td>Differential Scanning Calorimetry
and
Reasoned case</td><td>Napropamide-M technical
Batch No: UPH-08/DNE-263/TECH/20121226
Purity: 97.26% (total D- + L-isomer)</td><td><u>Reasoned case:</u>
The applicant stated that napropamide-M does not contain any groups that directly suggest explosives properties e.g. nitrates, chlorates, nitrate esters, aromatic nitro, aliphatic nitro, nitramine, azide, nitroso, perchlorate, acetylides.
In addition napropamide-M does not contain groups that are able to contribute to the explosive property when present alongside groups directed associated with explosivity (e.g. hydroxyl, carbonyl, ether, amino, sulphonic acid). There is no realistic possibility that the compound present a risk of explosion.
<table>
<tr><td>DSC Ref</td><td>A</td><td>B</td></tr>
<tr><td>Sample weight</td><td>2.068 mg</td><td>2.249 mg</td></tr>
<tr><td>Onset</td><td>315.01 ºC</td><td>292.67 ºC</td></tr>
<tr><td>ΔH</td><td>-75.145 J/g</td><td>-63.354 J/g</td></tr>
</table></td><td>The commission communication (2013/C 95/01) states that A.14 is an appropriate test method to follow when testing the explosive properties.
The method EEC A14 comprises three parts:
a) A test of thermal sensitivity</td><td>Y</td><td>Bates, G. (2014), J19544</td></tr>
</table>

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
			No significant exothermic event (very small events only) were observed when test substance was heated in a sealed crucible between 30ºC and 400ºC at the rate of 10ºC/minute and therefore showed no evidence of tendency to thermal explosivity. The test material (napropamide-M) does not constitute a explosivity hazard.	b) A test of mechanical sensitivity with respect to shock c) A test of mechanical sensitivity with respect to friction. The applicant has only addressed the thermal explosivity tendency but has not addressed any potential sensitivity with respect to shock or to friction. The DSC test performed and the reasoned case presented shows that napropamide-M does not have an indication of a tendency to be explosive. Acceptable		
B.2.12. SURFACE TENSION						
Surface tension **B.2.12/01**	EEC A5	Napropamide-M Batch No: UPH-08/DNE-263/PURE/20121222 Purity: 99.85% (total D- + L-isomer)	In accordance with EEC method A5, a 90% saturated solution in water was used for testing. Surface tension at 20ºC: 56.9 mN/m Surface tension at 40ºC:	Acceptable.	Y	Bates, G. (2014), J19544

<table>
<tr><th>Test or Study Annex Point</th><th>Guideline and method</th><th>Test material purity and specification</th><th>Used methods / Results</th><th>Comments (Acceptable / Non acceptable)</th><th>GLP</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>56.2 mN/m

The surface tension of napropamide-M at 20ºC is below 60mN/m therefore should be regarded as being a surface-active material.</td><td></td><td></td><td></td></tr>
<tr><td colspan="7">B.2.13. OXIDISING PROPERTIES</td></tr>
<tr><td>Oxidizing properties
B.2.13/01</td><td>EEC A17
And
Reasoned case</td><td>Napropamide-M technical
Batch No: UPH-08/DNE-263/TECH/20121226
Purity: 97.26% (total D- + L-isomer)</td><td><u>Reasoned case:</u>
The applicant stated that the molecular structure of napropamide-M does not contain any oxidising groups such as peroxide, chlorate, perchlorate, nitrate, bromate, chromate, etc. Therefore there is no realistic possibility that the technical material presents oxidation hazard. The applicant went onto conduct EEC A17 to further confirm this.
EEC A.17:
<u>Preliminary test:</u>
Cone test: The sample burned producing thick white fumes but did not produce a vigorous reaction. The sample burned to completion in 12 minutes. This was within the maximum burning rate of the reference mixture (1.5 minute).

<u>Train test:</u>
The following results were observed for the Test Item (napropamide-M)/Cellulose mixtures:
<table><tr><th colspan="2">Test Item/ Cellulose mixture</th><th rowspan="2">Time for flame to reach 200mm (min)</th><th rowspan="2">Observations</th></tr><tr><th>Test Item</th><th>Cellulose</th></tr><tr><td>90%</td><td>10%</td><td>3.33</td><td>Burned vigorously to completion</td></tr><tr><td>70%</td><td>30%</td><td>2.29</td><td>Burned vigorously to completion</td></tr><tr><td>50%</td><td>50%</td><td>3.17</td><td>Burned vigorously to completion</td></tr><tr><td>30%</td><td>70%</td><td>2.23</td><td>Burned vigorously to completion</td></tr><tr><td>10%</td><td>90%</td><td>3.34</td><td>Burned to completion</td></tr></table>Due to the observations, a barium nitrate/cellulose reference sample (60: 40 % w/w) was also tested.</td><td>Test method EEC A17 is sufficiently similar to the UN test method for classification according to CLP.

It is also further noted that the commission communication (2013/C 95/01) states that A.17 is an appropriate test method to follow.

Under the conditions of the test (EEC A17) the applicant has used one approach to show that the material napropamide-M does not possess oxidizing properties. An alternative approach (EEC A17) could have been to test the napropamide-M/cellulose mixture in an inert atmosphere, however the applicant has justified by one of the suggested approaches that it does not</td><td>Yes</td><td>Bates, G. (2014), J19544</td></tr>
</table>

Test or Study Annex Point	Guideline and method	Test material purity and specification	Used methods / Results	Comments (Acceptable / Non acceptable)	GLP	Reference
			The reference sample burn rate was found to be 2 minutes and 10 seconds (for the time for the flame to each 200 mm). Due to the positive ignition seen with napropamide-M with cellulose, an inert substance (Kieselguhr) was also tested in place of cellulose in mixture with napropamide-M (as per the suggested approach in EEC A17). Although the test item gave a positive ignition and burned with both cellulose and Kieselguhr it was concluded that it does not possess oxidising properties as defined by the test.	possess oxidising properties. Acceptable		
B.2.14. OTHER STUDIES						

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
B.2.1/01	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.1/02	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.1/03	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.2/01	Patel, A.H.	2013	Vapour pressure of napropamide-M purified Final report Company report No: 207-2-11-6176 Jai Research foundation, India GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.2/02	Peatman, M.H.	2014	Napropamide-M: Calculation of Henry's Law Constant Final report Company report No: UPL/16/01-HLC1 JSC International Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.3/01	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.4/01 - 02	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A

B.2.4/03	Marshall, I	2013	Provision of NMR and Chiral HPLC data for napropamide-M purified active ingredient (Batch: UPH-08/DNE-263/D-STD/20121221) Company report No: SEL/7234/1 Selcia Ltd, UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.4/04	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.4/05	Marshall, I	2013	Provision of NMR and Chiral HPLC data for napropamide-M purified active ingredient (Batch: UPH-08/DNE-263/D-STD/20121221) Company report No:SEL/7234/1 Selcia Ltd, UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.5/01 – B.2.6/01	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.7/01	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.7/02 -05	Bates, G	2016	Validation of method M844 for the determination of metabolites of napropamide-M in octanol and water phases for support of partition testing. Final report Company report No: J20144 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.8/01, B.2.9/01 - 02	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A
B.2.11/01 B.2.12/01 B.2.13/01	Bates, G	2014	Physical and chemical determinations on Napropamide-M technical and purified material Final report Company report No: J19544 GC Laboratories Ltd., UK GLP, Unpublished	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	N/A