

## APPENDIX 7

### FORMAT FOR THE COMPILATION OF *TIER II* SUMMARIES - ACTIVE SUBSTANCE

#### PART 1

#### Section 1 **Identity of the Active Substance; Physical and Chemical Properties of the Active Substance; Further Information on the Active Substance; Proposals including Justification of the Proposals for the Classification and Labelling of the Active Substance**

The example of a summary and assessment of data which follows is intended to illustrate the approach recommended for the preparation of *Tier II* summaries and assessments. The material included has not been critically assessed for its technical content. Although based on a real submission, the data included in the following summary and evaluation have been amended to protect the commercial interests of the owner of the data.

Applicants should be aware that these guidelines are intended to provide a degree of flexibility. Where in particular cases, it is more appropriate to present the data and information in another format, applicants may do so. In such cases it is recommended that the applicant discuss the format proposed with the Regulatory Authority of the Country to which application is to be made.

#### 1 **Identity of the active substance**

|         |                      |                           |  |
|---------|----------------------|---------------------------|--|
| IIA 1.1 | <b>Applicant</b>     | Contact person:           | Dr John Jones  |
|         |                      | Address:                  | Chemco<br>36 -39 Plant Street<br>Marlborough<br>Wiltshire<br>England |
|         |                      | Telephone:                | +44 (0) 1345 6789112   |
|         |                      | Fax:                      | +44 (0) 1345 4567890   |
| IIA 1.2 | <b>Manufacturer</b>  | Contact Person:           | Dr S. Smith  |
|         |                      | Address:                  | As above   |
|         |                      | Telephone:                | as above   |
|         |                      | Fax:                      | as above   |
| IIA 1.3 | <b>Common name</b>   | chemx (proposed ISO name) |  |
| IIA 1.4 | <b>Chemical Name</b> | IUPAC:                    |  |
|         |                      | CA:                       |  |

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**IIA 1.5      Manufacturer's development code numbers**

OEC 1000 and BJC 14 are both used as code numbers for the active substance (technical and pure material). BJC 14 is used in the early Chemistry Reports, while OEC 1000 is used in all other reports.

**IIA 1.6      CAS, EEC and CIPAC numbers**      CAS:      16335-17-2  
EEC:      Not assigned  
CIPAC:      Not assigned

**IIA 1.7      Molecular and structural formula, molecular mass**

Molecular Formula:

Structural Formula:

Molecular Mass :      440.37

**IIA 1.8      Method of manufacture of the active substance**

The information concerned is included with all other confidential information in Document J

**IIA 1.9      Specification of purity of the active substance**

The information concerned is included with all other confidential information in Document J

**IIA 1.10      Identity of isomers, impurities and additives together with the structural formula**

The information concerned is included with all other confidential information in Document J

**IIA 1.11      Analytical profile of batches**

The information concerned is included with all other confidential information in Document J

**2      Physical and chemical properties of the active substance**

| Test or Study & Data point  | Guideline and method   | Test material purity and specification             | Findings  | Comments   | GLP Y/N | Reference               |
|---|--|--|---|--|---------|-------------------------|
| Melting point, freezing point or solidification point (IIA 2.1.1) | OECD 102   | 99 % pure, lot number GHQ-9209-4531-A (Document J) | Mean range: 201.1 - 201.7 °C (mean of 3 measurements; accuracy, $\pm 0.1$ °C max)   |  | Y       | White T 1996a p 39      |
| Boiling point (IIA 2.1.2)   |  |  |   | Not relevant as the test material is not a liquid, nor is it a low melting substance |         |                         |
| Temperature of decomposition of sublimation (IIA 2.1.3)           |  |  |   | Not determined   |         |                         |
| Relative density (IIA 2.2)  | CIPAC MT3. [Capillary stoppered Pycnometer]                    | 99.5 % pure, lot number 30016916 (Document J)      | 1.518 g/cm <sup>3</sup> at 20.0 °C  |  | Y       | White T 1996a p 173-175 |
| Vapour pressure (IIA 2.3.1)                                       | OECD 104 (Gas saturation method)                               | 99.5 % pure, lot number 30016916 (Document J)      | 7.22 x 10 <sup>-7</sup> Pa at 35°C<br>1.87 x 10 <sup>-6</sup> Pa at 40°C<br>Conclusion:<br>3.05 x 10 <sup>-8</sup> Pa at 20 °C<br>and 8.81 x 10 <sup>-8</sup> Pa at 25°C (by extrapolation)                           | chemx is not volatile at ambient temperatures.                                       | Y       | White T 1996a p 177-179 |
| Henry's law constant (IIA 2.3.2)                                  | Calculated using solubility at 3 pH values and vapour pressure |  | Henry's Law constant at 20°C (calculated):<br>pH 5: 8.15 x 10 <sup>-07</sup> Pa/m <sup>3</sup> /mol<br>pH 7: 8.83 x 10 <sup>-09</sup> Pa/m <sup>3</sup> /mol<br>pH 9: 2.97 x 10 <sup>-08</sup> Pa/m <sup>3</sup> /mol |  |         | White T 1996a p 181-183 |
| Colour and physical state (IIA 2.4.1)                             |  | 99.5 % pure, lot number 30016919 (Document J)      | white powder (Munsell colour N 9.5/90 %R)   |  |         | White T 1996a p 13      |
| Odour (IIA 2.4.2)   |  | 99.5 % pure, lot number 30016919 (Document J)      | no odour  |  |         | White T 1996a p 13      |

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| Test or Study & Data point                           | Guideline and method               | Test material purity and specification             | Findings   | Comments  | GLP Y/N | Reference               |
|--|------------------------------------|--|--|---|---------|-------------------------|
| UV/VIS, IR, NMR, MS spectra (as) (IIA 2.5.1)         | UV, IR, H-NMR, C-NMR and mass spec | 99.5 % pure, lot number 30016919 (Document J)      | UV (aqueous methanol, pH > xx)<br>IR (KBr)<br><sup>1</sup> H-NMR (300MHz, IBM AF-300 FT NMR)<br><sup>13</sup> C-NMR (75MHz IBM AF-300 FT NMR)<br>UV Absorption Characteristics:<br>Basic (aqueous methanol, pH > 10)<br>$\lambda_{\max} = 208 \text{ nm}$ , $\epsilon = 187,150 \text{ L.mol}^{-1}.\text{cm}^{-1}$<br><br>Optical purity is not required as OEC 1000 is not a resolved isomer. | Absorption in the range 300 to 330nm. is indicative of a potential for photodegradation in natural sunshine.        | Y       | White T 1996a p 31-38   |
| UV/VIS, IR, NMR, MS spectra (impurities) (IIA 2.5.2) |                                    |  | no data presented  | There are no impurities which are considered to be of toxicological, ecotoxicological or environmental significance | Y       |                         |
| Solubility in water (IIA 2.6)                        | EEC A.8 (flask method)             | 99 % pure, lot number GHQ-9209-4531-A (Document J) | pH 5: 17.60 ± 2.71 ppm<br>pH 7: 1626.8 ± 39.8 ppm<br>pH 9: 482.44 ± 8.35 ppm<br>all at 20°C<br>(all results are given at the 95% confidence interval, n = 3)   | Chemx is moderately soluble in water at environmental pH values.  | Y       | White T 1996a p 43-63   |
| Solubility in organic solvents (IIA 2.7)             | OECD 105 (flask method)            | 99.5 % pure, lot number 30016916 (Document J)      | n-heptane: <0.001 g/l at 20°C<br>xylene: 0.16 g/l at 20°C<br>1,2-dichloroethane: 4.35 g/l at 20°C<br>methanol: 0.33 g/l at 20°C<br>acetone: 0.71 g/l at 20°C<br>ethyl acetate: 1.01 g/l at 20°C  |   | N       | White T 1996a p 175-177 |

| Test or Study & Data point   | Guideline and method          | Test material purity and specification  | Findings   | Comments   | GLP Y/N | Reference              |
|--|-------------------------------|---|--|--|---------|------------------------|
| n-octanol/water partition coefficient (IIA 2.8)  | OECD 107 (Shake flask method) | 99 % pure, lot number GHQ-9209-4531-A (Document J)  | at pH 5, log P <sub>ow</sub> < 1<br>at pH 7, log P <sub>ow</sub> < 1<br>at pH 9, log P <sub>ow</sub> < 1   | At pH 9 there were difficulties in that some degradation of the as occurred in the buffer solution.<br>At pH 5 the difference between the high and low concentration was greater than the ± 0.3 log units recommended. | Y       | White T 1996a p 64-120 |
| Hydrolysis rate at pH 4,7 and 9 under sterile conditions in the absence of light (IIA 2.9.1) | OECD 111                      | [ <sup>14</sup> C]-chem2-chemx<br>[ <sup>14</sup> C]-chem3-chemx<br>99 % pure, specific radioactivity x.xx MBq/mg | pH 4: half-life = 7.0 days at 25°C, 0.83 days at 40°C<br>pH 5: half-life = 48 days at 25°C, 6.0 days at 40°C<br>pH 7: half-life = 168 days at 25°C, 16 days at 40°C<br>pH 9: half-life = 156 at 25°C, 15 days at 40°C  | The only significant hydrolysis products are xxxxxxx (metabolite 2), metabolite 3. Minor products formed each accounted for < 1% of the applied radioactivity.   | Y       | White T 1995           |
| Direct photo-transformation (IIA 2.9.2)  | FIFRA 162-2                   | [ <sup>14</sup> C]-chem2-chemx<br>[ <sup>14</sup> C]-chem3-chemx<br>99 % pure, specific radioactivity x.xx MBq/mg | Experimental photolytic half-life of chem2-chemx and chem3-chemx (radiolabelled at different sites) in sterile aqueous buffer solution (pH 7.0) at 25°C: 36.3 hours and 33.0 hours respectively.<br><br>Conversion to 12-hour sunlight days results in half-lives of 3.x days (chem2) and x.x days (chem3) respectively.<br><br>The main degradation products were metabolite 1, metabolite 2, and metabolite 3. These accounted for relative distributions of radioactivity from 5.09 - 28.34% at some time during the photolysis.<br><br>Overall accountabilities for the study were 96.8% of the applied radioactivity for the photolyzed solutions.<br><br>Photolysis products: see attachment |  | Y       | White T 1993a          |

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| Test or Study & Data point                               | Guideline and method  | Test material purity and specification                                       | Findings   | Comments  | GLP Y/N | Reference               |
|--|---|--|--|---|---------|-------------------------|
| Quantum yield of direct photo-transformation (IIA 2.9.3) | BBA, Part IV, 6-1 $\equiv$ OECD Draft Guideline (Feb. 1995) Irradiation in a Heraeus "Suntest" apparatus - wavelength > 290nm | [ <sup>14</sup> C]-chem2-chemx 99 % pure, specific radioactivity x.xx MBq/mg | A half-life value of 5.7 hours and a DT <sub>90</sub> value of 18.9 hours were calculated using first-order reaction kinetics<br><br>Quantum yield calculated to be $\phi = 1.81 \times 10^{-3}$ . | Lifetime was calculated by using direct phototransformation, for mid-day sunlight in the top millimeters of a natural aquatic system, utilising the simulation model GCSOLAR - at the water surface: 3.4 days in spring, 2.4 days in summer, 8.2 days in autumn and 22 days in winter. calculated. Real lifetime was calculated by consideration of the solar light intensity incident upon the upper layer of the water, penetration of light into the water and absorption of light by water dissolved organic matter. Using the absorption spectrum of a typical Rhine River water sample, the lifetimes were calculated to be 2.4, 2.8, 3.2 and 3.8 days (summer) and 21.7, 25.3, 29.2 and 33.4 days (winter) at depths of 0, 10, 20 and 30 cm respectively. Another model developed by Frank and Klöpfer provided similar results. | Y       | White T 1993b           |
| Dissociation constant (IIA 2.9.5)                        | OECD 112  | 99.5 % pure, lot number 30016916 (Document J)                                | pK <sub>a</sub> = 3.51 at 20°C<br><br>Dissociation in water does not occur. Chemx is not a salt.   | The test deviated from OECD method 112 in that the pKa results from the 3 replicated data sets ranged from 3.43 to 3.68 and hence exceeded the limit of 0.1 log units.  | Y       | White T 1996a p 161-237 |
| Estimated photochemical oxidative degradation (IIA 2.10) |   |  | no data presented  | This calculation was not carried out as the chemx is essentially not volatile (see point 2.3.1, vapour pressure and point 2.3.2, Henry's Law constant).   |         | White T 1996a p 238-329 |

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| Test or Study & Data point      | Guideline and method | Test material purity and specification        | Findings  | Comments  | GLP Y/N | Reference               |
|---------------------------------|----------------------|---|---|---|---------|-------------------------|
| Flammability (IIA 2.11.1)       | EEC A.10             | 98.9 % pure, lot number 30016919 (Document J) | The test material did not ignite, did not support combustion, and is not flammable. |   | Y       | White T 1996a p 238-329 |
| Auto-flammability (IIA 2.11.2)  | EEC A.16             | 98.9 % pure, lot number 30016919 (Document J) | Chemx does not have a self-ignition temperature lower than its melting temperature  |   | Y       | White T 1996a p 238-329 |
| Flash point (IIA 2.12)          |                      |   | no data presented   | Not determined since chemx is not a liquid at temperatures < 40°C |         |                         |
| Explosive properties (IIA 2.13) | EEC A.14             | 98.9 % pure, lot number 30016919 (Document J) | Mechanical sensitivity:- negative<br>Thermal sensitivity:- negative                 |   | Y       | White T 1996a p 238-329 |
| Surface Tension (IIA 2.14)      | EEC A.5              | 98.9 % pure, lot number 30016919 (Document J) | 66.6 dyne/cm  |   |         | White T 1996a p 161-237 |
| Oxidizing properties (IIA 2.15) | EEC A.17             | 98.9 % pure, lot number 30016919 (Document J) | The test material was did not act as an oxidising or reducing agent                 |   | Y       | White T 1996a p 238-329 |

**Attachment**

**Chemx metabolite key : names, structures & studies where found**

[ Number ] in Tier II text refers to ID Number below

| ID No. | Trivial Name | Chemical Abstracts Name | Structure | Where Found   |
|--------|--------------|-------------------------|-----------|---|
| 1      | chemx        |                         |           | Wheat forage, wheat straw   |
| 2      | metabolite 1 |                         |           | Hydrolysis, aerobic soil, aquatic sediment, wheat forage, wheat straw, rotation crops, rat (urine and faeces) |
| 3      | metabolite 2 |                         |           | Hydrolysis, aerobic soil, aquatic sediment, aqueous photolysis  |
| 4      | metabolite 3 |                         |           | Aerobic soil, aquatic sediment, wheat forage, wheat straw, rat (urine and faeces)                             |

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3      **Further information on the active substance**

IIA 3.1      **Function**      Herbicide

IIA 3.2      **Effects on harmful organisms**

IIA 3.2.1      **The nature of the effects on harmful organisms**      Contact and residual action.

IIA 3.2.2      **Translocation in plants**

Chemx is translocated in plants both apoplastically and symplastically.

IIA 3.3      **Field of use envisaged**      Agriculture

IIA 3.4      **Harmful organisms controlled and crops or products protected or treated**

IIA 3.4.1      **Details of existing and intended use**

**Table IIA 3.4.1-1      Effect of timing and application rate on the effectiveness of chemx applied in wheat to control *Wild oats* <sup>(1)</sup>**

| Application Rate<br>g as / ha<br>[No of Applications] | Timing Of<br>Application | Mean % Weed<br>Control<br>{no. of results} | Mean Relative<br>Yield <sup>(2)</sup><br>{no. of results} | Number of<br>Seasons<br>tested |
|---|--------------------------|--|---|--------------------------------|
| 1. Ireland  |                          |  |   |                                |
| xx g + S  | 12-34                    | 39.1(9)                                    | 121.7 (3)   | 2                              |
| xx g + S  | 12-34                    | 23.8 (9)                                   | 148.7 (3)   | 2                              |
| xx g + S  | 12-18                    | 51.4 (3)                                   | 165.5 (3)   | 2                              |
| 2. UK   |                          |  |   |                                |
| xx g + S  | 12-39                    | 72.3 (18)                                  | 109.5 (9)   | 3                              |
| xx g + S  | 12-39                    | 80.3 (25)                                  | 133 (8)   | 3                              |
| xx g + S  |                          | no data                                    |   |                                |
| 3. Germany<br>in-house trials +<br>contract trials    |                          |  |   |                                |
| xx g  | 21-32                    | 53 (21)                                    | 115 (8)   | 3                              |
| xx g  | 21-32                    | 61 (16)                                    | 123 (4)   | 3                              |
| xx g  | 21-32                    | 75 (27)                                    | 125 (12)  | 3                              |
| xx g  | 21-32                    | 81 (7)                                     | -   | 2                              |

(1) Prepared on the basis of trials over three seasons in the Northern region of the EU (Ireland, France, Germany, UK, Denmark and Belgium).

(2) Yield at harvest relative to the yield of the untreated control (100). “+S” = with surfactant

**Observation :** Where infestation levels are high an application of xx g as / ha is required to achieve satisfactory control and yield benefit. Such conditions occur in most seasons in the Northern region of the EU. Full details are given in the Biological Dossier.



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#### IIA 3.4.2 **Details of harmful organisms against which protection is afforded**

Chemx is recommended for use as a spring post-emergence treatment in wheat to control a number of weeds including *Avena fatua*, *Bromus sp.*, *Galium Aparine* and various other broad leaved weeds.

#### IIA 3.4.3 **Effects achieved on crops**

There is no effect on the crop other than to remove competition from weeds which allows the full yield potential to be reached and improves ease of harvesting.

#### IIA 3.5 **Mode of action**

##### IIA 3.5.1 **Details of biochemical and physiological mechanisms and biochemical pathways**

Chemx is a sulfonylurea herbicide. On this basis it is believed like other members of the class, its mode of action involves inhibition of acetolactate synthase in the aliphatic amino acid pathway. Acetolactate synthase is the first enzyme in the pathway that makes the aliphatic amino acids valine, isoleucine and leucine. These are essential amino acids and are only made in plants.

Following application meristematic growth stops immediately. Affected plants appear dark green and stunted. This is followed by a reddening of the stem base. The next phase of plant death is characterized by a very slowly developing necrosis. Death can take 3-6 weeks to occur and the speed of death is dependent upon the rate of plant growth. (Beyer EM *et al* 1987).

##### IIA 3.5.2 **Chemical name (IUPAC and CA), ISO common name, CAS number, EEC number, CIPAC number, empirical and structural formula and molecular mass of metabolite or degradation product known to exert the intended effect.**

The intended effect is exerted by the active ingredient, chemx.

##### IIA 3.5.3 **Processes, mechanisms, reactions, rate of conversion, rate limiting step, environmental and other factors affecting the rate and extent of conversion of active substance to active metabolites and degradation products.**

Not relevant - see IIA 3.5.2 above.

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**IIA 3.6 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies**

Details on the occurrence of resistance and a resistant management strategy is included in the Biological dossier (Volume 32).

**IIA 3.7 Material Safety Data Sheet (MSDS) for the active substance**

The material safety data sheet for chemx is provided in Document KII (IIA 3.7/01).

**IIA 3.8 Procedures for destruction or decontamination**

**IIA 3.8.1 Controlled incineration**

As chemx does not have a halogen content greater than 60%, pyrolytic behaviour under controlled conditions is not required.

The recommended means of safe disposal is by controlled incineration at an approved chemical waste facility. This is a standard process and no further detailed instructions are required.

**IIA 3.8.2 Others** No other means of safe disposal are proposed.

**IIA 3.9 Procedures for the decontamination of water in case of an accident**

Like other sulfonylurea herbicides there is not a readily available method for neutralisation or decontamination of water. As chemx is water soluble, it will not form a layer on top of water bodies which could easily be removed. Any chemical or additive, which could be used to decontaminate water is likely to be more harmful than chemx itself.

On this basis precautions must be taken to avoid contamination for example :

Minimise spread - products containing chemx should not be dumped, spilled, rinsed or washed into sewers or public waterways.

When off-loading, ensure vehicle is in a bunded area, and products containing chemx should be stored in a bunded area.

If in a worst case situation, chemx were to contaminate water in excessive volumes (*i.e.* several hundred fold increase in exposure from its normal use), as a consequence of its very low toxicity (see Sections 3 and 6) it is unlikely to have any effect other than to aquatic plants and algae. In addition the half-life as a consequence of aqueous photolysis (see point 2.9) is fairly short and so breakdown in the top 30 cm will be relatively fast. On the basis of the results of the water sediment study presented in section 5, it is believed that chemx would partition fairly readily to sediment where it would be broken down. In the case of such a spill contaminated water should not be used for irrigation purposes for at least 30 days.

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**IIA 3.10 Recommended methods and precautions concerning handling, storage, transport or fire**

**Hazards identification:** On the basis of available information chemx is not expected to produce any significant adverse health or environmental effects when the recommended use instructions are followed.

**Fire Fighting Measures:**

Flash Point: NA, solid granular material

Hazardous Products of Combustion: None known

Extinguishing Media: In case of fire, use water (flood with water), dry chemical, CO<sub>2</sub>, or alcohol foam.

Unusual Fire and Explosion Hazards: None

Fire Fighting Equipment: Fire fighters and others exposed to products of combustion should wear self-contained breathing apparatus. Equipment should be thoroughly decontaminated after use.

**Transport :** Not classified for IMO or IATA.

**Handling & Storage:** Good industrial practice in housekeeping and personal hygiene should be followed. Avoid contact with eyes skin and clothing. When using do not eat, drink or smoke. Wash hands thoroughly after handling. Store only in original container.

**IIA 10 PROPOSALS FOR THE CLASSIFICATION AND LABELLING OF THE ACTIVE SUBSTANCE**

|                              |      | <b>Justification for the proposal</b>  |
|------------------------------|------|--|
| <b>Hazard symbol :</b>       | None |  |
| <b>Indication of danger:</b> | None | The toxicological and ecotoxicological studies conducted with chemx support the classification proposed - see Sections 3 and 6 of the <i>Tier II</i> summary for the active substance. |
| <b>Risk phrases:</b>         | none |  |
| <b>Safety phrases:</b>       | None |  |

