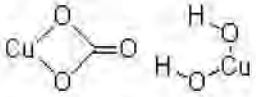
Section A2	Identity of Active Substance
IUCLID: 1.1.1	A2.1 – A2.9, copper carbonate

Subsection (Annex Point)		Official use only
2.1 Common name (IIA2.1)	Basic copper carbonate	X
2.2 Chemical name (IIA2.2)	Copper(II) carbonate—copper(II) hydroxide	
2.3 Manufacturer's development code number(s) (IIA2.3)	(1:1) None.	
2.4 CAS No and EC numbers (IIA2.4)	Non-entry field	
2.4.1 CAS-No	*If relevant CAS-No. for mixture of isomers* 12069-69-1	
Isomer 1	Not applicable	
Isomer n	Not applicable	
2.4.2 EC-No	*EINECS, ELINCS or No longer polymer-No* 235-113-6	
Isomer 1	Not applicable	
Isomer n	Not applicable	
2.4.3 Other	*If possible give registration numbers of other institutions, e.g. CIPAC* The CIPAC code number for copper compounds is 45.	X
2.5 Molecular and structural formula, molecular mass (IIA2.5)	Non-entry field	
2.5.1 Molecular formula	*according to Hill or CAS system* $CH_2Cu_2O_5$	
2.5.2 Structural formula		
2.5.3 Molecular mass	*Give molecular mass of a.s. in g/mol* 221.1	
		X
	Short description of the used method	
2.6 Method of manufacture of the active substance (IIA2.1)	[redacted]	

Section A2 Identity of Active Substance
IUCLID: 1.1.1 A2.1 – A2.9, copper carbonate

[redacted]

2.7	**Specification of the purity of the active substance, as appropriate (IIA2.7)**	[redacted]	G/l	[redacted]	% v/v	X
2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	See separate standard format. *Give maximum content of active isomer and ratio isomer/diastereomers if relevant*				X
2.8.1	**Isomeric composition**	Not applicable.				
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Copper is obtained from reclaimed/recycled sources, e.g. scrap metal and spent etchant from the electronics (printed circuit board) industry.				

	Evaluation by Competent Authorities Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	
2.7 Specification of the purity	[redacted]

Section A3	Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point IUCLID: 2.1	OECD Guideline 102 'Melting Point/Melting EC Directive 92/69 Method A1 'Melting/Freezing Temperature'	**purity:** [redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room temperature	**result:** Copper carbonate, wet dense grade does not undergo melting at temperatures up to 400°C. A loss of water was observed from 86°C (359K) and a chemical change occurred at 206°C (479)K.		Yes	(1) valid without restriction	[redacted] 2000. Copper Carbonate Test Substances: Determination of the Physico-Chemical Properties (Appearance, pH, Oxidation/Reduction, EC Tests A1, A3 and A6). Covance Laboratories Ltd. Report No. 529/3-D2141 (unpublished)	
3.1.2 Boiling point IUCLID: 2.2				Not required, as boiling point will occur at temperatures greater than 360°C, based on			TNG Data Waiver A3.1.2	

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
				melting point.				
3.1.3 Bulk density/ relative density IUCLID: 2.3	EC Directive 92/69 Method A3; OECD Guideline 109 (1995); and OPPTS 830.7300.	**purity:** [redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room temperature	**relative density:** 3.4779 to 3.4829 **mean relative density:** 3.480 +/- 0.002 Test temperature: 21.4°C	Actual measurement temperature was 21°C and not 20°C, however, it is considered this makes no significant difference to the result as the change in density with temperature for most solids is negligible over a few degrees range. Therefore, any inaccuracy may be expected to be within overall experimental error.	Yes	(1) valid without restriction	[redacted] 2000. Copper Carbonate Test Substances: Determination of the Physico-Chemical Properties (Appearance, pH, Oxidation/Reduction, EC Tests A1, A3 and A6). Covance Laboratories Ltd. Report No. 529/3-D2141 (unpublished)	
3.2 Vapour Pressure (IIA3.2) IUCLID: 2.4				It is not possible to determine a vapour pressure due to the high melting point (and hence high boiling point) of copper carbonate, wet			TNG Data Waiver A3.2	

Section A3	Physical and Chemical Properties of Active Substance							
Subsection (Annex Point)	**Method**	**Purity/ Specification**	**Results** Give also data on test pressure, temperature, pH and concentration range if necessary	**Remarks/ Justification**	**GLP (Y/N)**	**Reliability**	**Reference**	**Official use only**
3.2.1 Henry´s Law Constant (Pt. I-A3.2) IUCLID: 2.4				Henry's Law Constant is not possible to calculate without a value for vapour pressure.			TNG Data Waiver A3.2.1	
3.3Appearance (IIA3.3) 3.3.1 Physical state	Conducted in accordance with: OPPTS 830.6303. Conducted in	**purity:** [redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room temperature **purity:**	Copper carbonate, wet dense grade was described as a moist powder.		Yes	(1) without restriction	[redacted] 2000. Copper Carbonate Test Substances: Determination of the Physico-Chemical Properties (Appearance, pH, Oxidation/Reduction, EC Tests A1, A3 and A6). Covance Laboratories Ltd. Report No. 529/3-D2141 (unpublished)	

3.3.2 Colour	accordance with: OPPTS 830.6302	[redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room Temperature	Copper carbonate, wet dense grade was described as green.		Yes	(1)Without restriction	[redacted] 2000. Copper Carbonate Test Substances: Report No. 529/3-D2141 (unpublished)	
3.3.3 Odour	Conducted in accordance with: OPPTS 830.6304	**purity:** [redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room temperature	Copper carbonate, wet dense grade was described as having no odour readily detectable at 21oC.		Yes	(1)Without restricton	[redacted] 2000. Copper Carbonate Test Substances: Report No. 529/3-D2141 (unpublished)	

Section A3	Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.4 Absorption spectra (IIA3.4)								
3.4.1 UV/VIS **IUCLID: 1.1.2**	OECD Guideline 101 (1981)	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	**Molar absorption coefficient (dm3.mol-1.cm-1):** 294 **Medium:** Acidic (pH 1.2) **Wavelength:** 245 nm	Molarity of test solutions were calculated using a molecular weight of 221.1 g.mol-1 An acidic test medium was used due to the negligible water solubility at neutral or alkaline pH.	Yes	(1) without Restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No: 1645/007 (unpublished)	
3.4.2 IR **IUCLID: 1.1.2**	Copper Carbonate, wet dense (0.0018g) was mixed with ground potassium bromide (0.1850g). This mixture was scanned over	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	The major absorbances obtained from the IR spectrum, were: **3750 to 2950 (cm-1)**: O-H stretch (broad) **1450 to 1350 (cm-1)**: ionic carbonate **925 to 850 (cm-1)**: ionic carbonate It was not possible to positively identify the		Yes	(1)without restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No:	

	the range 4400 to 450 cm-1 using potassium bromide as a reference		test material from the IR spectrum , however, the IR spectrum was consistent with the proposed chemical structure.				1645/007 (unpublished)	
3.4.3 NMR **IUCLID: 1.1.2**				Determination of NMR spectra is not applicable to simple inorganic salts, such as copper carbonate, wet dense, which is practically insoluble in the solvents required to carry out an NMR spectra. Any solvents which can be used, would form an acid digestion.			TNG Data Waiver A3.4.3	
3.4.4 MS **IUCLID: 1.1.2**				Determination of MS spectra is not applicable to metals, as MS is the molecular fragmentation at certain energy levels. On this basis, MS analysis of copper oxide would provide no useful information.			[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No:	

							1645/007 (unpublished)	
3.5 Solubility in water (IIA3.5) **IUCLID: 2.6.1** Water solubility (Ambient pH) IUCLID: 2.6.1	*including effects of pH (5-9)* EC Directive 92/69 Method A6	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	**result:** 4.68 x 10-3 to 1.59 x 10-3 g/l **temperature:** 20oC +/- 0.5oC **pH:** 6.2-6.8 A decreasing concentration in water solubility against time was noted, possibly due to precipitation of the copper ions as the carbonate or hydroxide salt. Samples tested at 30.0oC +/- 0.5oC and 10.0oC +/- 0.5oC showed no temperature dependent changes on solubility.		Yes	(1)without restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico- chemical properties. SafePharm Laboratories. Project No: 1645/007 (unpublished	

Water solubility (Acidic pH) IUCLID: 2.6.1	EC Directive 92/69 Method A6	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	**result:** >1.16 g/l **temperature:** 20oC +/- 0.5oC **pH:** 5.6 – 5.8 Solubility of the test material was dependent on the acid availability.	An increase in the pH of the sample solution was noted as the test material degraded to soluble copper salts. This neutralised the acid, resulting in saturation due to the insolubility of the test material at ambient pH. Further solubility could be achieved by increasing the acidic pH of the sample solution.	Yes	(1)without restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No: 1645/007 (unpublished)	
Water solubility: (Basic pH) IUCLID: 2.6.1	EC Directive 92/69 Method A6	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	**result:** < 1.0 x 10-5 g/l **temperature:** 20oC +/- 0.5oC **pH:** 8.7 to 8.8		Yes	(1) without restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No: 1645/007	

							(unpublished)	
3.6 Dissociation constant (-) **IUCLID: 2.12**				A determination of the dissociation constant was not carried out due to the chemical composition of copper carbonate, wet dense as addition of acid to solutions of copper carbonate would result in the formation of carbon dioxide.			TNG Data Waiver A3.6	
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1) **IUCLID: 2.6.1**			**Result:** Solubility of copper in monoethanolamine = 3.07 x 10^5 mg/l	refer to TNG Data Waiver A3.7		(4) assignable	Anonymous (2004) In house information from protim solignum	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2) **IUCLID: 2.14**				A determination of the stability in organic solvents is unnecessary, as the products in which copper carbonate, wet dense will be used are exclusively			T14G Data Waiver A3.8	

				aqueous in nature and will not contain organic solvents.				
3.9 Partition coefficient n-octanol/water (IIA3.6) **IUCLID: 2.5**	Hansch, L.A. and Elkins, C., 1971. Partition coefficients and their uses. Chem Rev. 71: 525-616		**result:** 0.00000085 **temperature:** 20oC **pH:** 1.6	It is generally considered that the determination of octanol/water partition coefficients for copper from sparingly soluble salts is impractical for technical reasons. However, given the relatively high water solubility of copper sulphate, it has been possible to determine an octanol/water partition coefficient for copper using this salt.			Pirot, F., Panisset, F., Agache, P. and Humbert, P., 1996. Simultaneous absorption of copper and zinc through human skin in vitro. Influence of counter-ion and vehicle. Skin Pharmacol. 9: 43-52.	
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7) **IUCLID: 2.14**				Not required, based on value for melting point.			TNG Data Waiver A3.10	

3.11 Flammability, including autoflammability and identity of combustion products (IIA3.8) **IUCLID: 2.9**	EC Directive 92/69 Method A10	**purity:** [redacted] **specification:** As given in section 2 **batch no:** 482-03 to 543-03 **stability:** stable at room temperature	The test material failed to ignite after exposure to a bunsen flame for two minutes in a preliminary screening test. As a result, copper carbonate, wet dense has been determined to be not highly flammable.	The moisture content of the test material was 13.28 %.	Yes	(1) without restriction	[redacted] (2004) Copper (II) carbonate – copper (II) hydroxide (1:1): Determination of general physico-chemical properties. SafePharm Laboratories. Project No: 1645/007 (unpublished)	
3.12 Flash-point (IIA3.9) **IUCLID: 2.7**				A Flash-point value was not determined, as this is not relevant to solid compounds, such as copper carbonate, wet dense.			T14G Data Waiver A3.12	
3.13 Surface tension (IIA3.10) **IUCLID: 2.6.2**				A determination of surface tension is not applicable, as copper carbonate, wet dense has a very low water solubility.			T14G Data Waiver A3.13	

3.14 Viscosity (-) **IUCLID: 2.13**				A determination of viscosity is not applicable to a solid, such as copper carbonate, wet dense.			T14G Data Waiver A3.14	
3.15 Explosive properties **(IIA3.11)** **IUCLID: 2.10**				Based on the chemical composition and experience in use, it is considered that this test would give a negative result for copper carbonate, wet dense.			T14G Data Waiver A3.15	
3.16 Oxidizing properties (IIA3.12) **IUCLID: 2.11**	OPPTS 830.6314	**purity:** [redacted] **specification:** As given in section 2 **pH:** 8.87 (1% (w/v) dispersed in distilled water) **synthesis batch:** 29308/2/RW **stability:** Stable at room temperature	Copper carbonate, wet dense, showed no signs of oxidizing properties which could result in violent reactions to the test substances used.	The oxidation/reduction properties of copper carbonate, wet dense were tested with monoammonium phosphate, potassium permanganate, powdered zinc and water.	Yes	(1) without restriction	[redacted] 2000. Copper Carbonate Test Substances: Determination of the Physico-Chemical Properties (Appearance, pH, Oxidation/Reduction, EC Tests A1, A3 and A6). Covance Laboratories Ltd. Report No. 529/3-D2141 (unpublished)	

3.17 Reactivity towards container material (IIA3.13) **IUCLID: 8.8**	Based on OPPTS 830.6320 and ASTM G 31-72	**specification:** As given in section 2 **synthesis batch:** 29788/1 **stability:** Stable at room temperature	In the absence of any significant changes in weight or appearance, it can be concluded that all the commercial packaging was resistant to chemical attack by copper carbonate, wet dense.	Commercial packaging for copper carbonate, wet dense consisted of a green and grey printed plastic sack.	Yes	(1) without restriction	[redacted] 2001. Copper Carbonate (Dry Light and Wet Dense): Determination of Accelerated Storage Stability and Corrosion Characteristics. SafePharm Laboratories Ltd. Laboratory ProjectID: 453/018 (unpublished)	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Results	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A5 IUCLID: 7.1-7.5	**Effectiveness against target organisms and intended uses**	
Subsection (Annex Point)		**Official use only**
5.1 Function **(IIA5.1)**	[redacted]	
5.2 Organism(s) to be controlled and products, organisms or objects to be protected **(IIA5.2)**	[redacted]	
5.2.1 Organism(s) to be controlled (IIA5.2)	[redacted]	

Section A5 IUCLID: 7.1-7.5	**Effectiveness against target organisms and intended uses**	
	[redacted]	
5.2.2 Products, organisms or objects to be protected (IIA5.2)	[redacted]	
5.3 Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)	[redacted]	
Section A5 IUCLID: 7.1-7.5	**Effectiveness against target organisms and intended uses**	

	[redacted]	
5.3.1 Effects on target organisms (IIA5.3)	[redacted]	
5.3.1.1 Wood-destroying basidiomycete fungi	[redacted]	
Section A5 IUCLID: 7.1-7.5	[redacted]	

	[redacted]	
5.3.1.2 Soft rotting fungi	[redacted]	
5.3.1.3 Wood destroying	[redacted]	
Section A5 **IUCLID: 7.1-7.5**	[redacted]	
insects	[redacted]	

5.3.1.4 Termites	[redacted]	
Section A5 IUCLID: 7.1-7.5	**Effectiveness against target organisms and intended uses**	

	[redacted]	
5.3.2 Likely concentrations at which the A.S. will be used (IIA5.3)	[redacted]	
5.3.2.1 PT08	[redacted]	
5.4 Mode of action (including time delay) (IIA5.4)	[redacted]	
5.4.1 Mode of action	[redacted]	
Section A5 IUCLID: 7.1-7.5	**Effectiveness against target organisms and intended uses**	
	[redacted]	

5.4.2 Time delay	[redacted]	
5.5 Field of use envisaged (IIA5.5)	[redacted]	
5.5.1 MG02: Preservatives	[redacted]	
5.6 User (IIA5.6)	[redacted]	
5.6.1 Industrial	[redacted]	
5.6.2 Professional	[redacted]	
5.6.3 General public	[redacted]	
5.7 Information on the occurrence or possible occurrence of the development of resistance and	[redacted]	

Section A5 IUCLID: 7.1-7.5		Effectiveness against target organisms and intended uses	
	appropriate management strategies (IIA5.7)		
5.7.1	Development of resistance	[redacted]	
5.7.2	Management strategies	[redacted]	
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	[redacted]	

Section A5 IUCLID: 7.1-7.5	Effectiveness against target organisms and intended uses	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and methods	[redacted]	

Section A5 IUCLID: 7.1-7.5	Effectiveness against target organisms and intended uses	
Conclusion	[redacted]	
Reliability		
Acceptability	[redacted]	
Remarks	[redacted]	
	COMMENTS FROM ...	
Date	*Give date of comments submitted*	
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	
Remarks		

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
[redacted]		[redacted]
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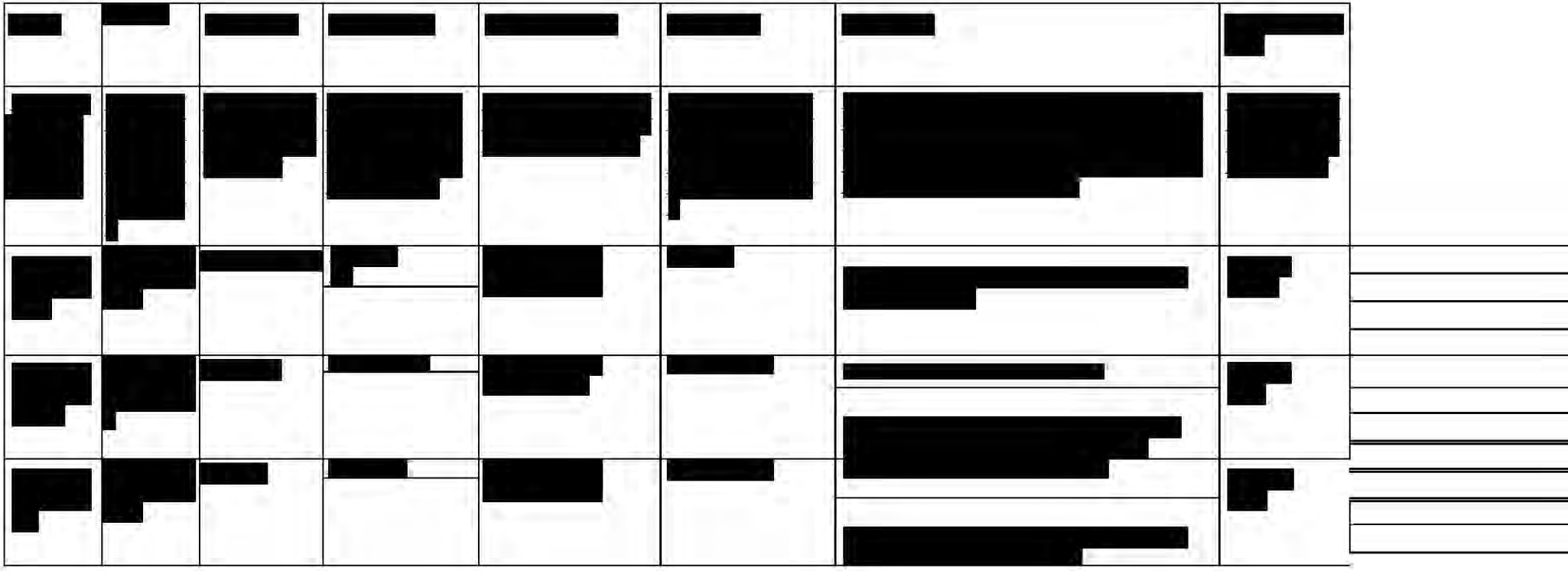
[redacted]		[redacted]

[redacted]



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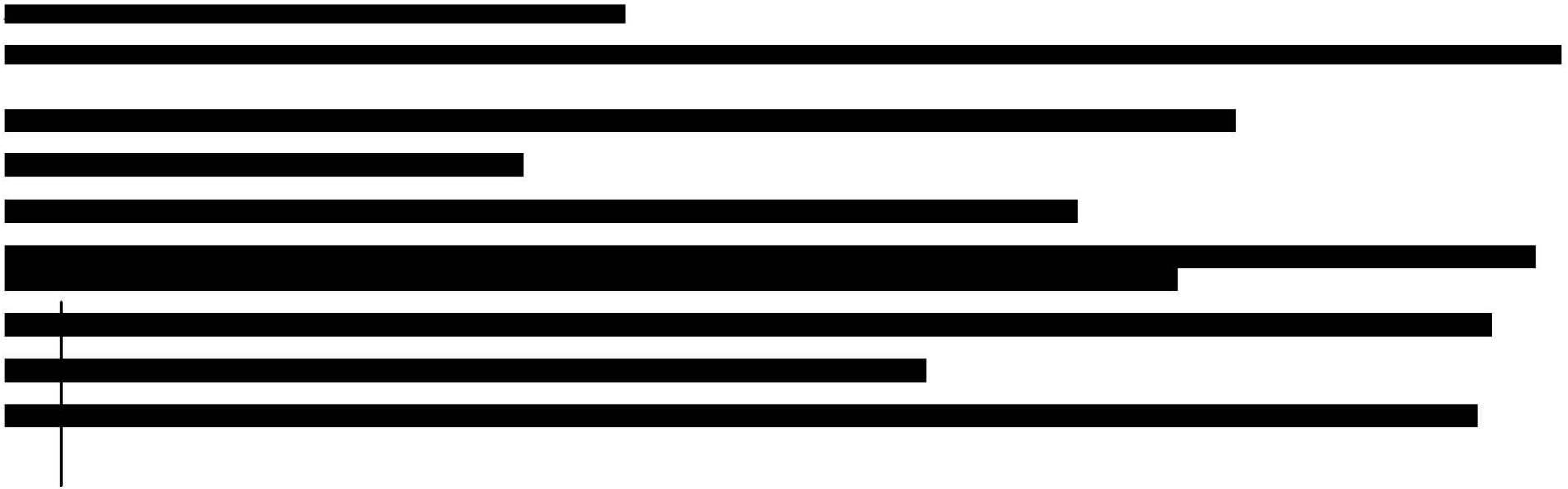

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[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

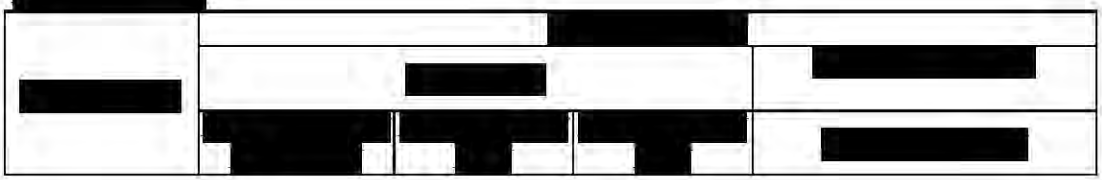
Section A5(1) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (against wood-destroying Basidiomycete fungi and insects)	
	REFERENCE	Official use only
1. Reference	[redacted]	
2. Data protection	[redacted]	
Data owner	[redacted]	
Criteria for data protection	[redacted]	
3. Guideline study	[redacted]	
4. Deviations	[redacted]	
	5. CONTENTS OF THE REVIEW	
6. Introduction	[redacted]	
7. Literature data	[redacted]	
'Initial toxicity' to wood-destroying basidiomycete fungi	[redacted]	

Section A5(1) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (against wood-destroying Basidiomycete fungi and insects)**	
'Initial toxicity' to wood-destroying insects	[redacted]	
Permanence of toxicity	[redacted]	
8. Results and discussion		
'Initial toxicity' to wood-destroying basidiomycete fungi	[redacted]	
'Initial toxicity' to wood-destroying insects	[redacted]	
Permanence of toxicity	[redacted]	
	9. APPLICANT'S SUMMARY AND CONCLUSION	
10. Summary of the review	[redacted]	XI

Section A5(1) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (against wood-destroying Basidiomycete fungi and insects)**	
	[redacted]	
11. Conclusion	[redacted]	
12. Reliability	[redacted]	
13. Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks	[redacted]	
	COMMENTS FROM	
Date	*Give date of the comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	

Section A5(1) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (against wood-destroying Basidiomycete fungi and insects)**	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

[redacted]



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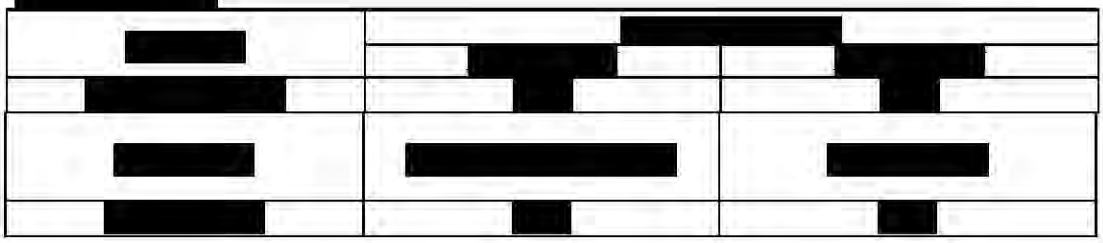

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Section A5(2) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (against wood-destroying Basidiomycetes)	
	REFERENCE	Official use only
14. Reference	[redacted]	
15. Data protection	[redacted]	
Data owner	[redacted]	
Criteria for data protection	[redacted]	
16. Guideline study	[redacted]	
17. Deviations	[redacted]	
	18. CONTENTS OF THE REPORT	
19. Introduction	[redacted]	
20. Monograph toxic limit data	[redacted]	
21. Results and discussion	[redacted]	X
	22. APPLICANT'S SUMMARY AND CONCLUSION	
23. Summary of the review	[redacted]	

Section A5(2) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (against wood-destroying Basidiomycetes)**	
	[redacted]	
24. **Conclusion**	[redacted]	X X
25. **Reliability**	[redacted]	
26. **Deficiencies**	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks		
	COMMENTS FROM	
Date	*Give date of the comments submitted*	

Section A5(2) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (against wood-destroying Basidiomycetes)	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Section A5(3) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (copper tolerance in wood-destroying fungi)	
	1 REFERENCE	Official use only
1.1 Reference	[redacted]	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	
1.2.3 Criteria for data protection	[redacted]	
	[redacted]	
2.1 Guideline study	[redacted]	
2.2 GLP	[redacted]	
2.3 Deviations	[redacted]	
	3 MATERIALS AND METHODS	
3.1 Test material		
3.1.1 Fungal Isolates	[redacted]	
3.1.2 Preservative solutions	[redacted]	
3.2 Test method		
3.2.1 Copper tolerance agar screening test	[redacted]	

Section A5(3) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (copper tolerance in wood-destroying fungi)**	
	[redacted]	
3.2.2 Standard laboratory test EN 113	[redacted]	
3.2.3 Electron paramagnetic resonance spectroscopy (EPR)	[redacted]	
	4 RESULTS AND DISCUSSION	
4.1 Screening test		
4.1.1 Copper (II) sulphate	[redacted]	

4.1.2 Copper amine preservative	[redacted]	
4.1.3 Chromated copper	[redacted]	

Copper carbonate

Section A5(3) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (copper tolerance in wood-destroying fungi)**	
borate	[redacted]	
4.1.4 Potassium dichromate	[redacted]	

4.2 Standard laboratory test (EN 113)	[redacted]	
4.3 Conclusions	[redacted]	

Copper carbonate

Section A5(3) Annex Point IIA V.5.1 – V.5.1.3	**Efficacy Data (copper tolerance in wood-destroying fungi)**	

	[redacted]	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	

Section A5(3) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (copper tolerance in wood-destroying fungi)**	
	[redacted]	
5.3 Conclusion	[redacted]	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks	[redacted]	

Section A5(3) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (copper tolerance in wood-destroying fungi)**	
	COMMENTS FROM	
Date	*Give date of the comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

Section A5(4) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	1 REFERENCE	Official use only
1.1 Reference	[redacted]	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	
1.2.3 Criteria for data protection	[redacted]	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	[redacted]	
2.2 GLP	[redacted]	
2.3 Deviations	[redacted]	
	3 MATERIALS AND METHODS	
3.1 Test material		
3.1.1 Fungal Isolates	[redacted]	
3.1.2 Preservative solutions	[redacted]	
3.2 Test method	[redacted]	

Section A5(4) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	[redacted]	
	4 RESULTS AND DISCUSSION	
4.1 Screening test	[redacted]	
4.2 Conclusions	[redacted]	

Section A5(4) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	[redacted]	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]

Section A5(4) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks		
	COMMENTS FROM	
Date	*Give date of the comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

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[redacted]	[redacted]											
				[redacted]				[redacted]				[redacted]
				[redacted]				[redacted]				
				[redacted]				[redacted]				
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[redacted]	[redacted]
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[redacted]	[redacted]
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[redacted]	[redacted]														
				[redacted]											
				[redacted]				[redacted]				[redacted]			
[redacted]				[redacted]				[redacted]				[redacted]			

[redacted]

[redacted]

Section A5(5) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	1 REFERENCE	Official use only
1.1 Reference	[redacted]	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	
1.2.3 Criteria for data protection	[redacted]	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	[redacted]	
2.2 GLP	[redacted]	
2.3 Deviations	[redacted]	
	3 MATERIALS AND METHODS	
3.1 Test materials		
3.1.1 Preservative materials	[redacted]	
3.1.2 Test organisms	[redacted]	
3.2 Test method	[redacted]	

Section A5(5) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (efficacy against soft rotting fungi)	
	[redacted]	
	4 RESULTS AND DISCUSSION	
4.1 Surface colonisation of sawdust	[redacted]	
4.2 Quantitative decay data	[redacted]	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	

Section A5(5) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	[redacted]	
5.3 Conclusion	[redacted]	x
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks	[redacted]	
	COMMENTS FROM	
Date	*Give date of the comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.*	

Section A5(5) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against soft rotting fungi)**	
	Discuss if deviating from view of rapporteur member state	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

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		[redacted]			
		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	X			

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[redacted]	[redacted]	[redacted]			
		[redacted]			
		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]			

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
	1 REFERENCE	Official use only
1.1 Reference	[redacted]	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	
1.2.3 Criteria for data protection	[redacted]	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	[redacted]	
2.2 GLP	[redacted]	
2.3 Deviations	[redacted]	
	3 MATERIALS AND METHODS	
3.1 Test material		
3.1.1 Preservative	[redacted]	
3.1.2 Termite test species	[redacted]	

3.1.3 Treated samples	[redacted]	

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
	[redacted]	
3.2 Test method	[redacted]	
	4 RESULTS AND DISCUSSION	
4.1 *Coptotermes formosanus* Tests	[redacted]	

4.1.1 Weight loss/visual rating	[redacted]	

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
4.1.2 Termite survival	[redacted]	
4.2 *Reticulitermes flavipes* Tests	[redacted]	
4.2.1 Weight loss/visual rating	[redacted]	
4.2.2 Termite survival	[redacted]	
4.3 Conclusions	[redacted]	

	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
	[redacted]	

5.2 Results and discussion	[redacted]	x
5.3 Conclusion	[redacted]	

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
	[redacted]	X x
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks		
	COMMENTS FROM	
Date	*Give date of the comments submitted*	

Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*

Section A5(6) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against termites)**	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Section A5(7) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (efficacy against wood-destroying fungi and insects)	
	1 REFERENCE	Official use only
1.1 Reference	[redacted]	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	
1.2.3 Criteria for data protection	[redacted]	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	[redacted]	X1
2.2 GLP	[redacted]	
2.3 Deviations	[redacted]	
	3 MATERIALS AND METHODS	
3.1 Basidiomycetes test according to EN 113	[redacted]	
3.2 Soft Rot Tests according to prENV 807	[redacted]	
3.3 Tests against *Hylotrupes bajulus*	[redacted]	
3.4 Tests against	[redacted]	

Section A5(7) Annex Point IIA V.5.1 – V.5.1.3	Efficacy Data (efficacy against wood-destroying fungi and insects)	
Termites	[redacted]	
	4 RESULTS AND DISCUSSION	
4.1 Basidiomycetes test according to EN 113	[redacted]	
4.2 Soft Rot Tests according to prENV 807	[redacted]	
4.3 Tests against *Hylotrupes bajulus*	[redacted]	
4.4 Tests against Termites	[redacted]	
4.5 Conclusions	[redacted]	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	X2)

Section A5(7) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against wood-destroying fungi and insects)**	
	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	[redacted]	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	

Section A5(7) **Annex Point IIA V.5.1 – V.5.1.3**	**Efficacy Data (efficacy against wood-destroying fungi and insects)**
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM
Date	*Give date of the comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

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[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]			[redacted]
		[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]					
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Copper carbonate

Table A5(7)-4. Summary table of experimental data on the effectiveness of Copper against target organisms.

Section A5.4.1(2) Annex Point IIA V.5.4	Mode of Action (against termites)	
	REFERENCES	Official use only
27. References	[redacted]	
28. Data protection	[redacted]	
Data owner	[redacted]	
Criteria for data protection	[redacted]	
29. Guideline study	[redacted]	
30. Deviations	[redacted]	
	31. REVIEW OF PUBLISHED LITERATURE	
	[redacted]	
	32. APPLICANT'S SUMMARY AND CONCLUSION	
33. Summary of the	[redacted]	

Section A5.4.1(2) Annex Point IIA V.5.4	Mode of Action (against termites)	
review	[redacted]	
34. Reliability	[redacted]	
35. Conclusion	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks	[redacted]	
	COMMENTS FROM ... *(specify)*	
Date	*Give date of comments submitted*	
Comments	*Discuss if deviating from view of rapporteur member state*	
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*	

Section A5.4.1 Annex Point IIA V.5.4	Mode of Action (against wood-rotting fungi)	
	REFERENCE	Official use only
36. Reference	[redacted]	
37. Data protection	[redacted]	
Data owner	[redacted]	
Criteria for data protection	[redacted]	
38. Guideline study	[redacted]	
39. Deviations	[redacted]	
	40. CONTENTS OF THE REVIEW	
	[redacted]	
	41. APPLICANT'S SUMMARY AND CONCLUSION	
42. Summary of the review	[redacted]	
43. Reliability	[redacted]	
44. Conclusion	[redacted]	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	

Section A5.4.1 Annex Point IIA V.5.4	Mode of Action (against wood-rotting fungi)	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	[redacted]	
Remarks		
	COMMENTS FROM	
Date	*Give date of the comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

Section A5	Effectiveness against target organisms and intended uses
IUCLID: 7.1-7.5	

Subsection (Annex Point)		Official use only
5.8 Likely tonnage to be placed on the market per year (IIA5.8)	*Including imported quantities. Indicate also quantities for use other than biocides.* [redacted]	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate*
IUCLID: 5.1.1/01	*Specify type of test (Limit Test, LD_{50}, special investigation)* **A6.1.1(01), Acute Oral Toxicity**

1 REFERENCE

1.1 Reference

Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages) If necessary, copy field and enter other reference(s).

[redacted] (2001). Acute Oral Toxicity Study of Copper Carbonate Dry Light in Rats. Covance Laboratories, Inc.

Report No. 7180-100 (unpublished).

1.2 Data protection

Yes

(indicate if data protection is claimed)

1.2.1 Data owner

Give name of company

Wood Preservative Copper Taskforce

1.2.2 Criteria for data protection

Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:

Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

Yes - the study was conducted according to the following test guidelines;

OECD Guidelines, No. 401. Acute Oral Toxicity (February 24, 1987)

EPA. Prevention, Pesticides and Toxic Substances; OPPTS 870.1100 Acute Toxicity Testing - Background; Health Effects Test Guidelines (August 1998).

(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")

2.2 GLP

Yes

(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)

2.3 Deviations

Yes

At test initiation the animals were approximately 8 to 13 weeks of ages (opposed to 8 to 12 as specified in the protocol). This deviation is not considered to have had an adverse effect on the outcome.

(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

3 MATERIALS AND METHODS

In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values

	as appropriate.	
3.1 Test material	Dry copper carbonate *or give name used in study report*	
3.1.1 Lot/Batch number	*List lot/batch number if available* Lot/batch number: No. 907	
3.1.2 Specification	As given in section 2 Deviating from specification given in section 2 as follows *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.2.1 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Light green powder	
3.1.2.2 Purity	*Give purity in % of active substance* [redacted]	X
3.1.2.3 Stability	*Describe stability of test material* Stable at room temperature	
3.2 Test Animals	Non-entry field	
3.2.1 Species	Rat	
3.2.2 Strain	Crl:CD(SD)IGS BR	
3.2.3 Source	Charles River Laboratories, Portage, Michigan, USA	
3.2.4 Sex	Male and Female	
3.2.5 Age/weight at study initiation	Age/weight at study initiation: The animals were aged between 8 and 13 weeks old and weighed approximately 214-298 g at the start of the study.	
3.2.6 Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups* 5 males and 5 females	
3.2.7 Control animals	No	
3.3 Administration/ Exposure	Oral *Fill in respective route in the following, delete other routes*	
3.3.1 Postexposure period	14 days	
	Oral	
3.3.2 Type	Gavage	
3.3.3 Vehicle	Moistened with distilled water	
3.3.4 Concentration in vehicle	500 and 2000 mg/kg bw	
3.3.5 Total volume	5 ml/kg bw	

applied	
3.3.6 Controls	Not applicable – no controls were used in the study
Examinations	Clinical observations were conducted at 1, 2.5 and 4 hours following test material administration and daily thereafter for 14 days. Mortality checks were conducted twice a day for 13 days after test material administration and again on the morning of Day 15. Bodyweights were determined before test material administration (Day 1). Additional bodyweights were determined on Day 8 and at either mortality during post-exposure period or sacrifice at test termination. All animals, whether found dead during the study, sacrificed in a moribund condition or euthanised at test termination, were subject to an abbreviated macroscopic necropsy examination. Any abnormalities were noted.
Method of determination of LD_{50}	The LD_{50} was determined from mortality data. No statistical analysis was employed.
Further remarks	Not applicable

4 RESULTS AND DISCUSSION

describe findings. if appropriate, include table. sample tables are given below.

4.1 Clinical signs

No effects / describe significant effects referring to data in results table

MORTALITY:

No mortality was observed at 500 mg/kg bw dose level. All 10 animals treated at 2000 mg/kg bw were either found dead (four males and five females) or sacrificed in a moribund condition (one male) within 7 days of test material administration. For further details please refer to Table A6_1-1.

BODYWEIGHTS

All animals surviving to the end of the observation period exhibited bodyweight gains during the study, with the exception of one female which exhibited an insignificant loss of 2 g during the second week. For further details please refer to Table A6_1-1.

X

CLINICAL SIGNS

The only clinical signs observed in animals treated at 500 mg/kg were non-formed faeces and a dark stained urogenital area. All animals at this dose level returned to a normal appearance by Day 9. Clinical signs of toxicity observed in the animals treated at the 2000 mg/kg bw dose group prior to death or moribund sacrifice included hunched posture, hypoactivity, red-stained face, green-tinted/black mucoid/non-formed faeces, few faeces, dark stained urogenital area, cold to touch, dyspnea and prostration. For further details please refer to Table A6_1-1.

4.2 Pathology *No effects / describe significant effects referring to data in results table*

The macroscopic necropsy examination conducted at termination of the animals treated at 500 mg/kg did not reveal any visible lesions. Test material related lesions observed in the 2000 mg/kg dose group pertained to abnormally coloured fluid contents in the gastrointestinal tract. All other findings were indicative of an acute death. For further details please refer to Table A6_1-1.

4.3 Other *Describe any other significant effects*

Not applicable

4.4 LD_{50} *Give LD_{50} male, females, males + females*
State if no lethal effect at maximal dose

The estimated LD_{50} values were determined to be between 500 and 2000 mg/kg bw for males, females and both sexes combined

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods *Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines*

In this study, copper carbonate dry light was evaluated for its acute oral toxicity potential in male and female rats when administered as a single gavage dose at levels of 500 and 2000 mg/kg bw. There was a 14 day post exposure period to determine clinical observations, bodyweight changes and mortality. At the end of the study the animals were sacrificed and subjected to pathological examinations.

The study was conducted according to OECD (401 – Acute Oral Toxicity) and EPA (OPPTS 870.1100 Acute Toxicity Testing) guidelines. The study was also conducted according to GLP.

At test initiation the animals were approximately 8 to 13 weeks of ages (opposed to 8 to 12 as specified in the protocol). This deviation is not considered to have had an adverse effect on the outcome.

5.2 Results and discussion *Summarize relevant results; discuss dose-response relationship*

No mortality was observed in the 500 mg/kg dose group. The only clinical signs observed were non-formed faeces and dark stained urogenital area. All animals treated at 2000 mg/kg died or were sacrificed in a moribund condition within 7 days of test material administration. Based on the mortality observed in the study, the estimated oral LD_{50} values in rats were determined to be between 500 and 2000 mg/kg for males, females and the sexes combined.

Based on the results of this study, the acute oral toxicity caused by copper carbonate was sufficient to classify the substance as 'Harmful if Swallowed' under Commission Directive 93/21/EC)

5.3 Conclusion Non-entry field

5.3.1 Reliability *Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4*

(1) valid without restriction

5.3.2 Deficiencies No

(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Guidelines and quality assurance • [redacted]

Materials and Methods • [redacted]

Results and discussion • [redacted]

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/01	**A6.1.1(01), Acute Oral Toxicity**
	A6_1-1. [redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	* [redacted]
3.1	**COMMENTS FROM ...**
3.2 Date	*Give date of comments submitted*
3.3 Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1-1. Summary of Acute Toxicity Results

Dose mg/kg	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
500 mg/kg males	0/5	-	Dark stained urogenital area was observed from Day 2 to Day 8.
500 mg/kg females	0/5	-	Dark stained urogenital area was observed from Day 3 to Day 7.
2000 mg/kg males	5/5	4-8* days	Two to three days following test substance administration clinical observations included non-formed faeces, dark stained urogenital areas, red stained face, hypoactivity, and hunched posture. All individuals exhibited a light green, granular semifluid in the gastro-intestinal tract. Other observations included dark red/brown stains in the perineum/perianal area, ocular and nasal discharge and extended lumen
2000 mg/kg females	5/5	3-7 days	Two days after test substance administration clinical signs included non-formed faeces, dark stained urogenital area, prostration, dyspnea, cold to touch, hypoactivity and a red stained face. Four individuals exhibited a light green, granular semifluid in the gastro-intestinal tract. Other observations included green stains in the perineum/perianal area along with moist material and an extended lumen.
LD_{50} value	Between 500 – 2000 mg/kg bw for males, females and both sexes combined		

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/02	**A6.1.1(02), Acute Oral Toxicity**

Official use only

1 REFERENCE

1.1 Reference

Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)
If necessary, copy field and enter other reference(s).

[redacted] (1990). Acute Oral Toxicity Test of 'Kupferkarbonat Griin Gefallt 54/56% Cu' in Rats. International Bio Research. Report No. 10-04-0714-90 (unpublished)

1.2 Data protection

Yes

(indicate if data protection is claimed)

1.2.1 Data owner

Give name of company

Wood Preservative Copper Taskforce

1.2.2 Criteria for data protection

Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:

Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

Yes - the study was conducted to the following test guidelines:

OECD Guidelines, No. 401. Acute Oral Toxicity (February 24, 1987).

EEC Directive 84/449/EEC. (September 19, 1984).

(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")

2.2 GLP

Yes

(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)

2.3 Deviations

No

(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

3 MATERIALS AND METHODS

In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.

3.1 Test material

As given in section 2

or give name used in study report

3.1.1 Lot/Batch number *List lot/batch number if available*

Section A6.1.1		**Acute Oral Toxicity in the Rat (LD_{50})**	
Annex Point IIA6.1.1		*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*	
IUCLID: 5.1.1/02		**A6.1.1(02), Acute Oral Toxicity**	
		Not reported	
3.1.2	Specification	As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.2.1	Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Powder	
3.1.2.2	Purity	*Give purity in % of active substance* [redacted]	X
3.1.2.3	Stability	*Describe stability of test material* Stable at room temperature	
3.2 Test Animals		Non-entry field	
3.2.1	Species	Rat	
3.2.2	Strain	Crl.: (WI) BR - Wistar	
3.2.3	Source	Firma Charles River Wiga, Germany	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	Males weighed 220-314 g and females weighed 181-262 g.	
3.2.6	Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups* 5 males and 5 females	
3.2.7	Control animals	No	
3.3 Administration/ Exposure		Oral *Fill in respective route in the following, delete other routes*	
3.3.1	Postexposure period	14 days	
		Oral	
3.3.2	Type	Gavage	
3.3.3	Vehicle	Carboxymethylcellulose	
3.3.4	Concentration	Following a preliminary range finding test with a dose of 2000 mg/kg the final doses were 1000, 1500 and 2000 mg/kg.	
3.3.5	Concentration in vehicle	10, 15 and 20%	X
3.3.6	Total volume applied	1.8 – 3.1 ml	
3.3.7	Controls	Not applicable	

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/02	**A6.1.1(02), Acute Oral Toxicity**
3.4 Examinations	Clinical observations were recorded after 10 minutes, 1, 2, 6, 24 hours and once daily thereafter up to Day 14 following test substance administration. The bodyweights of test organisms were recorded immediately before treatment (Day 0) and surviving animals reweighed on Day 7 and Day 14 (termination). Animals found dead or killed in extremis were immediately necropsied. The surviving animals were sacrificed after 14 days and gross pathological examinations performed.
3.5 Method of determination of LD_{50}	The LD_{50} values were carried out by probit analysis.
3.6 Further remarks	Not applicable
	4 RESULTS AND DISCUSSION *Describe findings. If appropriate, include table. Sample tables are given below.*
4.1 Clinical signs	*No effects / describe significant effects referring to data in results table* Severe clinical symptoms related to CNS-symptoms, coordination, reflexes and automatic functions were observed with dose related intensity up to 9 days post administration. For further details, refer to Table A6.1.1. Weight gains were reduced in surviving animals. In the 1500 and 2000 mg/kg dose groups some weight losses were observed. For further details, refer to Table A6.1.1. X
4.2 Pathology	*No effects / describe significant effects referring to data in results table* Gross pathological examination at 14 days post administration revealed no test article dependent findings in any of the dose groups. Those macroscopic changes observed were attributable to the sacrificing procedure or to minor variations which often occur spontaneously in rats of this strain and age. In contrast, severe macroscopic changes of the gastro-intestinal tract were observed in all mid and high dose animals killed in extremis or died spontaneously. The findings are considered to be test article-related. For further details refer to Table A6.1.1
4.3 Other	*Describe any other significant effects* Not applicable

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/02	**A6.1.1(02), Acute Oral Toxicity**
4.4 LD_{50}	*Give LD_{50} male, females, males + females* Males - 1434 mg/kg Females - 1291 mg/kg Male and females combined - 1385 mg/kg

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods *Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines*

The aim of this study was to determine the acute oral toxicity of copper carbonate to male and female rats. The test concentrations were 1000, 1500 and 2000 mg/kg bw. During a 14-day post exposure period the test animals were assessed for clinical observations, bodyweight change and mortality. At the end of the study all animals were sacrificed and subject to pathological examination.

The study was conducted according to GLP and the following guidelines;

OECD Guidelines, No. 401. Acute Oral Toxicity (February 24, 1987).

EEC Directive 84/449/EEC. (September 19, 1984).

5.2 Results and discussion *Summarize relevant results; discuss dose-response relationship.*

Severe clinical symptoms were observed up to 9 days post administration. There were reduced weight gains in all test animals. Gross pathological examinations at 14 days revealed no test article dependant findings in any of the dose groups. However, all mid and high dose animals killed in extremis or died spontaneously revealed characteristic gastro-intestinal alterations, which were considered to be test article related.

The resulting LD50 values were 1434, 1291 and 1385 mg/kg for males, females and both sexes combined respectively. Based on these results and according to EU directive 83/467/EEC copper carbonate should be classified as 'Harmful if Swallowed' under Commission Directive 93/21/EC)

5.3 Conclusion Non-entry field

5.3.1 Reliability *Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4*

1

5.3.2 Deficiencies No

Section A6.1.1	**Acute Oral Toxicity in the Rat (LD_{50})**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/02	**A6.1.1(02), Acute Oral Toxicity**

(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and	*Discuss if deviating from view of rapporteur member state*
discussion Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1-1. Summary of Findings for Acute Oral Toxicity

Dose mg/kg	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
1000 males	0/5	-	Clinical observations included reduced activity, general reactions, body tone and skin turgor. Additional signs were piloerection, diarrhoea, paleness in skin/mucous membrane and test organisms adopted a squatting position. One animal was killed in extremis and pathological investigations determined residues of the test article in the stomach and green discolouration of the intestine. After 14 days observation period, pathological findings included a white cover on the mucous membrane of the stomach in one male and one female, foamy yellow contents in the intestine, swollen liver and spleen, pale kidneys and hydrometra in the genital system of one female.
1000 females	2/5	Day 7	
1500 males	4/5	Day 2 – Day 8	Clinical observations included reduced activity and general reactions. Additional signs were pilorection, diarrhoea, paleness in skin/mucous membrane and test organisms adopted a squatting position. Pathological findings of animals killed in extremis prior to test termination included marbled lung, green discoloured and swollen mucous membrane of the stomach After 14 days, pathological findings included swollen mucous membranes in the stomach and intestine of one male and two females. One organism had an enlarged and darkened spleen.
1500 females	3/5	3 hours – Day 6	
2000 males	4/5	Day 3 – Day 9	Clinical observations included reduced activity, general reactions, body tone and skin turgor. Additional signs were pilorection, diarrhoea, paleness in skin/mucous membrane and test organisms adopted a squatting position. Pathological findings in animals killed in extremis included swollen mucous membranes, green discoloration and mucous membrane and corrosion in the stomach of 3 males and 3 females. Four males and three females had hyperaemic and green discolouration of the intestine. Other findings were reduced and discoloured spleen and abnormal coloured kidney. After 14 days two individuals had enlarged and dark discoloured spleen. Other pathological findings included a marbled liver and lung, enlarged and dark coloured spleen, marbled and discoloured kidney and inflated and green coloured intestine.
2000 females	3/5	4 hours – Day 7	
LD_{50} value	Male – 1434 mg/kg Female – 1291 mg/kg Males and Females – 1385 mg/kg		

Section A6.1.1		**Acute Oral Toxicity in the Rat (LD_{50})**	
Annex Point IIA6.1.1		*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*	
IUCLID: 5.1.1/03		**A6.1.1(03), Acute Oral Toxicity**	
		1 REFERENCE	Official use only
1.1	**Reference**	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)* *If necessary, copy field and enter other reference(s).* [redacted] (2002) Cupric Oxide: Acute Oral Toxicity in the Rat – Acute Toxic Class Method. SafePharm Laboratories. Report No. 1645/001 (unpublished).	
1.2	**Data protection**	Yes *(indicate if data protection is claimed)*	
1.2.1	Data owner	*Give name of company* Wood Preservative Copper Taskforce	
1.2.2	Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes – the study was conducted according to the following test guideline: OECD Guidelines for the Testing of Chemicals No. 423 "Acute Oral Toxicity – Acute Toxic Class Method" (adopted 17 December 2001) *(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2	**GLP**	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	X
2.3	**Deviations**	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
		3 MATERIALS AND METHODS *In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.*	
3.1	**Test material**	Copper Oxide *or give name used in study report*	
3.1.1	Lot/Batch number	*List lot/batch number if available* Lot/Batch number: 02-0084	

Section A6.1.1 **Annex Point IIA6.1.1** **IUCLID: 5.1.1/03**		**Acute Oral Toxicity in the Rat (LD_{50})** *Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)* **A6.1.1(03), Acute Oral Toxicity**	
3.1.2	Specification	As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	X
3.1.2.1	Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Brown/black powder	
3.1.2.2	Purity	*Give purity in % of active substance* [redacted]	
3.1.2.3	Stability	*Describe stability of test material* Stable at room temperature	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Rat	
3.2.2	Strain	Sprague-Dawley	X
3.2.3	Source	Charles River (UK) Ltd, Margate, Kent, UK	
3.2.4	Sex	Male	X
3.2.5	Age/weight at study initiation	Test animals were at least 200 g and were approximately 8 weeks old.	
3.2.6	Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups* 3 (2 groups both dosed 2000 mg/kg bw)	
3.2.7	Control animals	No	
3.3	**Administration/ Exposure**	Oral *Fill in respective route in the following, delete other routes*	
3.3.1	Postexposure period	14 days	
		Oral	
3.3.2	Type	Gavage	
3.3.3	Concentration	Gavage — Two groups dosed at: 2000 .. mg/kg bw	
3.3.4	Vehicle	Arachis oil BP	
3.3.5	Concentration in vehicle	200 mg/ml	
3.3.6	Total volume applied	10 ml/kg	
3.3.7	Controls	Not applicable – no control animals used in study	
3.4	**Examinations**	Clinical observations, mortality, bodyweights and necropsy. Observations for death or toxicity were taken 0.5, 1, 2 and 4	

hours after dosing and then once daily for fourteen days. Individual bodyweights were measured prior to dosing and seven and fourteen days after treatment. All animals were subjected to gross pathological examination after death.

3.5 Method of determination of LD_{50}

LD_{50} was determined from mortality data and not by statistical analysis.

4 RESULTS AND DISCUSSION

Describe findings. If appropriate, include table. Sample tables are given below.

4.1 Clinical signs

No effects / describe significant effects referring to data in results table

There were no signs of systemic toxicity at any observation time point in any of the treated animals.

4.2 Pathology

No effects / describe significant effects referring to data in results table

No abnormalities were noted at necropsy.

4.3 Other

Describe any other significant effects

There were no mortalities among any of the treated animals at study termination.

All animals showed expected gains in bodyweight over the study period.

4.4 LD_{50}

Give LD_{50} male, females, males + females
State if no lethal effect at maximal dose

There were no mortalities or signs of systemic toxicity among any of the animals treated with copper oxide at the test concentration of 2000 mg/kg b.w. An LD_{50} of >2500 mg/kg b.w can be estimated using the flow chart in annex 2d of OECD Guidelines for the Testing of Chemicals No. 423 "Acute Oral Toxicity – Acute Toxic Class Method" (adopted 17 December 2001).

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines

The study was performed to assess the acute oral toxicity of copper oxide following a single oral administration by gavage in the Sprague-Dawley rat. A group of three fasted male rats were treated with the test material at a dose level of 2000 mg/kg bw administered as a suspension in Arachis oil BP. This was followed by a further group of three fasted males treated with the same dose level.

The animals were observed for deaths or overt signs of

		toxicity at 0.5, 1, 2 and 4 hours after dosing and subsequently once daily for 14 days. The individual bodyweights were recorded prior to dosing, 7 and 14 days after treatment. At the end of the observation period, the animals were sacrificed and subject to gross pathological examination. The study was conducted according to OECD Guidelines for the Testing of Chemicals No. 423 "Acute Oral Toxicity – Acute Toxic Class Method" (adopted 17 December 2001). The study was also conducted according to GLP. No deviations from the test guidelines, or deficiencies in the method were reported.	X
5.2	**Results and discussion**	*Summarize relevant results; discuss dose-response relationship.* There were no mortalities or signs of systemic toxicity among any of the animals treated with copper oxide at the test concentration of 2000 mg/kg b.w. All animals showed expected gains in bodyweight over the study period and there were no abnormalities noted at necropsy. An LD_{50} of >2500 mg/kg b.w can be estimated using the flow chart in annex 2d of OECD Guidelines for the Testing of Chemicals No. 423 "Acute Oral Toxicity – Acute Toxic Class Method" (adopted 17 December 2001). The test material does not meet the criteria for classification according to EU labelling regulations Commission Directive 93/21/EEC.	
5.3	**Conclusion**	Non-entry field	
5.3.1	Reliability	*Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4* (1) valid without restriction	
5.3.2	Deficiencies	No *(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)*	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	• [redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.1		**Acute Oral Toxicity - LD_{50} Test in the Rat**
Annex Point IIA6.1.1		*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/04		**A6.1.1(04)**

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] X 1994. Test to Evaluate the Acute Toxicity Following a Single Oral Administration (LD50) in the Rat. Pharmakon Europe. Report No. 44193 (unpublished). *Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages) If necessary, copy field and enter other reference(s).*	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Wood Preservatives Copper Task Force	
1.2.2	Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes – the study was conducted according to the following test guidelines: OECD No. 401 (1987) EEC 92/69 – Annex V – Method B1 (1992) – 93/21 (1993) *(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2	**GLP**	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
2.3	**Deviations**	Yes The bodyweights of three females were noted beyond the norms (120-180 g) 117 and 119 g. It was reported that these deviations were not considered to have affected the outcome of the objectives of the study. *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
		3 MATERIALS AND METHODS *In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.*	
3.1	**Test material**	As given in section 2 *or give name used in study report*	X
3.1.1	Lot/Batch number	844	

Section A6.1.1	**Acute Oral Toxicity - LD_{50} Test in the Rat**	
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*	
IUCLID: 5.1.1/04	**A6.1.1(04)**	
3.1.2 Specification	As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	X
3.1.2.1 Description	Powder, blue crystals *If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)*	
3.1.2.2 Purity	[redacted] *Give purity in % of active substance*	
3.1.2.3 Stability	Stable at room temperature *Describe stability of test material*	
3.2 Test Animals	Non-entry field	
3.2.1 Species	Rat	
3.2.2 Strain	Sprague-Dawley	
3.2.3 Source	Iffa-Crédo, B.P. 0109 (69592 L'Arbresle Cedex, France)	
3.2.4 Sex	Males and females	
3.2.5 Age/weight at study initiation	Age: 5-7 weeks Weight of males: 130 - 230 g Weight of females: 120 – 180 g	
3.2.6 Number of animals per group	5 males and 5 females per dose group *Give number specify, if there are differences for example for treatment and recovery groups*	
3.2.7 Control animals	Yes – 5 males and 5 females	
3.3 Administration/ Exposure	Oral *Fill in respective route in the following, delete other routes*	
3.3.1 Postexposure period	14 days	
	Oral	
3.3.2 Type	Gavage	
3.3.3 Concentration	Gavage 0 (control), 447, 562, 708 and 893mg/kg bw	
3.3.4 Vehicle	Purified water	
3.3.5 Concentration in vehicle	0, 2.235, 2.810, 3.540, 4.465 % (w/v)	
3.3.6 Total volume applied	20 ml/kg	
3.3.7 Controls	Vehicle only	
3.4 Examinations	Clinical observations, mortality, bodyweights and necropsy. Animals were observed for clinical signs and mortality 15 minutes and 1, 2 and 4 hours after administration of the test material, followed by daily observations for the 14 day study period. Bodyweights were measured the day before	

		treatment, immediately before treatment, on day 8 and at death. All animals were subjected to gross pathological examination after death.
3.5	**Method of determination of LD_{50}**	Bliss, Litchfield and Wilcoxon, *or other*

RESULTS AND DISCUSSION

Describe findings. If appropriate, include table. Sample tables are given below.

Section A6.1.1 Annex Point IIA6.1.1 IUCLID: 5.1.1/04		**Acute Oral Toxicity - LD_{50} Test in the Rat** *Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)* **A6.1.1(04)**
3.6	**Clinical signs**	The major modifications noted during clinical observations were prostration and subdued behaviour from 15 minutes after the treatment to 4 hours. Greenish diarrhoea was also observed from 1-4 hours after the treatment. Some cases of infrequent stools were noted on Day 2. No clinical signs were observed in the control group. For further details see Table A6_1-1 *No effects / describe significant effects referring to data in results table*
3.7	**Pathology**	There were no macroscopically detectable abnormalities detected in any of the control test organisms. There were no abnormalities detected in any of the animals sacrificed on study termination. Detected abnormalities in animals that died during the observation period included stomach distension by a greenish liquid (1 female 447 mg/kg, 1 female 562 mg/kg, 1 male 708 mg/kg), congested intestines (1 male 447 mg/kg, 2 males 893 mg/kg) and a discoloured liver (1 female 447 mg/kg). *No effects / describe significant effects referring to data in results table*
3.8	**Other**	Bodyweights: Body weight change in the treated animals of the 447 mg/kg dose group and the males in the 562 mg/kg dose group were similar to those in the control groups (although mean weights were statistically lower than controls in males in the 562 mg/kg dose group on day 8 only). The mortality rate observed in the other dose groups did not allow analysis of body weight changes. Mortality – see Table A6_1-1 *Describe any other significant effects*
3.9	**LD_{50}**	LD_{50} for males and females by the Bliss' method – 482 mg/kg (403-575 mg/kg) LD_{50} for males and females by the Litchfield & Wilcoxon method 481 mg/kg (400-580 mg/kg) *Give LD_{50} male, females, males + females* *State if no lethal effect at maximal dose*
		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	An acute oral toxicity test was carried out according to OECD (No. 401) and EU (EEC 92/69 – Annex V – Method B1 (1992) – 93/21 1993) guidelines in Sprague-Dawley rats. Five males and five females were tested at each dose level

of 0 (control), 447, 562, 708 and 893 mg/kg bw. Copper sulphate was administered by gavage with purified water utilised as the vehicle.

The only protocol deviation was the bodyweights of three females which were noted to be beyond the norms (120-180 g) 117 and 119 g. This was not considered to have any affect on the outcome of the study.

Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines

4.2 Results and discussion

The oral LD_{50} of copper sulphate was determined to be 481-482 mg/kg.

There were no mortalities in the control groups. Mortality demonstrated a dose-response relationship with 2/5 test organisms dying in the 447 mg/kg group and all test organisms dying in the highest (893 mg/kg) dose group.

The major modifications noted during the clinical observations were prostration and subdued behaviour from 15 minutes after the treatment to 4 hours. Greenish diarrhoea was also observed from 1 hour to 4 hours after the treatment. Some cases of infrequent stools were noted on Day 2 (except in the 447 mg/kg dose group). No clinical signs were observed in the control groups.

Some cases of stomach distension by a greenish liquid and intestines slightly congested were observed in animals which died during the observation period. No macroscopically detectable abnormality was noted in animals sacrificed at study termination.

Body weight change in the treated animals of the 447 mg/kg dose group and the males in the 562 mg/kg dose group were similar to those in the control groups (although mean weights were statistically lower than controls in males in the 562 mg/kg dose group on day 8 only).

Summarize relevant results; discuss dose-response relationship.

4.3 Conclusion Non-entry field

4.3.1 Reliability (1) valid without restriction

Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4

4.3.2 Deficiencies No

(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)

Evaluation by Competent Authorities

Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

Section A6.1.1	**Acute Oral Toxicity - LD_{50} Test in the Rat**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/04	**A6.1.1(04)**

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table A6_1-1. **Table for Acute Toxicity**

Section A6.1.1 **Acute Oral Toxicity - LD_{50} Test in the Rat**

Annex Point IIA6.1.1 *Specify section no., heading, route and species as appropriate*
Specify type of test (Limit Test, LD_{50}, special investigation)

IUCLID: 5.1.1/04 **A6.1.1(04)**

Dose mg/kg	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
Contro l males	0/5	-	No clinical signs were observed
Control females	0/5	-	
447 males	2/5	2 hours	All animals displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in one animal, 1-hour after dosing. Greenish diarrhoea was observed in 2 test organisms 2-4 hours after dosing. Infrequent stools were observed in 6 test organisms on Day 2. All surviving test organisms returned to normal from Day 3
447 females	2/5	2 hours-2 days	
562 males	2/5	2-4 hours	All animals displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in three animals, 1-2 hours after dosing. Greenish diarrhoea was observed in 3 test organisms 2 hours to 2 days after dosing. Infrequent stools were observed in 3 test organisms on Day 2. All surviving test organisms returned to normal from Day 3
562 females	5/5	1 hour-2 days	
708 males	4/5	1 hour-2 days	Seven displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in three animals, 15 minutes after dosing. Greenish diarrhoea was observed in 2 test organisms 2-4 hours after dosing. Infrequent stools were observed in 1 test organism on Day 2. The one surviving test organisms returned to normal from Day 3
708 females	5/5	1-4 hours	
893 males	5/5	1-2 hours	Nine animals displayed subdued behaviour 15 minutes after dosing. Prostration was observed in one animal fifteen minutes after dosing and four animals, 1-hour after dosing. Greenish diarrhoea was observed in 2 test organisms 1 hour after dosing. All animals had died 2 hours after dosing.
893 females	5/5	1-2 hours	
LD_{50} value	481-482 mg/kg		

Section A6.1.1	**Acute Oral Toxicity - LD_{50} Test in the Rat**
Annex Point IIA6.1.1	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.1/04	**A6.1.1(04)**

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1-1. Table for Acute Toxicity

Section A6.1.1 **Acute Oral Toxicity - LD_{50} Test in the Rat**

Annex Point IIA6.1.1 *Specify section no., heading, route and species as appropriate*
Specify type of test (Limit Test, LD_{50}, special investigation)

IUCLID: 5.1.1/04 **A6.1.1(04)**

Dose mg/kg	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
Contro l males	0/5	-	No clinical signs were observed
Control females	0/5	-	
447 males	2/5	2 hours-2 days	All animals displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in one animal, 1-hour after dosing. Greenish diarrhoea was observed in 2 test organisms 2-4 hours after dosing. Infrequent stools were observed in 6 test organisms on Day 2. All surviving test organisms returned to normal from Day 3
447 females	2/5	2 hours	
562 males	2/5	2-4 hours	All animals displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in three animals, 1-2 hours after dosing. Greenish diarrhoea was observed in 3 test organisms 2 hours to 2 days after dosing. Infrequent stools were observed in 3 test organisms on Day 2. All surviving test organisms returned to normal from Day 3
562 females	5/5	1 hour-2 days	
708 males	4/5	1 hour-2 days	Seven displayed subdued behaviour 15 minutes after dosing, although this had returned to normal 2 days following treatment. Prostration was observed in three animals, 15 minutes after dosing. Greenish diarrhoea was observed in 2 test organisms 2-4 hours after dosing. Infrequent stools were observed in 1 test organism on Day 2. The one surviving test organisms returned to normal from Day 3
708 females	5/5	1-4 hours	
893 males	5/5	1-2 hours	Nine animals displayed subdued behaviour 15 minutes after dosing. Prostration was observed in one animal fifteen minutes after dosing and four animals, 1-hour after dosing. Greenish diarrhoea was observed in 2 test organisms 1 hour after dosing. All animals had died 2 hours after dosing.
893 females	5/5	1-2 hours	
LD_{50} value	481-482 mg/kg		

Section A6.1.2	**Acute Dermal Toxicity in Rabbits (LD_{50})**
Annex Point IIA6.1.2	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.3(01)	**A6.1.2(01), Acute Dermal Toxicity**

Official use only

1 REFERENCE

1.1 Reference

Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)
If necessary, copy field and enter other reference(s).

[redacted]. (2001). Copper Carbonate: Acute Dermal Toxicity (Limit Test) in the Rat. SafePharm Laboratories. Project No. 453/008R (unpublished).

1.2 Data protection

Yes

(indicate if data protection is claimed)

1.2.1 Data owner

Give name of company

Wood Preservative Copper Taskforce

1.2.2 Criteria for data protection

Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:

Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

Yes – the study was carried out according to the following test guidelines;

Commission Directive 92/69/EEC Method B3 Acute Toxicity (Dermal).

OECD Guidelines for the Testing of Chemicals No. 402 'Acute Dermal Toxicity' (adopted 24 February 1987).

EPA Health Effects Test Guidelines OPPTS 870.1200 Acute Dermal Toxicity, August 1998.

(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")

2.2 GLP

Yes

(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)

2.3 Deviations

No

(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

3 MATERIALS AND METHODS

In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.

Section A6.1.2	**Acute Dermal Toxicity in Rabbits (LD_{50})**
Annex Point IIA6.1.2	*Specify section no., heading, route and species as appropriate*
IUCLID: 5.1.3(01)	*Specify type of test (Limit Test, LD_{50}, special investigation)*
	A6.1.2(01), Acute Dermal Toxicity
3.1 Test material	As given in section 2
	or give name used in study report
3.1.1 Lot/Batch number	*List lot/batch number if available*
	26694/4/ROX
3.1.2 Specification	As given in section 2
	Deviating from specification given in section 2 as follows
	(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):
3.1.2.1 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)*
	Green powder
3.1.2.2 Purity	*Give purity in % of active substance* X
	[redacted]
3.1.2.3 Stability	*Describe stability of test material*
	Stable and room temperature
3.2 Test Animals	Non-entry field
3.2.1 Species	Rat
3.2.2 Strain	Sprague-Dawley CD (Crl:CD(SD) IGS BR)
3.2.3 Source	Charles River (UK) Ltd, Margate, UK.
3.2.4 Sex	Male and female
3.2.5 Age/weight at study initiation	At the start of the study, the males weighted 225-242 g and the females 204-230 g, and were approximately 8 weeks old.
3.2.6 Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups*
	5 males and 5 females.
3.2.7 Control animals	No
3.3 Administration/ Exposure	Dermal
	Fill in respective route in the following, delete other routes
3.3.1 Post-exposure period	14 days
	Dermal
3.3.2 Area covered	10 % of body surface
3.3.3 Occlusion	Semi-occluded
3.3.4 Vehicle	Distilled water
3.3.5 Concentration in vehicle	2000 mg/kg bw

3.3.6 Total volume applied	Not reported
3.3.7 Duration of exposure	24 hours
3.3.8 Removal of test substance	Distilled water was used to remove any residual material.
3.3.9 Controls	Not applicable
3.4 Examinations	Mortality and clinical signs: The test animals were observed for deaths or overt signs of toxicity 0.5, 1, 2 and 4 hours after dosing and subsequently once daily for 14 days. Dermal examination: After removal of the dressings and subsequently once daily for 14 days, the test sites were examined for evidence of primary irritation. Scoring system: Draize scoring system. Bodyweights: Individual bodyweights were recorded prior to application of the test material on Day 0 and on Days 7 and 14. Pathology: At the end of the study all animals were sacrificed and subjected to gross necropsy examination. This consisted of an external examination and opening of abdominal and thoracic cavities. The appearance of any macroscopic abnormalities was recorded.
3.5 Method of determination of LD_{50}	Mortality data was used to determine the LD_{50}. To statistical analysis were applied to the data.
3.6 Further remarks	

4 RESULTS AND DISCUSSION

Describe findings. If appropriate, include table. Sample tables are given below.

4.1 Clinical signs	*No effects / describe significant effects referring to data in results table* Mortality: No deaths occurred during the study period. Clinical observations: There were no signs of systemic toxicity noted during the study period. Dermal reactions: Staining was noted at the treatment sites of all males one day after dosing. The staining did not affect

	the evaluation of skin responses. There were no signs of dermal irritation. Bodyweight: All animals showed expected gain in bodyweight during the study period.
4.2 Pathology	*No effects / describe significant effects referring to data in results table* No abnormalities were noted at necropsy.
4.3 Other	*Describe any other significant effects* Not applicable
4.4 LD_{50}	The acute dermal median lethal dose (LD50) in male and female Sprague-Dawley rats was found to be greater than 2000 mg/kg bw.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods	*Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines* A group of ten animals (5 male and 5 female) were given a single, 24-hour, semi-occluded dermal application of undiluted copper carbonate to intact skin at a dose level of 2000 mg/kg bw. Clinical signs and bodyweight development were monitored during the study. All animals were subjected to gross necropsy examination. The study was GLP compliant and was conducted in accordance with the following guidelines; Commission Directive 92/69/EEC Method B3 Acute Toxicity (Dermal). OECD Guidelines for the Testing of Chemicals No. 402 'Acute Dermal Toxicity' (adopted 24 February 1987). EPA Health Effects Test Guidelines OPPTS 870.1200 Acute Dermal Toxicity, August 1998.

Section A6.1.2	**Acute Dermal Toxicity in Rabbits (LD_{50})**
Annex Point IIA6.1.2	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.3(01)	**A6.1.2(01), Acute Dermal Toxicity**

5.2 Results and discussion *Summarize relevant results; discuss dose-response relationship.*

There was no mortality, signs of clinical observations or dermal reactions noted in any of the test organisms during the study. The acute dermal median dose (LD50) of the test material in Sprague Dawley strain rats was found to be greater than 2000 mg/kg bw.

The test material does not meet the criteria for classification and will not require labelling for dermal toxicity in accordance with EU labelling regulations Commission Directive 93/21/EEC.

5.3 Conclusion Non-entry field

5.3.1 Reliability *Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4*

1

5.3.2 Deficiencies No

(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

Section A6.1.2	**Acute Dermal Toxicity in Rabbits (LD_{50})**
Annex Point IIA6.1.2	*Specify section no., heading, route and species as appropriate* *Specify type of test (Limit Test, LD_{50}, special investigation)*
IUCLID: 5.1.3(01)	**A6.1.2(01), Acute Dermal Toxicity**

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.4 **Annex Point IIA6.4.1** **IUCLID : 5.2.1(01)**	**Acute Dermal Irritation in the New Zealand White Rabbit** *Specify section no., heading and species as appropriate* **A6.1.4(01), Acute Dermal Irritation**	**Official use only**
	REFERENCE	
3.4 Reference	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)* *If necessary, copy field and enter other reference(s).* [redacted]2001). Copper Carbonate: Acute Dermal Irritation in the Rabbit. SafePharm Laboratories Limited. Report No. 453/009R (unpublished)	
3.5 Data protection	Yes *(indicate if data protection is claimed)*	
3.5.5 Data owner	*Give name of company* Wood Preservative Copper Taskforce	
3.5.6 Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]	
	5 GUIDELINES AND QUALITY ASSURANCE	
5.1 Guideline study	Yes - the study was conducted according to the following test guidelines: Commission Directive 92/69/EEC Method B4 Acute Toxicity (Skin Irritation). OECD Guidelines for the Testing of Chemicals No. 404 'Acute Dermal Irritation/Corrosion' (adopted 17 July 1992). EPA Health Effects Test Guidelines OPPTS 870.2500 Acute Dermal Irritation. August 1998. *(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
5.2 GLP	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
5.3 Deviations	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
	6 MATERIALS AND METHODS *In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.*	
6.1 Test material	Copper carbonate	

6.1.5 Lot/Batch number	*List lot/batch number if available* Lot/batch number: 26694/4/ROX
6.1.6 Specification	As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*
Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Green Powder
Purity	*Give purity in % active substance* [redacted] X
Stability	*Describe stability of test material* Stable at room temperature
6.2 Test Animals	Non-entry field
6.2.5 Species	Rabbit
6.2.6 Strain	New Zealand White
6.2.7 Source	David Percival Ltd, Moston, Sandbach, Cheshire, UK
6.2.8 Sex	Male
6.2.9 Age/weight at study initiation	At the start of the study the animals weighed 2.74-2.90 kg and were 12-16 weeks old.
6.2.10 Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups* 3
6.2.11 Control animals	No
6.3 Administration/ Exposure	Dermal
6.3.5 Application	Non entry field
Preparation of test substance	Test substance was prepared by mixing 0.5 grams of test substance with 0.5 ml of distilled water, immediately before application.
Test site and Preparation of Test Site	*State site: dorsal area of the trunk/left/right side of the trunk* *Shaved skin or other* *State skin cleaning method and used agents* On the day prior to test substance administration, fur of the test animals was clipped free from the dorsal/flank area. No other information was reported.
6.3.6 Occlusion	Semi-occluded
6.3.7 Vehicle	Distilled water
6.3.8 Concentration in vehicle	Not applicable.

6.3.9 Total volume applied	0.5 g
6.3.10 Removal of test substance	The test site was swabbed with distilled water to remove any residual material. *(give solvent, detergents)*
6.3.11 Duration of exposure	4-hours
6.3.12 Postexposure period	72-hours
6.3.13 Controls	Not applicable.
6.4 Examinations	Irritation. Test sites were examined for irritation 1 hour after removal of the patches and 24, 48 and 72 hours later.
6.4.5 Clinical signs	No
6.4.6 Dermal examination	Yes
scoring system	*State scoring system* Draize scoring system
Examination time points	Approximately 1, 24, 48 and 72 hours following removal of the test material, the test sites were examined for evidence of primary irritation.
6.4.7 Other examinations	No other examinations were taken.
6.5 Further remarks	The pH of a 10 % w/v aqueous preparation of the test material was determined as 8.5.
	7 RESULTS AND DISCUSSION *Describe findings. If appropriate, include table. Sample tables are given below.*
7.1 Average score	Non-entry field
7.1.5 Erythema	*Give average score for all animals at 24, 48, 72 h* The average score at all examination time points was 0.
7.1.6 Edema	*Give average score for all animals at 24, 48, 72 h* The average score at all examination time points was 0.
7.2 Reversibility	*Name effect and give time for reversion.* Not applicable
7.3 Other examinations	*Give results* No other examinations were taken.
7.4 Overall result	There was no evidence of skin irritation noted during the study.
	8 APPLICANT'S SUMMARY AND CONCLUSION
8.1 Materials and	*Give concise description of method; give test guidelines no. and discuss*

methods	*relevant deviations from test guidelines* This study was conducted to assess the irritancy potential of copper carbonate to the skin of the New Zealand White rabbit. A group of 3 male New Zealand White rabbits were given a single, 4-hour, semi-occluded dermal application of copper carbonate moistened with distilled water to intact skin. Irritancy was determined 1, 24, 48 and 72 hours after the test substance was removed. The study was conducted according to Commission Directive 92/69/EEC Method B4 Acute Toxicity (Skin Irritation), OECD Guidelines for the Testing of Chemicals No. 404 'Acute Dermal Irritation/Corrosion' (adopted 17 July 1992) and EPA Health Effects Test Guidelines OPPTS 870.2500 Acute Dermal Irritation. August 1998. The study was also conducted according to GLP. No deviations from the test guidelines, or deficiencies in the method were reported.
8.2 Results and discussion	*Summarize relevant results; discuss dose-response relationship.* The test material produced a primary irritation index of 0.0 and was classified as NON IRRITANT to rabbit skin according to the Draize classification scheme. No corrosive effects were noted.
8.3 Conclusion	The test material did not meet the criteria for classification as irritant or corrosive to skin according to the EU labelling regulations Commission Directive 93/21/EEC.
8.3.5 Reliability	*Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4* (1) valid without restriction.
8.3.6 Deficiencies	No *(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)*

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Section A6.1.4
Annex Point IIA6.4.1
IUCLID : 5.2.1(01)

Acute Dermal Irritation in the New Zealand White Rabbit

Specify section no., heading and species as appropriate

A6.1.4(01), Acute Dermal Irritation

Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

	Comments from ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 6.1.4	**Acute Eye Irritation in the New Zealand White Rabbit**
Annex Point IIA6.1.4	*Specify section no., heading and species as appropriate*
IUCLID : 5.2.2(01)	**A6.1.4(02), Acute Eye Irritation**

Official use only

1 REFERENCE

1.1 Reference

Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)
If necessary, copy field and enter other reference(s).

[redacted]. (2001). Copper Carbonate: Acute Eye Irritation in the Rabbit. SafePharm Laboratories Limited. Report No. 453/010R (unpublished)

1.2 Data protection

Yes
(indicate if data protection is claimed)

1.2.1 Data owner

Give name of company

Wood Preservative Copper Taskforce

1.2.2 Criteria for data protection

Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:

Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

Yes - the study was conducted according to the following test guidelines:

Commission Directive 92/69/EEC Method B5 Acute Toxicity (Eye Irritation/Corrosion).

OECD Guidelines for the Testing of Chemicals No. 405 'Acute Eye Irritation/Corrosion' (adopted 24 February 1987).

EPA Health Effects Test Guidelines OPPTS 870.2400 Acute Eye Irritation, August 1998.

(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")

2.2 GLP

Yes
(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)

2.3 Deviations

No
(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

3 MATERIALS AND METHODS

In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.

Section 6.1.4	**Acute Eye Irritation in the New Zealand White Rabbit**
Annex Point IIA6.1.4	*Specify section no., heading and species as appropriate*
IUCLID : 5.2.2(01)	**A6.1.4(02), Acute Eye Irritation**

3.1	**Test material**	Copper carbonate *or give name used in study report*
3.1.1 Lot/Batch number	*List lot/batch number if available*	Lot/batch number: 26694/4/ROX
3.1.2 Specification		As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*
3.1.2.1 Description		*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Green powder
3.1.2.2 Purity		*Give purity in % active substance* [redacted]
3.1.2.3 Stability		*Describe stability of test material* Stable at room temperature
3.2	**Test Animals**	Non-entry field
3.2.1 Species		Rabbit
3.2.2 Strain		New Zealand White
3.2.3 Source		David Percival Ltd, Moston, Sandbach, Cheshire, UK.
3.2.4 Sex		One male and two females
3.2.5 Age/weight at study initiation		At the start of the study the animals weighed 2.73-2.81 kg and were twelve to sixteen weeks old.
3.2.6 Number of animals per group	*Give number* *specify, if there are differences for example for treatment and recovery groups*	3.
3.2.7 Control animals		No controls were used in the study, the untreated eye of each test animal served as a control.
3.3	**Administration/ Exposure**	
3.3.1 Preparation of test substance		The test substance was used as supplied with no additional preparation.
3.3.2 Amount of active substance instilled		0.1 ml (91 mg)
3.3.3 Exposure period		72-hours
3.3.4 Postexposure period		14 days
3.4	**Examinations**	Ocular damage/irritation. Approximately 1, 24, 48 and 72 hours after treatment, the eyes were assessed for signs of ocular damage and irritation.

X

3.4.1 Ophthalmoscopic examination: yes

3.4.1.1 Scoring system: *state scoring system and give time table of examinations, describe the terms slight, moderate, etc., if these terms are used*

Draize scoring system and modified Kay and Calandra classification system.

3.4.1.2 Examination time points: Assessment of ocular damage/irritation was made approximately 1 hour and 24, 48 and 72 hours following treatment.

3.4.2 Other investigations: *for example: effect of rinsing*

Any other ocular effects were also noted. Additional observations were made in two treated eyes on Days 7 and 14 to assess the reversibility of the ocular effects.

3.5 Further remarks: The pH of a 10 % w/v aqueous preparation of the test material was determined as 8.5.

RESULTS AND DISCUSSION

Describe findings. If appropriate, include table. Sample tables are given below.

3.6 Clinical signs: *No effects / describe significant effects referring to data in results table*

Not reported

3.7 Average score: Non-entry field

3.7.1 Cornea: *Give average score for all animals at 24, 48, 72 h*

See table A6.1.4 Acute Eye Irritation.

3.7.2 Iris: *Give average score for all animals at 24, 48, 72 h*

See table A6.1.4 Acute Eye Irritation.

3.7.3 Conjunctiva: Non-entry field

3.7.3.1 Redness: *Give average score for all animals at 24, 48, 72 h*

See table A6.1.4 Acute Eye Irritation.

3.7.3.2 Chemosis: *Give average score for all animals at 24, 48, 72 h*

See table A6.1.4 Acute Eye Irritation.

3.8 Reversibility: *Name effect and give time for reversion.*

Yes - One treated eye appeared normal at the 48-hour observation and two other treated eyes appeared normal at the 14-day observation.

3.9 Other: *Describe any other significant effects*

Green residual test material around the eyelids of the treated eye was noted in two animals one hour after treatment.

Diffuse or translucent corneal opacity was noted in two treated eyes at 24 and 48-hour observations with diffuse

corneal opacity at the 72-hour and 7-day observations. Vascularisation of the cornea was noted in two treated eyes at the 7-day observation.

Iridial inflammation was noted in one treated eye one hour after treatment and in two treated eyes at the 24 and 48-hour observations. No other iridial effects were noted.

Moderate conjunctival irritation were noted in all treated eyes one hour after treatment with minimal to moderate conjunctival irritation at the 24-hour observation. Moderate conjunctival irritation was noted in two treated eyes at the 48-hour observation with minimal conjunctival irritation at the 72-hour observation.

For further details please refer to the attached document Table A6.1.4 Acute Eye Irritation.

3.10 Overall result

The test material produced a maximum group mean score of 20.0 and was classified as a moderate irritant to the rabbit eye according to a modified Kay and Calandra classification system.

The test material did not meet the criteria for classification as an eye irritant according to EU labelling regulations Commission Directive 93/21/EEC.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines

This study was conducted to assess the irritancy potential of copper carbonate to the eye of the New Zealand White rabbit.

Three New Zealand White rabbits (2 females, 1 male) were given a single dose of 0.1 ml copper carbonate (91 mg) applied directly into the conjunctival sac of the right eye. The left eye remained untreated and was used for control purposes. Assessment of ocular damage/irritation was made 1, 24, 48 and 72 hours following treatment, according to the Draize scoring system and a modified version of the Kay and Calandra classification system. Any other ocular effects were also noted.

Additional observations were made in two treated eyes on

		days 7 and 14 to assess the reversibility of the ocular effects. The study was conducted according to Commission Directive 92/69/EEC Method B5 Acute Toxicity (Eye Irritation/Corrosion), OECD Guidelines for the Testing of Chemicals No. 405 'Acute Eye Irritation/Corrosion' (adopted 24 February 1987) and EPA Health Effects Test Guidelines OPPTS 870.2400 Acute Eye Irritation, August 1998. The study was also conducted according to GLP. No deviations from the test guidelines, or deficiencies in the method were reported.
4.2	**Results and discussion**	*Summarize relevant results; discuss dose-response relationship.* A single application of the test material to the non-irrigated eye of three rabbits produced diffuse or corneal opacity, iridial inflammation and moderate conjunctival irritation. Vascularisation of the cornea was noted in two treated eyes at the 7-day observation. One treated eye appeared normal at the 48-hour observation and two treated eyes appeared normal at the 14-day observation.
4.3	**Conclusion**	The test material produced a maximum group mean score of 20.0 and was classified as a moderate irritant to the rabbit eye according to a modified Kay and Calandra classification system. The test material did not meet the criteria for classification as an eye irritant according to EU labelling regulations Commission Directive 93/21/EEC.
4.3.1 Reliability		*Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3, or 4* (1) valid without restriction
4.3.2 Deficiencies		No *(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)*

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

Evaluation by Rapporteur Member State

Date [redacted]

Materials and Methods [redacted]

Section 6.1.4	**Acute Eye Irritation in the New Zealand White Rabbit**
Annex Point IIA6.1.4	*Specify section no., heading and species as appropriate*
IUCLID : 5.2.2(01)	**A6.1.4(02), Acute Eye Irritation**

	[redacted]
Results and discussion	[redacted]
	[redacted]
Conclusion	[redacted]
	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	

TABLE A6.1.4 ACUTE EYE IRRITATION - SUMMARY OF RESULTS

	CORNEA		IRIS	CONJUNCTIVA		
	(Degree of opacity)	(Area of Opacity)	(Congestion)	Redness	Chemosis	Discharge
Score (average of animals investigated)	**0-4**	**0-4**	**0-2**	**0-3**	**0-4**	**0-3**
1 hour	0	0	0.33	1.66	1.33	2
24 hour	1	1	0.66	1.66	1.66	1.66
48 hour	1	1	0.66	1.33	1.33	0.66
72 hour	0.66	1	0	0.66	0.66	0
Average 24h, 48h and 72h	0.88	1	0.44	1.22	1.22	0.77
Area effected	Not reported	Not reported	Not reported	Not reported	Not reported	Eyelids
Maximum average score (including area affected, max 110)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Reversibility	Completely reversible	Completely reversible	Completely reversible	Completely reversible	Completely reversible	Completely reversible

Official use only

5 REFERENCE

5.1 Reference

Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)
If necessary, copy field and enter other reference(s).

[redacted] (2001). Copper Carbonate: Skin Sensitization in the Guinea Pig – Magnusson and Kligman Maximisation Method. SafePharm Laboratories Limited. Report No. 453/011R (unpublished).

5.2 Data protection

Yes
(indicate if data protection is claimed)

5.2.1 Data owner

Give name of company

Wood Preservative Copper Taskforce

5.2.2 Criteria for data protection

Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:

Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation]

6 GUIDELINES AND QUALITY ASSURANCE

6.1 Guideline study

Yes - the study was carried out according to the following test guidelines:

Commission Directive 96/54/EC Method B6 Acute Toxicity (Skin Sensitisation).

OECD Guidelines for the Testing of Chemicals No. 406 'Skin Sensitisation' (adopted 17 July 1992).

(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")

6.2 GLP

Yes
(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)

6.3 Deviations

No
(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

7 MATERIALS AND METHODS

In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.

7.1 Test material

Copper carbonate
or give name used in study report

7.1.1 Lot/Batch number	*List lot/batch number if available* Lot/batch number: 26694/4/ROX
7.1.2 Specification	As given in section 2 *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*
7.1.2.1 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Green powder
7.1.2.2 Purity	*Give purity in % of active substance* [redacted] X
7.1.2.3 Stability	*Describe stability of test material* Stable at room temperature
7.1.2.4 Preparation of test substance for application	*a) for induction: used as delivered or other; state solvent* Distilled water was added to the test material. *b) for challenge: used as delivered or other; state solvent* Distilled water was added to the test material.
7.1.2.5 Pretest performed on irritant effects	Yes
7.2 Test Animals	Non-entry field
7.2.1 Species	Guinea pigs *state reason for non-standard species*
7.2.2 Strain	Dunkin Hartley
7.2.3 Source	David Hall Limited, Burton-on-Trent, Staffordshire, UK.
7.2.4 Sex	Male
7.2.5 Age/weight at study initiation	At the start of the study the test animals weighed 300-357 g and were approximately 8-12 weeks old.
7.2.6 Number of animals per group	10 test animals were used in the main study. *Specify, if there are differences e. g. for treatment and recovery groups*
7.2.7 Control animals	Yes – 5 control animals were used in the main study.
7.3 Administration/ Exposure	State study type: Adjuvant *Adjuvant / Non-Adjuvant*
7.3.1 Induction schedule	day 0 – day 7 On day 0, an area of 40 mm x 60 mm of hair was clipped from each animal using veterinary clippers and three pairs of 0.1 ml intradermal injections were made on either side of the mid-line. The injections were: a) Freund's Complete Adjuvant plus distilled water at a ratio of 1:1

b) 0.1 % w/w formulation of the test material in distilled water
c) 0.1 % w/w formulation of the test material in a 1:1 preparation of Freund's Complete Adjuvant plus distilled water.

Approximately 24 and 48 hours later, the degree of erythema at the test material injection sites (injection b) was evaluated.

On day 7, the same area was clipped again on each animal and treated with a topical application of test material (50 % w/w in distilled water) and held in place with occlusive dressing for 48 hours. After 1 and 24 hours, the degree of erythema and oedema was evaluated after removal of the dressings.

Induction of the control animals was performed in an identical manner as for the test animals, except that the test material was ommitted.

The scoring schedule for erythema was derived from 'Modified OECD Test Guideline 406, 1992 and Method B6 Skin Sensitisation of Commission Directive 96/54/EEC' and the scoring schedule for oedema was taken from Draize, J.H. 1977.
see table A_6.1.5 (1) in appendix

7.3.2	Way of Induction	Intradermal and topical Topical induction was kept in place with an occlusive dressing.
7.3.3	Concentrations used for induction	Intradermal induction: 0.1% w/w in distilled water (causing mild to moderate irritation) Topical Induction: 50% w/w in distilled water (causing mild to moderate irritation)
7.3.4	Concentration Freunds Complete Adjuvant (FCA)	See section 3.3.1
7.3.5	Challenge schedule	day 21; see Table_A_6.1.5(1) in appendix

On day 21, an area of 50 mm x 70 mm on both flanks was clipped free of hair and a filter paper patch loaded with test material at the maximum non-irritant concentration (5 % w/w in distilled water) was applied to the right flank of each animal and held in place with surgical tape and an occlusive

	dressing. To ensure the maximum non-irritant concentration was used at challenge, the test material was applied in a similar method to the left flank at a concentration of 2 % w/w in distilled water. The dressings were kept in place for 24 hours, and approximately 24 and 48 hours after challenge dressing removal, the degree of erythema and oedema was evaluated. Any other reactions were also recorded. See Section 3.3.1 for scoring schedules used.
7.3.6 Concentrations used for challenge	Topical challenge: 5 % w/w and 2 % w/w in distilled water (usually maximum non-irritant concentration)
7.3.7 Rechallenge	No
7.3.8 Scoring schedule	24h and 48h after challenge
7.3.9 Removal of the test substance	*give time and solvent (water or other)* After 24h, the dressing was removed and the challenge sites swabbed with cotton wool soaked in distilled water to remove residual material.
7.3.10 Positive control substance	2-Mercaptobenzothiazole
7.4 Examinations	*Non-entry field*
7.4.1 Pilot study	Yes - the concentrations of test material to be used at each stage of the main study were established by sighting tests, in which groups of guinea pigs were treated with various concentrations of test material to select the concentration for intradermal induction, topical induction and topical challenge, respectively. Intradermal induction sighting test: Intradermal injections (0.1 ml/site) were given at concentrations of 0.1, 0.5, 1 and 5% w/w in distilled water. The degree of erythema was assessed at 24, 48, 72 hours and 7-days after injection, but the degree of oedema was not recorded. Evidence of systemic toxicity was also recorded. Topical induction sighting test: Two guinea pigs (intradermally treated with Freund's Complete Adjuvant 9 days earlier) were treated with 5, 10, 25 and 50% w/w of test material in distilled water for an exposure period of 48 hours. The degree of erythema and

oedema was evaluated at 1, 24 and 48 hours after dressing removal.

Topical challenge sighting test:

Concentrations of the test material at 5, 10, 25 and 50% w/w in distilled water were applied to two guinea pigs under occlusive dressings for an exposure period of 24 hours. The degree of erythema and oedema was evaluated at 1, 24 and 48 hours after dressing removal.

8 RESULTS AND DISCUSSION

Describe findings. If appropriate, include table. Sample tables are given below.

8.1 Results of pilot studies

give information on dose selection, i.e. maximum non irritant concentration, if available

Intradermal induction sighting test:

The highest concentration causing only mild to moderate skin irritation which was well tolerated systemically (0.1% w/w) was selected for the intradermal induction stage of the main study.

Topical induction sighting test:

The highest concentration applied causing only mild to moderate dermal irritation which was well tolerated systemically (50% w/w) was selected for the topical induction stage of the main study.

Topical challenge sighting test:

The highest non irritant concentration of the test material and one lower concentration were selected for the topical challenge stage of the main study (5% and 2% w/w in arachis oil BP).

See Section 3.3.1 for scoring schedules used.

4.1.1 Other findings

Three out of the four animals given test material at concentrations of 0.5, 1 and 5% w/w in the intradermal induction sighting test were humanely killed due to the severity of reactions. Desquamation was also noted in both animals in the topical sighting test for induction application at test material concentrations of 10 and 50% w/w.

8.2 Results of test

See Tables A 6.1.5 (1) and A 6.1.5 (2)

8.2.1 24h after challenge *Number of animals with signs of allergic reactions / number of animals*

0/10

No test animals showed signs of erythema or oedema at either the 2 % or 5 % w/w challenge concentration. Green-coloured staining was noted at the challenge sites of all test and control animals.

8.2.2 48h after challenge *Number of animals with signs of allergic reactions / number of animals*

0/10

No test animals showed signs of erythema or oedema at either the 2 % or 5 % w/w challenge concentration. Green-coloured staining was noted at the challenge sites of 5/10 test animals at the 2 % w/w challenge concentration and 2/10 animals at the 5 % w/w challenge concentration. Green-coloured staining was noted in 4/5 control animals at both the 2 % and 5 % w/w challenge concentrations.

8.2.3 Other findings

None reported

8.3 Overall result

No skin reactions were noted at the challenge sites of the test or control animals at the 24 or 48-hour observations at the 2% and 5% w/w concentrations.

It was concluded that the test substance did not induce any sensitisation reactions in the guinea-pig.

9 APPLICANT'S SUMMARY AND CONCLUSION

9.1 Materials and methods

Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines

The study was performed to assess the contact sensitisation potential of copper carbonate in the albino guinea pig. Ten test and five control animals were used for the study. Two phases were involved; an induction of a response by intradermal injection and topical application, and a topical challenge of that response. Based on the results of sighting tests, the concentrations of the test material for the induction and challenge phases were selected as;

Intradermal induction: 0.1% w/w in distilled water

Topical Induction: 50% w/w in distilled water

Topical challenge: 2 and 5% w/w in distilled water

On day 0, approximately 24 and 48 hours after the initial intradermal induction injection (0.1% w/w), the degree of erythema was evaluated. Seven days later, the same area used for the intradermal injection was treated with a topical application of test material (50% w/w). The degree of erythema and oedema was evaluated 1 and 24 hours after removal of the patches. Induction of the control animals was performed in an identical manner as for the test animals, except that the test material was omitted.

On day 21, test material was applied at the maximum non-irritant concentration (5% w/w) and a lower concentration (2% w/w) as challenge doses. Approximately 24 and 48 hours after removal of the challenge doses, the degree of erythema and oedema was evaluated and any other skin reactions were recorded.

See Section 3.3.1 for scoring schedules used.

The study was conducted according to Commission Directive 96/54/EC Method B6 Acute Toxicity (Skin Sensitisation) and OECD Guidelines for the Testing of Chemicals No. 406 'Skin Sensitisation' (adopted 17 July 1992). The study was also conducted according to GLP.

No deviations from the test guidelines, or deficiencies in the method were reported.

9.2 Results and discussion

Summarize relevant results; discuss dose-response relationship.

No skin reactions were noted at the challenge sites of the test or control animals at the 24 or 48-hour observations at the 2% and 5% w/w concentrations. Therefore, under the conditions of the test, the test material produced a 0% (0/10) sensitisation rate and was classified as a non-sensitiser to guinea pig skin.

9.3 Conclusion

The test material did not meet the criteria for classification as a sensitiser according to EU labelling regulations Commission Directive 93/21/EEC.

9.3.1 Reliability

Based on the assessment of materials and methods include appropriate

	reliability indicator 0, 1, 2, 3, or 4
	(1) valid without restriction
9.3.2 Deficiencies	No
	(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

TABLE A_6.1.5 (1)
DETAILED INFORMATION INCLUDING INDUCTION/CHALLENGE/SCORING SCHEDULE FOR SENSITISATION TEST

INDUCTION/ CHALLENGE	DAY OF TREATMENT	APPLICATION	OBSERVATIONS/REMARKS
INDUCTION 1 Intradermal injection	0	3 intradermal injections made as follows; • FCA & distilled water in ratio 1:1 • 0.1% w/w formulation of the test material in distilled water • 0.1% formulation of the test material in a 1:1 preparation of FCA plus distilled water. Degree of erythema quantified at 24 and 48 hours following injections.	Moderate and confluent erythema was observed in all test animals at all time points except one animal at 48 hours which showed discrete or patchy erythema. In the control animals, three animals at 24 hours showed discrete erythema and at 48 hours no signs of erythema were observed. No other signs of irritation were noted.
Pre-treatment for non irritating substance	There was no pre-treatment for non irritating substance		
INDUCTION 2 Topical induction	7	Filter paper with test material (50% w/w in distilled water) was applied to skin for 48 hours. Degree of erythema and oedema quantified 1 and 24 hours following removal of patch.	Green-coloured staining was noted at the challenge sites of all test animals. The staining did not affect evaluation of skin responses. At 1-hour all test animals showed moderate and confluent erythema. At 24-hours test animals showed discrete/patchy erythema to moderate and confluent erythema. No signs of irritancy were noted in any of the controls.
CHALLENGE Topical challenge	21	Filter paper with 5 % w/w test material in distilled water was applied to each animal. To ensure a maximum non-irritant concentration was used at challenge, the test material was also applied at 2% w/w in distilled water. The test material was removed after 24 hours. After 24 and 48 hours following challenge dressing removal, the degree of erythema and oedema was quantified.	Green-coloured staining was noted at the challenge sites of all test animals after 24 hours and in 5/10 test animals at the 2 % w/w challenge concentration and 2/10 animals at the 5 % w/w challenge concentration **after 48 hours**. All control animals showed green-coloured staining after 24 hours and 4/5 control animals at both the 2 % and 5 % w/w challenge concentrations showed staining also **after 48 hours**. The staining did not affect evaluation of skin responses. No skin reactions were noted at the challenge sites of the test or control animals at the 24 or 48-hour observations at the 2% and 5% w/w concentrations.

FCA – Freund's Complete Adjuvant

COMMENTS FROM ...	
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

TABLE A_6.1.5 (1)
DETAILED INFORMATION INCLUDING INDUCTION/CHALLENGE/SCORING SCHEDULE FOR SENSITISATION TEST

INDUCTION/ CHALLENGE	DAY OF TREATMENT	APPLICATION	OBSERVATIONS/REMARKS
INDUCTION 1 Intradermal injection	0	3 intradermal injections made as follows; • FCA & distilled water in ratio 1:1 • 0.1% w/w formulation of the test material in distilled water • 0.1% formulation of the test material in a 1:1 preparation of FCA plus distilled water. Degree of erythema quantified at 24 and 48 hours following injections.	Moderate and confluent erythema was observed in all test animals at all time points except one animal at 48 hours which showed discrete or patchy erythema. In the control animals, three animals at 24 hours showed discrete erythema and at 48 hours no signs of erythema were observed. No other signs of irritation were noted.
Pre-treatment for non irritating substance	There was no pre-treatment for non irritating substance		
INDUCTION 2 Topical induction	7	Filter paper with test material (50% w/w in distilled water) was applied to skin for 48 hours. Degree of erythema and oedema quantified 1 and 24 hours following removal of patch.	Green-coloured staining was noted at the challenge sites of all test animals. The staining did not affect evaluation of skin responses. At 1-hour all test animals showed moderate and confluent erythema. At 24-hours test animals showed discrete/patchy erythema to moderate and confluent erythema. No signs of irritancy were noted in any of the controls.
CHALLENGE Topical challenge	21	Filter paper with 5 % w/w test material in distilled water was applied to each animal. To ensure a maximum non-irritant concentration was used at challenge, the test material was also applied at 2% w/w in distilled water. The test material was removed after 24 hours. After 24 and 48 hours following challenge dressing removal, the degree of erythema and oedema was quantified.	Green-coloured staining was noted at the challenge sites of all test animals after 24 hours and in 5/10 test animals at the 2 % w/w challenge concentration and 2/10 animals at the 5 % w/w challenge. All control animals showed green-coloured staining after 24 hours and 4/5 control animals at both the 2 % and 5 % w/w challenge concentrations showed staining also. The staining did not affect evaluation of skin responses. No skin reactions were noted at the challenge sites of the test or control animals at the 24 or 48-hour observations at the 2% and 5% w/w concentrations.

FCA – Freund's Complete Adjuvant

TABLE A_6.1.5 (2) RESULTS OF SKIN SENSITISATION TEST

	Number of animals with signs of allergic reactions /number of animals in group			
	Negative Control	Test Group		Positive Control
		5%	2%	2-mercaptobenzothiazole
Scored after 24-hours	0/5	0/10	0/10	-
Scored after 48-hours	0/5	0/10	0/10	9/10 10/10 9/10 10/10 10/10 9/9

			Official use only
		10 REFERENCE	
1.1	**Reference**	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)* *If necessary, copy field and enter other reference(s).* Turnlund, J.R., Keen, C.L. and Smith, R.G. (1990). Copper status and urinary and salivary copper in young men at three levels of dietary copper. Am. J. Clin. Nutr. **51**: 658-64 (published).	
1.2	**Data protection**	No *(indicate if data protection is claimed)*	
1.2.1	Data owner	*Give name of company* Public domain	
1.2.2			
1.2.3	Criteria for data protection	Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others: No data protection claimed	
		11 GUIDELINES AND QUALITY ASSURANCE	
11.1	**Guideline study**	No. This was a non-regulatory study carried out in human volunteers. The experimental protocol was reviewed and approved by the Committee for Protection of Human Subjects, University of California, Berkeley, and by the US Department of Agriculture Human Studies Committee. This study was conducted to establish the effect of the amount of dietary copper on the copper nutriture of young men. Data from a study demonstrating the effect on copper absorption and balance are reported in study summary A6.2.4. *(If yes, give guidelines; if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
11.2	**GLP**	No. This was a non-regulatory study carried out in human volunteers. *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
11.3	**Deviations**	Yes. Refer to section 5.3.2 for a general discussion of deviations and deficiencies. *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
		12 MATERIALS AND METHODS	
		In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.	
12.1	**Test material**	Cu^{2+} Copper sulphate	
12.1.1	Lot/Batch number	Not available	
12.1.2	Specification	Deviating from specification given in section 2 as follows *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	

Section A6.2	**Metabolism in mammals**
Annex Point IIA6.2	*Specify section no., heading and species as appropriate*
IUCLID: 5.0/01	**A6.2(01), Homeostasis of copper**

12.1.2.1 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* Aqueous solution
12.1.2.2 Purity	*Give purity in % of active substance* [redacted]
12.1.2.3 Stability	*Describe stability of test material* Not available
12.1.2.4 Radiolabelling	*give structural location of radio labelling, give reason if not labelled* Not deemed necessary for the purposes of this study.
12.2 Test Animals	Non-entry field
12.2.1 Species	Human volunteers
12.2.2 Strain	Not applicable
12.2.3 Source	Not applicable
12.2.4 Sex	Male
12.2.5 Age/weight/height at study initiation	*Young adults recommended* Age: 22 to 35 years. Weight: 57 to 93 kg. Height: 165 to 190 cm.
12.2.6 Number of volunteers per group	*Give number* *Specify, if there are differences for example for treatment and recovery groups* 11 volunteers were involved in this study (12 originally; one volunteer left the study).
12.2.7 Controls	No
12.3 Administration/ Exposure	*(fill in respective route in the following, delete other routes)* Oral administration of copper sulphate in the diet.
12.3.1 Duration of treatment	The total duration of treatment was 90 days. The study was divided into three metabolic periods (MP). Each volunteer received: 1) an adequate-copper diet (1.68 mg/day) for 24 days, followed by 2) a low-copper diet (0.79 mg/day) for 42 days, and then 3) a high-copper diet (7.53 mg/day) for 24 days.
12.3.2 Exposure scenario	The diet was administered daily, 7 days a week. The diet used throughout the study contained low-copper food items, a liquid formula calorie supplement with added minerals and fiber, and a multivitamin tablet. The food and formula in the diet contained ~0.4 mg Cu before copper was added. A solution containing $CuSO_4$ was added to the liquid formula at each meal to achieve the desired copper content of the total diet.
12.4 Examinations	Non-entry field
12.4.1 Body weight	*yes/no (give time periods for determinations).* Yes. Body weight was monitored over the course of the study.

X

12.4.2 Urine collections	yes/no (give time periods for determinations). Yes. Complete urine collections were made throughout the study. 24 hour collections were diluted to 2000g and acidified with 1 ml concentrated HCl per 100 ml urine. Daily collections were inverted several times to ensure homogeneity and subsamples were combined into 6 day pools for each subject.
12.4.3 Blood collections	yes/no (give time periods for determinations). Yes. Blood samples were taken at the beginning of the study, at the end of each MP, and at the midpoint of MP 2 for complete blood counts and blood chemistry analysis. Blood was also drawn every 7 or 8 days from subjects 7-12 to monitor copper status (plasma copper, ceruloplasmin, and erythrocyte superoxide dismutase (SOD)). Blood was drawn less frequently from subjects 2-6. Plasma copper was determined 9 times in these five subjects, while ceruloplasmin and SOD were determined 5 times. Heparinised samples were centrifuged at 1100 x g for 15 minutes, plasma was transferred to polypropylene tubes, frozen and stored for later analysis.
12.4.4 Saliva collections	yes/no (give time periods for determinations). Yes. Saliva collections: Parotid saliva was collected ≥ 2 hours after the noon meal for determination of copper concentration at the beginning of the study, at the end of each MP, and at the mid-point of MP 2. Parotid saliva was collected by placing a teflon collection cup over the Stensen's duct, stimulating salivary flow by placing a few drops of lemon juice on the tongue, and collecting fluid through plastic tubing into polypropylene tubes. Samples were frozen for later analysis.
12.4.5 Sweat collections	*yes/no (give time periods for determinations).* Yes. Sweat was collected for 3 day periods near the end of each MP by taping a plastic sweat collection bag to an area including the upper arm, shoulder and axillary area of one arm. At the end of the collection period, the bag was detached at a lower edge and sweat was drained into a polypropylene container. The bag and skin surface included in the collection area were rinsed with deionised water into the container and the samples were stored frozen. Successful collections were achieved in only three subjects.
3.5 Sample processing and analysis	Non-entry field.
3.5.1 Copper analysis	Plasma was thawed and 4.5 ml of 6.7% trichloroacetic acid (TCA) solution was added to 1.5 ml plasma in polypropylene tubes. Tubes were capped, agitated in a test-tube mixer for 10 s, and centrifuged at 1100 x g at 3°C for 30 minutes. Plasma copper was determined by flame AAS by use of an autosampler. A reference pool of human plasma and a reagent blank were analysed with each batch of samples. Urinary, salivary, and sweat copper were determined by furnace AAS using the autosampler. Urine was thawed, heated in a water bath at 50°C for 20-25 minutes, inverted several times and transferred to a test tube before analysis. Saliva was thawed and diluted with one or three parts deionised water before analysis. Sweat and rinse-water solutions were thawed, concentrated on a hot-plate to a volume of 100 ml, cooled and weighed before analysis.