Directive 98/8/EC concerning the placing of biocidal products on the market

Inclusion of active substances in Annex I or IA to Directive 98/8/EC

Assessment Report

Basic copper carbonate

Product-type 8
(Wood preservatives)

September 2011

Annex I - France

Basic Copper carbonate (PT 8)

Assessment report

FINALISED IN THE STANDING COMMITTEE ON BIOCIDAL PRODUCTS AT ITS MEETING ON 22/09/2011 IN VIEW OF ITS INCLUSION IN ANNEX I TO DIRECTIVE 98/8/EC

CONTENTS

1 – STATEMENT OF SUBJECT MATTER AND PURPOSE

This assessment report has been established as a result of the evaluation of basic copper carbonate as product-type 8 (wood preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I to the Directive.

Basic copper carbonate (CAS no 12069-69-1) was notified as an existing active substance, by the Wood Preservative Task Force (WPCTF) and by Spiess Urania (SU), hereafter referred to as the applicants, in product-type 8.
Two separate dossiers were submitted by the applicants.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.
In accordance with the provisions of Article 7(1) of that Regulation, the Commission designated France as Rapporteur Member State to carry out the assessment of basic copper carbonate on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for basic copper carbonate as an active substance in product-type was 28 March 2004, in accordance with Article 9(2) of Regulation (EC) No 1451/2007.

On 29 March 2004, the French competent authority received a dossier from the applicants. The Rapporteur Member State accepted the dossiers as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of the dossier on 28 and 30 September 2004 respectively.

On 10 May 2007 for Wood Preservative Copper Task Force and 19 February 2008 for Spiess Urania, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation reports, hereafter referred to as the competent authority reports. The Commission made the reports available to all Member States by electronic means on 23 July 2007 and 9 April 2008 respectively. The competent authority reports included a recommendation for the inclusion of basic copper carbonate in Annex I to the Directive for product-type 8.
In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 9 April 2008. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.
In order to review the competent authority reports and the comments received on them, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions agreed upon were presented at technical and competent authority meetings and the competent authority reports were amended accordingly.

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[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market, OJ L 123, 24.4.98, p.1

[2] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

On the basis of the final competent authority reports, the Commission proposed the inclusion of basic copper carbonate in the Annex I of Directive 98/8/EC and consulted the Standing Committee on Biocidal Products on 22/09/2011.
In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 22/09/2011.

Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include basic copper carbonate in the Annex I of Directive 98/8/EC for product-type 8.

The applicant is not currently placing nano forms of basic copper carbonate on the market. Therefore, the submitted dossier and the finalised assessment report don't cover potential nanoforms of this copper compound, should such forms exist.

The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 8 that contain basic copper carbonate. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.
For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[3], shall be taken into account.
However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing basic copper carbonate for the product-type 8, which will fulfill the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements in the following sections of this assessment report,

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

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[3] http://ec.europa.eu/comm/environment/biocides/index.htm

2 – OVERALL SUMMARY AND CONCLUSIONS

2.1 General substance information/general product information

The main identity and the physical/chemical properties of Basic Copper carbonate are given in Appendix 1 (Listing of endpoints). The active substance shall comply with the specification given in Appendix 1 of this report. The evaluation has established that for the active substance notified by both applicants, traces of metals of toxicological concern (arsenic, cadmium, lead and nickel) were identified among the manufacturing impurities.

The applicant is not currently placing nano forms of basic copper carbonate on the market. Therefore, the submitted dossier and the finalised assessment report don't cover potential nanoforms of this copper compound, should such forms exist.

2.1.1 Identity, physico-chemical properties and methods of analysis of the active substance

The active substance as manufactured is an equimolar mixture of copper (II) carbonate ($CuCO_3$) and copper (II) hydroxide ($Cu(OH)_2$) (CAS no. 12069-69-1) with a minimum purity of 95.7% for both applicants. It is also known as basic copper carbonate or more simply as copper carbonate. The active substance is the cupric ion Cu^{2+}, released by copper carbonate. Traces of metals of toxicological concern (arsenic, cadmium, lead and nickel) were identified among the manufacturing impurities.

The five sources of basic copper carbonate submitted in the dossier are accepted.See the confidential part for the specifications. However, to confirm the data presented in the dossier, a new 5-batch analysis is required at the product authorization stage to check the compliance of current production of each source to these specifications.

Copper carbonate is a green powder with no characteristic odour. It decomposes above 200°C before melting. It is not volatile (its vapour pressure has been theoretically. assessed to be $< 1.0 \times 10^{-5}$ Pa). Solubility in water is pH dependent (acidic conditions). pH increases as degradation release of cupric ion occurs. It does not have any flammable, explosive or oxidising properties.

Adequate analytical methods are available for the determination of copper and the known impurities in the active substance as manufactured. These methods were collaborately validated and are very widely used, but validation data on the active substance must be provided for the WPCTF. It must be highlighted that methods of analysis for the impurities arsenic, lead, cadmium and nickel were not provided by SU and a method of analysis for one impurity > 0.1% was not provided by the WPCTF and must be provided at the product authorization stage.

The analyses of copper in environmental matrices and body fluids and tissues are routinely performed in many laboratories. As these methods were collaborately validated and are very widely used, limited validation data were accepted. However validation data for the methods of analysis copper in soil and water for SU were not provided and must be provided before the product authorization stage.

2.1.2 Identity, physico-chemical properties and methods of analysis of the biocidal product

Two representative products were proposed:

- For the product SPU-01840-F (SU):

It contains 15.2% of copper carbonate.

The biocidal product is a dark blue liquid, with a fishy odour. Its pH is basic (pH = 10.2). It has a density of 1.174 g/mL. It has neither explosive nor oxidising properties. It has an auto-ignition temperature of 415°C.

- For the product ACQ-C2D (WPCTF):

It contains 13% of copper carbonate.

The biocidal product is an intense cobalt blue liquid, with a slight ammonia odour. Its pH is slightly basic since pH = 9.54 at 23°C. It has a relative density of 1.220. It has neither flammable nor explosive properties. It is a weak oxidising agent.

An appropriate analytical method is available for the determination of copper carbonate in the SU product but a validated analytical method must be provided at the product authorization stage for the WPCTF product.

2.1.3 Intended uses and Efficacy

- **Field of use / Function/ Mode of action**
    - **Field of uses**

Product Type 8 (PT) wood preservative

Basic copper carbonate is intended to be used as a preventive wood preservative for wood in Use class 1, 2,3 4-1 as defined in the EN 335[4]

The active substance is restricted to industrial use only, in timber treatment plants operated by trained personnel.

The representative biocidal products ACQ-C2D and SPU-01840-F are supplied respectively as water soluble and a water-miscible wood preservative concentrate. They are both applied by vacuum pressure for the treatment of timbers of Use Class (UC) 1, 2, 3 and 4-1 (up to UC 4-2 for the product ACQ-C2D). The product SPU-01840-F is also intended for applications by dipping.

- **Function**

The active substance acts as a fungicide and as an insecticide for preventive wood preservation (product type 8).

- **Mode of action**

As the active substance is the Cu^{2+} ion, copper carbonate is therefore described as the precursor to release of the cupric ion. As a consequence, most copper-containing formulations are described in terms of total copper.

Copper carbonate acts by prevention of fungal infestation.Upon contact with the fungicide layer, the spores passively take up copper II cations which hinder germination. Copper II cations also act as a feeding and cell poison in insects independent from the kind of application. The threshold concentration

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[4] Since 2007 and the revision of the EN335-1, use classes had replaced hazard classes.

is about 0.1% of elemental copper. Amongst others, the influence of copper II cations in the organism causes unspecific denaturation of proteins and enzymes. For this reason it also acts as a feeding and cell poison in insects.

- **Objects to be protected, target organism**

The target species are fungi (wood rotting basidiomycetes and soft rot fungi) and insects. Regarding insects, an efficacy against wood boring beetles and termites has been claimed by both applicants but for the product SPU-01840-F, no efficacy data against termites has been provided. It should be noticed that no claim concerning the efficacy of copper on blue stain and mould, although efficacy against these organisms is well known and documented.

Copper efficacy was examined for the following target organisms:

➢ For the product SPU-01840-F (SU):

Application mode	**Target organism**	**active substances rate**
Vacuum pressure timber impregnation and dipping	Fungi: Wood rotting basidiomycetes and soft rot fungi Insects: Wood boring beetles There is no claim concerning the efficacy of copper on blue stain and mould, although efficacy against these organisms is well known and documented.	In spite of the request of the applicant for a target concentration at 0.5 kg Cu^{2+}/m^3 (claimed in the dossier), **the evaluation of the submitted trials showed a minimum target concentration at 1 kg Cu^{2+}/m^3 sapwood loading (12 kg SPU-01840-F per m^3 wood) (ENV807+EN84) whatever the application method (vacuum pressure impregnation or dipping).** Please note that these data do not take into account the expected service life of wooden elements treated with copper based product and should be considered as an indicator only.

Regarding insects, an efficacy against termites and larvae of house longhorn beetle (*Hylotrupes bajulus*) has been claimed. However, regarding termites, some efficacy data have been provided on doc IIA but not for the representative biocidal product SPU-01840-F. A full efficacy data should be provided at product authorisation stage.

➢ For the product ACQ-C2D (WPCTF):

Application mode	**Target organism**	**active substances rate**
Vacuum pressure timber impregnation	Fungi: Wood rotting basidiomycetes and soft rot fungi Insects: Wood boring beetles and termites There is no claim concerning the efficacy of copper on blue stain and mould, although efficacy against these organisms is well known and documented.	The typical use of copper for each use class is likely to be : UC 1, 2, 3: ≤ 1.9 kg Cu/m^3 sapwood loading UC 4: ≤ 3.42 kg Cu/m^3 sapwood loading These data are based on the current state of the art concerning the practical uses of copper based products during the last decades, related to the expected life of wooden elements treated with copper based products

Taking into account of the potential influence of the formulation on the efficacy, concentrations proposed above of active substance copper should be considered as an indicator only.

- **Resistance**

According to the data submitted no development of resistance from the target fungi has been reported. Knowing that there are strains of some species of wood destroying fungi that exhibit tolerance to copper, additional biocides are used where necessary to control copper-tolerant strains of fungi.

According to the data submitted, no formation of resistance has to be expected regarding target insects. There is no evidence of insects being naturally tolerant or being able to develop resistance to copper at the level of copper used for biocidal purposes in wood preservation.

2.1.4 Classification and labelling

On the basis of a review of submitted data, the following classification and labelling is proposed:

- Active substance

Directive 67/548/EEC	
Class of danger	Xn - Harmful N - Dangerous to the environment
R phrases*	R20 Harmful by inhalation R22 Harmful if swallowed R50-R53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S phrases	S22 – do not breathe in dust S37/39 Wear suitable gloves and eye/face protection S60: This material and its container must be disposed of as hazardous waste S61: Avoid release to the environment. Refer to special instructions/safety data sheets
Regulation 1272/2008	
Classification and Hazard statements	Acute Tox. 4 /H332 – Harmful if inhaled Acute Tox. 4/H302 – Harmful if swallowed Aquatic Acute/H400 – Very toxic to aquatic life Aquatic chronic/H410 - Very toxic to aquatic life with long lasting effects

- Biocidal product SPU-01840-F (SU)

	Directive 67/548/EEC

Class of danger	Xi – Irritant Xn – Harmful N - Dangerous to the environment
R phrases	R22: Harmful if swallowed R21: Harmful in contact with skin R20: Harmful by inhalation R38: Irritating to skin R41: Risk of serious damage to eyes R51: Toxic to aquatic organisms R53: May cause long-term adverse effects in the aquatic environment.
S phrases	S25: Avoid contact with eyes S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection S38: In case of insufficient ventilation wear suitable respiratory equipment S45: In case of an accident or if you fell unwell seek medical S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/safety data sheets.
Regulation 1272/2008	
Classification and Hazard statements	Acute Tox. 4/H302/H332 Harmful if swallowed and by inhalation Skin Irrit. 2/H315 Causes skin irritation Eye Dam. 1/H318 Causes serious eye damage Aquatic chronic/H410 Very toxic to aquatic organisms and may cause long lasting effects in the aquatic environment

- Biocidal product: ACQ-C2D (WPCTF)

Directive 67/548/EEC	
Class of danger	C - Corrosive T - Toxic N - Dangerous to the environment
R phrases	R22: Harmful if swallowed R23: Toxic by inhalation R34: Corrosive R51: Toxic to aquatic organisms R53: May cause long-term adverse effects in the aquatic environment.
S phrases	S25: Avoid contact with eyes S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection S38: In case of insufficient ventilation wear suitable respiratory equipment S45: In case of an accident or if you fell unwell seek medical S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/safety data sheets.
Regulation 1272/2008	

Classification and Hazard statements	Acute Tox. 4/H302 Harmful if swallowed Acute Tox. 3/H331 Toxic if inhaled Skin Corr. 1B/H314 Causes skin burns and eye damages Aquatic chronic/H411 Toxic to aquatic life with long lasting effects

2.2 Summary of the risk assessment

2.2.1 Human health risk assessment

2.2.1.1 Hazard identification and effects assessment

Foreword

Copper is an essential metal for life and is employed in all human cells. The main daily dietary intake of copper in adults ranges between 1.5 and 3 mg/person/day of copper. Most human diets naturally contain between 1 and 2 mg/person/day of copper, with some containing up to 4 mg/person/day.
Copper is regulated by a homeostatic mechanism. Homeostasis can be described as the maintenance of a constant internal environment in response to changes in internal and external environments. Homeostatic maintenance requires the tightly coordinated control of copper uptake, distribution and efflux in cells and the organism as a whole. The ability of the body to control the uptake and excretion of copper makes this an important factor in considering the exposure and effects of essential elements like copper.

Copper is involved in the reactions and functions of many enzymes, including angiogenesis, neurohormone release, oxygen transport and regulation of genetic expression. In this scope, basic copper carbonate can be considered as a precursor, releasing cupric ion, which is the actual active substance. This explains that, while several endpoints were documented by studies directly performed with basic copper carbonate (acute toxicity, skin and eye irritation, sensitisation), other endpoints were documented by other copper salts (mainly copper sulphate).

In mammalian toxicity, it is also considered that the most toxic moiety of any copper salt is the Cu^{2+} ion. This can be shown through the comparison of the most soluble salt (copper sulphate) with other relatively insoluble copper salts, where the solubility, bioavailability and hence toxicity of these salts can vary – with copper sulphate representing the worst-case scenario. When the acute oral toxicity of this salt is compared with either copper oxide or copper carbonate, the data indicate that copper sulphate is more toxic and thus more bioavailable. Therefore all the properties described below for copper will also be applicable to copper carbonate.
This has also been confirmed in comparative bioavailability studies where copper sulphate was shown to be more or equally bioavailable in relation to the copper carbonate in poultry and swine.

Moreover, as presented in the table below (Table 2.1.1-1) the Copper sulphate is more toxic than the other copper compounds, and then using studies performed with copper sulphate could be considered as a worst-case.

Table 2.1.1-1: Comparative toxicity of the different Copper Salts

Copper salts	Solubility	Acute toxicity (LD_{50})		Irritation
		oral	dermal	
$CuSO_4$	317 g/L	482 mg/kg	>1000 mg/kg	R36/38
$CuCO_3$	1,5 mg/L	1400 mg/kg	>2000 mg/kg	NC*
CuO	0,3 mg/L	>2000 mg/kg	>2000 mg/kg	NC*
$Cu(OH)_2$	6.6µ/L	763 mg/kg	>2000 mg/kg	R41

***NC: No Classification**

Consequently, it is considered appropriate to adopt a conservative approach and read-across from copper sulphate to basic copper carbonate, recognising that this may result in over-estimation of effects of less bioavailable soluble substances.

Toxicokinetics

- Absorption

Oral absorption of copper has been investigated in human volunteer studies. Absorption of copper occurs primarily in the small intestine. Oral absorption rates have been shown to vary between 12.4 % for subjects with high copper diet and 55.6 % for subjects with a low-copper diet. Absorption rate for subjects with adequate diet is 36 %. Rats have been shown to absorb 30 to 50 %, although studies in rats have also shown that absorption can be reduced to 10 % at high dietary intakes, as in humans (SU - A6.2/01). Based on these studies, an oral absorption factor of 36 % is used in risk characterisation for humans and 25 % for animals. These values were agreed at the TMIII08.

Quantitative *in-vitro* measurements of human percutaneous copper absorption have been in the range 0.66 to 5.04% of the applied dose. For the purpose of risk assessment, a percutaneous absorption level of copper of 5% was chosen as the worst case value of copper penetration, under the optimum condition including when emulsifiers were added. This value has been agreed at the TMIII08 and is in line with the EU-VRAR for Copper.

No animal or human studies were available to supply an inhalation absorption level. Thus, the default absorption factor for pulmonary fraction of 100 % is used in risk characterisation as worst-case value of copper salts penetration.

- Distribution

Once absorbed by oral route, copper is bound to albumin and transcuprein and then rapidly transported to the liver where it is incorporated to ceruloplasmin, a transport protein that circulates in the organism and deliver the copper to other organs. It should be however noted that a minor fraction of the absorbed dose can directly be distributed to peripheral organs. In both humans and animals, copper is tightly regulated at a cellular level, involving metallothionein and metallochaperones. These regulating molecules prevent from the accumulation of potentially toxic, free copper ions within the cell. In addition to the liver, the brain is another organ which contains relatively high concentrations of copper.

- Metabolisation

Basic copper carbonate dissociates in cupric ion, carbonate ion and hydroxyl ion. The two latter ions will eventually combine with protons and will end as carbon dioxide and water.

- Elimination

Biliary excretion, with subsequent elimination in the faeces, represents the main route of excretion for copper in animals (rats) and humans, with an excretion rate approximately of 1.7 mg Cu/day in humans. Available data show that copper is excreted in the bile in a relatively inabsorbable form. Consequently, little enterohepatic absorption takes place. Biliary excretion of copper and elimination in the faeces is recognised to be essential to the homeostatic regulation of copper in animals and humans.

A small amount of copper is also excreted in urine and sweat.

Acute Toxicity

The acute oral toxicity of Copper carbonate in the rat is moderate: LD_{50} = 1350 mg/kg b.w. for males and 1495 mg/kg b.w. for females (SU - A6.1.1/01-02). The acute dermal toxicity judged by the percutaneous LD_{50} was low (> 2000 mg/kg bw for rats, both sexes) (SU - A6.1.2). In an acute inhalation toxicity study (SU - A6.1.3), the LC_{50} via inhalation was determined in the range of 1.03 to 5.20 mg/l air. Based on these data the test compound requires classification with the symbol "**Xn" with R22 "harmful if swallowed**", and **R20 "harmful by inhalation"**. No classification is required for the dermal route.

Local toxicity

Whereas no sign of skin irritation was reported with basic copper carbonate (SU - A6.1.4/01), a moderate eye irritation was noted through diffuse or translucent corneal opacity, iridal inflammation and moderate conjunctival irritation (SU - A6.1.4/02). However these findings do not meet criteria for a classification.

Basic copper carbonate was not considered as sensitising since all the animals tested in the maximisation test of Magnusson and Kligman displayed negative results (SU - A6.1.5/02).

Repeated-dose toxicity

With regard to oral repeated dose toxicity, the 90-day dietary study (A6.4.1/01-02) was considered to be the pivotal study for Cu^{2+} presented as copper sulphate pentahydrate. Based on kidney damages, consisting in an increase of cytoplasmic protein droplets, a NOAEL of 1000 ppm (16.3 and 17.3 mgCu/kg bw/day in male and female rats respectively) rats and was determined. Other findings such as liver inflammation and lesions of the forestomach were also reported at 2000 ppm and above (corresponding to doses from 34 mgCu/kg bw/day).The NOAEL of 16.3 mg/kg bw/d was used for the risk characterisation.

Mice equally displayed forestomach lesions when exposed through diet to copper sulphate for 92 days but this occurred at a much higher dose (4000 ppm, corresponding to 187 and 267 mgCu/kg bw/day in males and females, respectively). No other damage was observed in mice (WPCTF - A6.4.1/02).

There were no dermal repeated dose toxicity studies. However, these studies are not required considering the ability to read-across from the above oral study. Moreover, due to the lack of toxicity observed in the acute dermal toxicity of copper carbonate and the weak rate of dermal penetration, a toxic effect is not expected.

For repeated-dose toxicity, it was considered that due to the low inhalation exposure during the use of copper-containing wood preservative products, no sub-acute, sub-chronic and/or chronic inhalation studies was necessary.

Mutagenicity

- *In vitro* tests

There was no evidence of mutagenic activity in Salmonella typhimurium strains in the presence or absence of the metabolic activation system when tested with copper sulphate pentahydrate (A6.6.1).

Although limited, these *in vitro* data were deemed sufficient and no further *in vitro* assays were required, considering the results of the *in vivo* tests.

- *In vivo* tests

In vivo studies, conducted with copper sulphate pentahydrate, induced neither micronuclei in the polychromatic erythrocytes from the bone marrow of mice (SU - A6.6.4 or WPCTF – A6.6.4/01), nor DNA damage in a rat hepatocyte UDS assay (SU - A6.6.5 or WPCTF – 6.6.4/02).
Equivocal results of additional *in vivo* genotoxicity studies from the public domain (Bhunya and Pati, 1987; Agarwal *et al*., 1990; Tinwell and Ashby, 1990), but these studies do not meet the higher reliability criteria (1 or 2) under the BPD.

Copper is therefore considered as non genotoxic.

Carcinogenicity

No carcinogenic potential of copper sulphate was detected in rats and mice. However, all available data are of limited value to evaluate the carcinogenic potential of copper compounds. Study durations are in particular too short (<2 years) and group sizes are small for drawing formal conclusions. However, due to the lack of genotoxicity and considering that the expected level of exposure (as described in paragraph 2.2.1.2) is significantly lower than the usual dietary intake of copper (2-3 mg/day), there is no need to conduct new carcinogenicity studies according to OECD guideline 451/453.

Reproductive Toxicity

- Developmental toxicity

A developmental study in mice (A6.8.1/01) was submitted but suffers from major methodological deficiencies including no information on maternal toxicity and is neither adequate for classification and labelling nor for risk assessment. No teratogenicity study in the rabbit was submitted, although regulatorily required.

In spite of this lack of (valid) data regarding the developmental toxicity, no further developmental studies were requested for the following reasons:

- Copper is an essential element to foetal development in humans. At birth, the copper level in the newborn baby is about 15 mg, coming from the mother. The copper is absorbed across the placenta and is required for healthy growth and development, especially in blood maturation, bone development, heart development and function of 20 enzymes (Ralph and McArdle, 2001).

- The systemic exposure resulting from primary and secondary to copper is low. As a matter of comparison, it is significantly lower than the usual dietary intake of copper (2-3 mg/day).

- A two-generation oral reproduction study (A6.8.2/06), although not designed for extensively studying malformations, does not raise any particular suspicion of teratogenic potential of copper in the rat. Performed in accordance with OECD test guideline 416, it provides information on the effects of repeated exposure to the substance during all phases of the reproductive cycle including gestation. In particular, the study provides information on the reproductive parameters, and on development, growth and survival of offspring.

On the basis of the above-mentioned data, it is therefore not proposed to classify copper as a teratogenic compound by oral route.

- Fertility

According to the two-generation oral reproduction study in rats administered with copper sulphate pentahydrate (SU - A6.8.2 or WPCTF – A6.8.2/06), the NOAEL for reproductive toxicity for parental males was 1500 ppm (the highest concentration tested corresponding to 23.6 mg/kg bw/d), The NOAEL for parental females was only 1000 ppm (15.2-35.2 mg/kg bw/d), based on the reduced spleen weight at 1500 ppm. This reduction also occurred in F1 and F2 generations at the same dose level in both males and females. However the reduced spleen weights were not considered a reproductive endpoint as it did not affect growth and fertility.

Therefore as the results of this study do not indicate specific reproductive toxicity at the highest dose level tested, it is proposed that copper sulphate and basic copper carbonate should not be classified as reprotoxic compounds.

Neurotoxicity

From a neurotoxicological point of view, although copper has been recently suspected to be involved in the pathogenesis of the Alzheimer's disease and other prion-mediated encephalopathies, this assumption is only speculative and although no valid neurotoxicity study was submitted, no evidence of a neurotoxic potential of copper is suspected from the available studies in animals or in humans up to now. No further study was therefore deemed necessary.

Human data

Human data are based on both clinical studies and poisoning cases.
Clinical studies were performed in healthy volunteers in order to explore the effect of copper gluconate supplementation in the diet. Even if liver functions were identified as the critical endpoints, no evidence of hepatic damage was reported at 10 mg/day.
Poisoning cases consisted in suicide attempts, food and water contamination (cases of India Childhood Cirrhosis, cases of Childhood Idiopathic Toxicosis) and occupational diseases (through Bordeaux mixture exposure).
Acute symptoms resulted in metallic taste, salivation, epigastric pain, nausea, vomiting and diarrhoea. Anatomo-pathological examinations after self-poisoning (ingestion varying between 1 and 100 g of copper dissolved in water) revealed ulcerations of gastro-intestinal mucosa, hepatic damages (dilatation of central vein, cell necrosis and bile thrombi) and kidney lesions (congestion of glomeruli, swelling or necrosis of tubular cells and sometimes haemoglobin casts).
Chronic symptoms, occurred in a voluntary intoxication by daily ingestion of 30 mg of copper for 2 years and 60 mg during the third year, were malaise, jaundice, hepatomegaly and splenomegaly. Liver examination revealed micronodular cirrhosis. In the particular case of vineyard sprayers intoxication by the Bordeaux mixture (unknown doses), lung lesions with focal distribution were observed: alveoli filled with desquamated macrophages, granuloma in the alveoli septa and fibro-hyaline nodules.

2.2.1.2 Exposure assessment

Primary exposure

Professional exposure

- **ACQ-C2D (WPCTF)**

The product in concentrate form is supplied to the timber treatment plants where the timber is impregnated with diluted solutions in enclosed pressure vessels. The treated wood is removed from the vessel at the end of the process and held for drying during a post-treatment conditioning period, before being stored. The major occupational routes of exposure to copper are inhalation and skin contact.

Assuming proper hygiene measures are applied, oral exposure would normally not occur in the workplace.

Based on the "Handling, model 1" data from the TNsG on human exposure and following a tiered approach, following exposures were estimated, depending on Hazard Classes:

Table 2.2.1.2-1: Summary of exposure estimates: direct exposure to industrial workers

Task : Handling of wood and equipment during vacuum-pressure impregnation (including mixing and loading, and post-application)						
Users :	Trained industrial workers					
Frequency :	3 cycles/day , 5 hours/day, daily					
Tier - PPE	**Hazard Class**	**Inhalation exposure**		**Dermal exposure**		**Total exposure**
		Inhaled uptake mg as/day	Systemic dose mg as/kg bw/d	Deposit on skin mg as/day	Systemic dose mg as/kg bw/d	Systemic dose mg as/kg bw/d
Tier 1 : gloves, minimal clothing, no RPE	HC 1, 2 or 3	0.037	0.00061	90	0.075	0.076
	HC 4	0.068	0.00113	165	0.138	0.139
Tier 2 : gloves, protective clothing, no RPE	HC 1, 2 or 3	0.037	0.00061	20	0.017	0.018
	HC 4	0.068	0.00113	36	0.030	0.031

- **SPU 01840 F (SU)**

SPU 01840 F is supplied as a concentrate for dilution before use. It is in a form of an aqueous solution containing Copper (II) complexes (corresponding to 15.2% basic Copper carbonate or 8.4% Copper) and other active or non-active ingredients.

It is intended for use in industrial wood preservation to protect freshly cut wood against insects and fungal infestation. The process is carried out by specialised professionals through:

- mechanical dipping with an application solution with 1.26 % of Copper (or 15% aqueous solution of SPU 01840-F), and

- vacuum pressure impregnation (between 10 and 14 bar) with an application solution containing of 0.336 % Copper (or 4% aqueous solution of SPU 01840-F).

As a first tier approach for primary exposure (i.e. exposure of workers at treatment facilities), no Personal Protective Equipment (PPE) are taken into account (except gloves when models give only exposure under gloves).
A second tier was introduced with the following refinements: Tier 2 estimates are appropriate where the product is used by a specialised industrial /user group. This is the case with timber treatment plant operators who are required to have adequate knowledge and skill in handling hazardous chemicals they use. This is also true where protective measures such as instruction, training, exposure control and PPE are required by health and safety law to be in place.

The results of the human exposure assessments for each use/scenario are reported in following tables:

Table 2.2.1.2-2: Summary of exposure estimates for industrial workers during industrial dipping of wood

Industrial dipping (including mixing and loading, and post-application)					
Users :	Trained industrial workers				
Frequency :	5 cycles/day, 2.5 hours/day, daily				
Model :	**TNsGs Dipping model 1**				
Tier - PPE	**Inhalation exposure**		**Dermal exposure**		**Total exposure**
	Inhaled uptake mg as /day	Systemic dose mg as / kg bw	Deposit on skin mg as /day	Systemic dose mg as / kg bw	Systemic dose mg as / kg bw
Tier 1 : gloves, minimal clothing, no RPE	3.9×10^{-2}	6.56×10^{-4}	506.6	4.22×10^{-1}	4.23×10^{-1}
Tier 2 : gloves, protective clothing, no RPE	3.9×10^{-2}	6.56×10^{-4}	115.5	9.63×10^{-2}	9.69×10^{-2}

Table 2.2.1.2-3: Summary of exposure estimates for industrial workers during vacuum-pressure impregnation of wood

Vacuum-pressure impregnation (including mixing and loading, and post-application)					
Users :	Trained industrial workers				
Frequency :	3 cycles/day , 5 hours/day, daily				
Model :	**TNsGs handling model 1**				
Tier - PPE	**Inhalation exposure**		**Dermal exposure**		**Total exposure**
	Inhaled uptake mg as /day	Systemic dose mg as / kg bw	Deposit on skin mg as /day	Systemic dose mg as / kg bw	Systemic dose mg as / kg bw
Tier 1 : gloves, minimal clothing, no RPE	4.00×10^{-2}	6.65×10^{-4}	97.3	8.11×10^{-2}	8.17×10^{-2}
Tier 2 : gloves, protective clothing, no RPE	4.00×10^{-2}	6.65×10^{-4}	21.3	1.77×10^{-2}	1.84×10^{-2}

Non-professional exposure

Intended uses are restricted to professional application, so non-professional primary exposure are not expected.

Secondary exposure

The secondary human exposure assessment considers the potential for the exposure of adults in which they may come into contact with copper treated timber. The scenarios used in this assessment are those contained in the TNsG on Human Exposure part 2 page 77 and User guidance page 51. The following scenarios have been identified as being relevant for assessing the potential exposure of humans to amine copper treated timbers during and after their use:

• Adults (workers) - Chronic	Handling, cutting and sanding treated timbers
• Adults (consumers) - Acute	Handling, cutting and sanding treated timbers
• Children - Chronic	Playing on preserved timber playground equipment
• Infants - Chronic	Playing on preserved timber playground equipment and mouth contacts with the treated timber surface
• Infants - Acute	Chewing preserved timber off-cuts

➢ ACQ-C2D (WPCTF)

The results of the exposure assessment, depending on the Use Classes are reported in following tables:

Table 2.2.1.2-4: Summary of exposure estimates in secondary human exposure, for HC 4

Scenario	Route	Estimate *	PPE	Uptake mg as /day	Systemic dose mg as/ kg bw
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	**inhalation**	1	None	0.428	0.0071
			RPE	0.0428	0.00071
	dermal	1	None	5.7	0.0048
			Gloves	0.57	0.00048
		2	None	0.168	0.00014
			Gloves	0.0168	0.000014
	TOTAL	inhalation 1 + dermal 1	None	6.128	0.0119
			Gloves + RPE	0.6128	0.00119
		inhalation 1 + dermal 2	None	0.596	0.0072
			Gloves + RPE	0.0596	0.00072
Adults (consumers) - Acute Handling, cutting and sanding treated timbers	**inhalation**	1	None	0.428	0.0071
	dermal	1	None	5.7	0.0048
		2	None	0.168	0.00014
	TOTAL	inhalation 1 + dermal 1	None	6.128	0.0119
		inhalation 1 + dermal 2	None	0.596	0.0072
Children - Chronic Playing on playground structure outdoors	**dermal**	1	None	2.72	0.0090
		2	None	0.080	0.00027
Infants - Chronic Playing on playground structure outdoors and mouthing	**dermal**	1	None	2.72	0.014
		2	None	0.080	0.0004
	oral	1	None	171	6.2
		2	None	0.10	0.0036
	TOTAL	dermal 1 + oral 1	None	173.72	6.21
		dermal 2 + oral 2	None	0.18	0.004
Infants - Acute Chewing preserved timber off-cuts	**oral**	1	None	5.5	0.197
		2	None	0.096	0.0035

*: The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = 68μg/cm^2 (unrealistically conservative). Estimate 2 = 2μg/cm^2.

The use of PPE (protective gloves and mask) is considered only for professional users.

Table 2.2.1.2-5: Summary of exposure estimates in secondary human exposure, for HC 1-3

Scenario	Route	Estimate*	PPE	Uptake mg as /day	Systemic dose mg as / kg bw
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	inhalation	1	None	0.225	0.0038
			RPE	0.0225	0.00038
	dermal	1	None	3	0.0025
			Gloves	0.3	0.00025
		2	None	0.168	0.00014
			Gloves	0.0168	0.000014
	TOTAL	inhalation 1 + dermal 1	None	3.225	0.0063
			RPE +Gloves	0.3225	0.00063
		inhalation 1 + dermal 2	None	0.393	0.0039
			RPE +Gloves	0.0393	0.00039
Adults (consumers) - Acute Handling, cutting and sanding treated timbers	inhalation	1	None	0.225	0.0038
	dermal	1	None	3	0.0025
		2	None	0.168	0.00014
	TOTAL	inhalation 1 + dermal 1	None	3.225	0.0063
		inhalation 1 + dermal 2	None	0.393	0.0039
Children - Chronic Playing on playground structure outdoors	dermal	1	None	1.43	0.0047
		2	None	0.080	0.00027
Infants - Chronic Playing on playground structure outdoors and mouthing	dermal	1	None	1.43	0.0074
		2	None	0.080	0.00027
	oral	1	None	90	3.26
		2	None	0.10	0.0036
	TOTAL	dermal 1 + oral 1	None	91.43	3.27
		dermal 2 + oral 2	None	0.180	0.0039
Infants - Acute Chewing preserved timber off-cuts	oral	1	None	2.9	0.104
		2	None	0.096	0.0035

*: The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = 68µg/cm² (unrealistically conservative). Estimate 2 = 2µg/cm².

The use of PPE (protective gloves and mask) is considered only for professional users.

- **SPU 01840 F (SU)**

The results of the secondary exposure assessment are reported in the following table:

Table 2.2.1.2-6: Summary of estimates for indirect exposure scenarios

Scenario	Route	Estimate *	PPE	Uptake mg as/day	Systemic dose mg as/ kg bw
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	inhalation	1	None RPE	0.125 0.0125	0.0021 0.00021
	dermal	2	None Gloves	0.17 0.017	0.00014 0.000014
	TOTAL	2	None RPE + gloves	0.30 0.030	0.0022 0.00022
Adults (consumers) - Acute Handling, cutting and sanding treated timbers	inhalation	1	None	0.125	0.0021
	dermal	2	None	0.17	0.00014
	TOTAL	2	None	0.30	0.0022
Children - Chronic Playing on playground structure outdoors	dermal	2	None	0.08	0.00027
Infants - Chronic Playing on playground structure outdoors and mouthing	dermal	2	None	0.08	0.0004
	oral	2	None	0.10	0.0036
	TOTAL	2	None	0.18	0.0040
Infants - Acute Chewing preserved timber off-cuts	oral	2	None	0.096	0.0035

*: The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = $68 \mu g/cm^2$ (unrealistically conservative). Estimate 2 = $2 \mu g/cm^2$. Only the more relevant estimate for each scenario/route is reported here.
The use of PPE (protective gloves and mask) is considered additionally only for professional users.

2.2.1.3 Risk characterisation for human health

The human health risk characterisation is performed using both the AEL and the MOE approaches.

AELs determination

For each exposure scenario, an appropriate AEL is determined on the basis of the exposure frequency. Accordingly, three types of AELs are classically derived: $AEL_{short\text{-}term}$, $AEL_{medium\text{-}term}$ and $AEL_{long\text{-}term}$ corresponding to short-, medium- and long-term exposures respectively.
AELs are usually derived by applying the following formula:

$$AEL = \frac{NOAEL}{Assessment\ \ factors}$$

In the case of basic copper carbonate, all AELs ($AEL_{short\text{-}term}$, $AEL_{medium\text{-}term}$ and $AEL_{long\text{-}term}$) were derived on the basis of the NOAEL of 1000 ppm, corresponding to 16.3 mgCu/kg bw/day obtained in the 90-day oral rat study with copper sulphate (A6.4.1). An oral absorption rate of 25% was taken into account for calculating the systemic NOAEL as follows:

$$NOAELsystemic = 16.3\ x\ 0.25 = \ 4.1\ \ mgCu / kg\ bw / d$$

Although basic copper carbonate induced local effects (eye irritation) and copper sulphate induced a minimal to moderate hyperplasia of the squamous mucosa in the forestomach, no local AEC was derived as far as no local effect was detected in the absence of systemic effects. Local effects are therefore covered by systemic AELs.

Regarding the assessment factors, after refinement, a value of 50 (including an inter-species factor of 5 and an intra-species factor of 10)[5] was applied for deriving $AEL_{short\text{-}term}$ and $AEL_{medium\text{-}term}$. An additional factor of 2 was integrated for taking into account the duration extrapolation from subchronic to chronic exposures. An overall assessment factor of 100 was therefore adopted for deriving $AEL_{long\text{-}term}$. These refined assessment factors were agreed by the technical meeting.
These values are used as the reference margin of exposure (MOE_{ref}).

The following AELs were therefore derived:

- $AEL_{short\text{-}term} = 4.1 / 50 = 0.082$ mgCu/kg bw/day
- $AEL_{medium\text{-}term} = 4.1 / 50 = 0.082$ mgCu/kg bw/day
- $AEL_{long\text{-}term} = 4.1 / 100 = 0.041$ mgCu/kg bw/day

In the AEL approach, a risk is considered as acceptable if AEL > exposure.
In practice, exposure is expressed as a percentage of the AEL (%AEL). The risk is therefore considered as acceptable if %AEL < 100.
In the MOE approach, a risk is considered as acceptable if $MOE > MOE_{ref}$ (where $MOE = \frac{NOAEL}{Exposure}$).

ADI determination

As no food risk assessment was deemed necessary because of the negligible exposure through food, no ADI was derived.
An ADI value of 0.15 mgCu/kg bw/d is nevertheless available in the literature (EFSA, 2008)

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[5] Although the inter-species factor is usually set at 10, it was agreed at TM I09 it could be reduced from 10 to 5 in the case of copper compounds. This factor is composed of an allometric scaling subfactor (which is 4 for rats) and a residual subfactor of 2.5 accounting for the other interspecies variability. Whereas the allometric scaling subfactor was kept unchanged, it was proposed to reduce the residual subfactor from 2.5 to 1.25 on the basis of the extensive toxicokinetic data set in both humans and animals (rats) which demonstrates similarities between the two species in absorption, distribution and excretion of copper compounds.
This approach was accepted by the TCNES and subsequently agreed during the review process by SCHER.
The Biocides Technical Meeting adopted it as a refined tier in order to harmonise with the overall assessment factor used in the VRA.

Risk characterisation for primary exposure scenarios

Professional users

The %AELs and the Margins of Exposure (MOE) were calculated for long-term exposures as reported in the table below:

- **ACQ-C2D (WPCTF)**

Table 2.2.1.3-1: Summary of risk assessment for professional users during long-term exposure.

Task : Handling of wood and equipment during vacuum-pressure impregnation (including mixing and loading, and post-application)							
Users : Trained industrial workers							
Tier - PPE	**Hazard Class**	**Exposure path**	**Systemic dose (mgCu/kg bw/d)**	**MOE_{ref}**	**MOE**	**$AEL_{long-term}$ (mgCu/kg bw/d)**	**Expo as % AEL**
Tier 1 : gloves, minimal clothing, no RPE	HC 1, 2 or 3	Inhalation and dermal exposure	0.076	100	**53.9**	0.041	**185.4**
	HC 4	Inhalation and dermal exposure	0.139	100	**29.5**	0.041	**339.0**
Tier 2 : gloves, protective clothing, no RPE	HC 1, 2 or 3	Inhalation and dermal exposure	0.018	100	**227.8**	0.041	**43.9**
	HC 4	Inhalation and dermal exposure	0.031	100	**132.3**	0.041	**75.6**

When PPE (protective clothing and new gloves) are worn, it can be seen that the % of AEL and MOE become acceptable whatever the hazard class considered.
In conclusion, since the MOE is greater than the MOE_{ref} and the %AEL is lower than 100%, the risks for industrial users wearing PPE are considered to be acceptable even if chronically exposed.

- **SPU 01840 F (SU)**

Table 2.2.1.3-2: Summary of Risk assessment for professional users during long-term exposure

Exposure scenario	**systemic total dose (mgCu/kg bw/day)**	**MOEref**	**AEL long-term**	**% AEL**	**MOE**
Industrial uses – Primary exposure, dipping process					
All phases of exposure : Tier 1 (mixing and loading + application + post-application)	4.23×10^{-1}	100	0.041	**1032**	**9.7**
All phases of exposure : Tier 2 (mixing and loading + application + post-application)	9.69×10^{-2}	100	0.041	**236**	**42.3**
Industrial uses – Primary exposure, simple vacuum pressure impregnation process					
All phases of exposure : Tier 1 (mixing and loading + application + post-application)	8.17×10^{-2}	100	0.041	**199**	**50.2**
All phases of exposure : Tier 2 (mixing and loading + application + post-application)	1.84×10^{-2}	100	0.041	**45**	**222.8**

The scenario of the “dipping process” has a %AEL>100 and a $MOE<MOE_{ref}$ in the first tier. And even when PPE (protective clothing and new gloves) are worn, it can be seen that the % of AEL and MOE are still not acceptable[6].

For all other scenarios, when PPE are worn, % of AEL and MOE values are acceptable, the risks for industrial or professional user under the conditions specified above are then acceptable.

Conclusion: the risk for industrial or professional users under the conditions specified above is not acceptable for the “dipping process”, whereas the risk is acceptable for the simple-vacuum pressure impregnation process when PPE are worn.

Non-professional users

The biocidal product is foreseen to be used by trained professionals only. Thus, a risk characterisation for non-professionals is not relevant.

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[6] Even when assuming that industrial users, wearing PPE, would be acutely exposed, the risk remains unacceptable (%AEL = 118%, MOE = 42.3).

Risk characterisation for secondary (indirect) exposure scenarios

The %AELs and the Margins of Exposure (MOE) were calculated for secondary exposure scenarios as reported in the tables below:

- **ACQ-C2D (WPCTF)**

Table 2.2.1.3-3: Summary of risk assessment for secondary exposure / Use Class HC 1-3 (Copper loading: 1.80 kg/m^3)

Scenario	Exposure path	Estimate *	Total exposure (mgCu/kg bw/d)	MOE$_{ref}$	MOE	AEL (mgCu/kg bw/d)	Expo as % AEL
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	Inhalation and dermal	1 + PPE	0.0063 0.00063	100	651 6508	0.041	15.4 1.5
		2 + PPE	0.0039 0.00039	100	1051 10513	0.041	9.5 1.0
Adults (consumers) - Acute Handling, cutting and sanding treated timbers	Inhalation and dermal	1	0.0063	50	651	0.082	7.7
		2	0.0039	50	1051	0.082	4.8
Children - Chronic Playing on playground structure outdoors	dermal	1	0.0047	100	872	0.041	11.5
		2	0.00027	100	15185	0.041	0.7
Infants - Chronic Playing on playground structure outdoors and mouthing	Dermal and oral	1	3.27	100	**1.25**	0.041	**7975**
		2	0.0039	100	1051	0.041	9.5
Infants - Acute Chewing preserved timber off-cuts	oral	1	0.104	50	**39.4**	0.082	**127**
		2	0.0035	50	1171	0.082	4.3

*The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = 68µg/cm² (unrealistically conservative). Estimate 2 = 2µg/cm².

The use of PPE (protective gloves and mask) is considered only for professional users.

The % of AEL on the "Infant playing on playground structure outdoors and mouthing" scenario (Estimate 1) is very largely >100 % (and the MOE is < 100). However, it is considered that the exposure value is based on an unrealistic estimate of the dislodgeable copper. By using the more realistic estimate 2, it can be seen that the % of AEL and MOE become acceptable.

Likewise, the % of AEL on the "Infant chewing preserved timber off-cuts" scenario (Estimate 1) is also above 100 % (and the MOE is < 50). However, it is considered that the model in the TNsG Human Exposure is unrealistic as far as it is unlikely that an infant could chew a piece of timber 4cm x 4 cm x 1 cm and certainly would not be able to generate enough saliva to extract wood preservative from the inside of the block of treated wood. It is rather proposed that the infant can remove the dislodgeable residues of copper from the surface of the wood and ingest this material. Treated wood is very hard and is highly likely to be distasteful for the infants. The infant would probably also expel unpleasant tasting materials from his/her mouth. By taking into account these elements in the more realistic estimate 2, it can be seen that the % AEL > 100 and MOE < MOE$_{ref}$, risk is then considered as acceptable.

For all other *scenarii*, % of AEL and MOE values are acceptable in estimates 1 and 2, the risks for professionals and consumers under the conditions specified above are then acceptable.

Table 2.2.1.3-4: Summary of Risk assessment for secondary exposure / Use Class HC 4 (Copper loading: 3.42 kg/m^3)

Scenario	**Exposure path**	**Estimate** *	**Total exposure mg as / kg bw**	**MOE$_{ref}$**	**MOE**	**AEL (mgCu/kg bw/d)**	**Expo as % AEL**
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	Inhalation and dermal	1 + PPE	0.0119 0.00119	100	345 3445	0.041	29.0 2.9
		2 + PPE	0.0072 0.00072	100	569 5694	0.041	17.6 1.8
Adults (consumers) - Acute Handling, cutting and sanding treated timbers	Inhalation and dermal	1	0.0119	50	345	0.082	14.5
		2	0.0072	50	569	0.082	8.8
Children - Chronic Playing on playground structure outdoors	Dermal	1	0.0090	100	456	0.041	22.0
		2	0.00027	100	15185	0.041	0.7
Infants - Chronic Playing on playground structure outdoors and mouthing	Dermal and oral	1	6.21	100	**0.66**	0.041	**15146**
		2	0.004	100	1 025	0.041	9.8
Infants - Acute Chewing preserved timber off-cuts	Oral	1	0.197	50	**21**	0.082	**240**
		2	0.0035	50	1171	0.082	4.3

* The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = 68µg/cm² (unrealistically conservative). Estimate 2 = 2µg/cm².The use of PPE (protective gloves and mask) is considered only for professional users.

As previously for class HC 1, 2 and 3 uses, a refinement was necessary for scenarios “Infants playing on playground structure outdoors and mouthing” and “Infant chewing preserved timber off-cuts”. Since the estimate 1 was unrealistic, it is proposed to rather consider the more realistic estimate 2 (described above). It has been demonstrated that the risks are acceptable for these estimates 2.

For all other *scenarii*, % of AEL and MOE values are acceptable in estimates 1 and 2, the risks for professionals and consumers under the conditions specified above are then acceptable.

- **SPU 01840 F (SU)**

Table 2.2.1.3-5: Summary of risk assessment for secondary exposure

Scenario	Exposure path	Estimate *	Systemic dose mg as / kg bw	MOE_{ref}	MOE	AEL (mgCu/ kg bw/d)	Expo as % AEL
Adults (professional) - Chronic Handling, cutting and sanding treated timbers	Inhalation and dermal	2 RPE + gloves	0.0022 0.00022	100	1864 18636	0.041	5.4 0.54
Adults (consumers) – Acute Handling, cutting and sanding treated timbers	Inhalation and dermal	2	0.0022	50	1864	0.082	2.7
Children - Chronic Playing on playground structure outdoors	dermal	2	0.00027	100	15185	0.041	0.66
Infants – Chronic Playing on playground structure outdoors and mouthing	Dermal and oral	2	0.0040	100	1025	0.041	9.8
Infants - Acute Chewing preserved timber off-cuts	oral	2	0.0035	50	1171	0.082	4.3

*: The different estimates are due to refinements for the estimation of the dislodgeable copper concentration. Estimate 1 = 68µg/cm² (unrealistically conservative). Estimate 2 = 2µg/cm². Only the more relevant estimate for each scenario/route is reported here. The use of PPE (protective gloves and mask) is considered additionally only for professional users.

For all these *scenarii*, %AEL and MOE values show that no unacceptable risk are anticipated for people secondarily exposed.

Overall assessment of the risk for the use of the active substance in biocidal products

Application of basic copper carbonate as an approx. 0.34 % aqueous solution (elemental copper) in preventive wood protection (dipping/immersion and vacuum pressure process) is considered to represent an unacceptable risk for professional facility workers on Tier 1 level except for one scenario “cutting and sanding” which is a secondary exposure. Higher tier (Tier 2) reflecting actual measures of occupational safety further reduce any potential hazards and result in a satisfactory protection level for workers for the “simple vacuum pressure impregnation process” but **the “dipping process” still represents an unacceptable risk for workers even if PPE are worn for long-term exposure.**

Secondary (indirect) human exposures are considered to be devoid of unacceptable risk.

2.2.2 Environmental risk assessment

Copper is applied in wood preservatives in the form of aqueous solutions of copper salts. The environmentally relevant moiety and the active principle of Copper carbonate is the cupric ion (Cu^{2+}), which may be released to the environment at a low rate.

2.2.2.1 Fate and distribution in the environment

As a result of the unique fate of copper in water, soil, sediment and sludge, many of the data requirements listed in Section A7 of the Technical notes for Guidance are not applicable for inorganic compounds and metals in particular e.g. hydrolysis, photodegradation and sediment degradation. It is not applicable to discuss copper in terms of degradation half-lives or possible routes of degradation.

Copper carbonate as an inorganic compound is not subjected to biological degradation in any environmental compartment. The substance is non-volatile, hydrolytically stable and not biodegradable. Phototransformation in water is not expected. The strong adsorbance to organic carbon, manganese and iron oxides increases in soil with increasing pH.
The most important parameters determining the distribution of copper in the aquatic and soil compartment is adsorption onto solid materials and therefore the copper partitioning coefficients.
Partition coefficient in suspended matter
Kpsusp = 30,246 l/kg (log Kp (pm/w) = 4.48) (50th percentile)
Partition coefficient in sediment
Kpsed = 24,409 l/kg (log Kp(sed/w) = 4.39) (50th percentile)
Partition coefficient in soil
Kpsoil = 2 120 l/kg (log Kp (soil/w) = 3.33) (50th percentile)

As all metals, copper becomes complexed to organic and inorganic matter in waters, soil and sediments and this affects copper speciation, bioavailability and toxicity.

Because of the homeostasis of metals, BCF values are not indicative of the potential bioaccumulation. There is therefore limited evidence of accumulation and secondary poisoning of inorganic forms of metals, and biomagnification in food webs.

2.2.2.2 Environmental effect assessment

The risk assessment is carried out on the basis of total concentrations of copper in the environment taking into account the background plus added amount of copper. It was stated that this approach may be more reliable. The PEC values, initially calculated as “added values” were corrected in order to integrate the background concentrations in copper. Total copper concentrations were calculated in taking into account of the natural/pristine or the regional copper background concentrations (as agreed under the Council Regulation (EEC) 793/93 on Existing Substances - EU-RAR).

2.2.2.2.1 Freshwater compartment

For the freshwater pelagic compartment, 139 individual NOEC/EC10 values resulting in 27 different species-specific NOEC values, covering different trophic levels (fish, invertebrates and algae) were used for the PNEC derivation. The large intra-species variabilities in the reported single species NOECs were related to the influence of test media characteristics (e.g., pH, dissolved organic carbon, hardness) on the bioavailability and thus toxicity of copper. Species-specific NOECs were therefore calculated after normalizing the NOECs towards a series of realistic environmental conditions in Europe (typical EU scenario’s, with well defined pH, hardness and DOC). Such normalization was done by using chronic copper bioavailability models (Biotic Ligand Models), developed and validated

for three taxonomic groups (fish, invertebrates and algae) and additional demonstration of the applicability of the models to a range of other species. The species-specific BLM-normalized NOECs were used for the derivation of log-normal Species Sensitivity Distributions (SSD) and HC5-50 values (the median fifth percentile of the SSD), using statistical extrapolation methods.
The HC5-50 values of the typical EU scenarios ranged between 7.8 to 22.1 µg Cu/L. Additional BLM scenario calculations for a wide range of surface waters across Europe further demonstrated that the HC5-50 of 7.8 µg Cu/L, is protective for 90% of the EU surface waters and can thus be considered as a reasonable worst case for Europe in a generic context.

Copper threshold values were also derived for three high quality mesocosm studies, representing lentic and lotic systems. The mesocosm studies included the assessment of direct and indirect effects to large variety of taxonomic group and integrate potential effects from uptake from water as well as from food.
BLM-calculated HC5-50 values (Assessment Factor (AF)=1) were used as PNEC for the risk characterisation.

The AF=1 was chosen due to the certainty concerning 1) the mechanism of action; 2) the overall evaluation of the database; 3) the robustness of the HC5-50 values; 4) corrections for bioavailability (reducing uncertainty); 5) the sensitivity analysis with regards to DOC and read-across assumptions; 6) the factor of conservatism “built in into” the data and assessment (such as no acclimation of the test organisms and no pre equilibration of test media); 7) results from multi-species mesocosm studies and 8) comparison with natural backgrounds and optimal concentration ranges for copper, an essential metal.

The HC5-50, with an AF=1, was used to derive a PNEC$_{\mathbf{freshwater}}$ of 7.8 µg Cu/l for Europe in a generic context in absence of site-specific information on bioavailability parameters (pH, DOC, hardness).

2.2.2.2.2 Sediment compartment

The sediment PNEC included using a weight of evidence approach considering different sources and tiered approaches of information: (1) sediment ecotoxicity data, (2) pelagic ecotoxicity data in combination with Kd values derived through different approaches, (3) soil ecotoxicity data and soil bioavailability models and (4) mesocosm/field ecotoxicity.

High-quality chronic benthic NOECs for six benthic species, representing 62 NOEC values were retained for the PNEC derivation. NOEC values were related to sediment characteristics (e.g., Organic Carbon (OC) and Acid Volatile Sulphides (AVS)), influencing the bioavailability and thus toxicity of copper to benthic organisms. The derivation of the freshwater HC5-50sediment for copper was therefore based on the OC-normalized dataset, containing only low-AVS sediments. Using the log-normal species sensitivity distribution a freshwater HC5-50sediment of 1741 mg Cu/kg OC was derived through the statistical extrapolation method.

Using the equilibrium partitioning (EP) approach, the derived HC5-50sediment (EP) values were comparable or higher than the HC5-50 derived from whole sediment tests. The comparison between the sensitivity of soil and benthic organisms added weight to the HC5-50 from whole sediment tests. The same did sediment threshold values and benthic NOECs that were obtained from four mesocosm studies and one field cohort study.

The AF of 1 was chosen due to the certainty concerning 1) weight of evidence provided; 2) the overall quality of the database; 3) the robustness of the HC5-50 values; 4) corrections for bioavailability (reducing uncertainty); 5) the conservative factor built into the system (no acclimation of the test organisms and only low AVS sediments retained); 6) validations from multi-species mesocosm studies and field studies and 7) comparison with natural backgrounds and optimal concentration ranges.

In case of natural sediments both the amount of AVS and organic carbon present in the sediment has dictated the observed effect levels for copper and were used for the risk characterisation. In absence of AVS data, a default AVS value of 0.77 µmol/kg dry weight was used. This value corresponded to the 10th percentile of the AVS obtained from a wide Flemish monitoring database and additional AVS data from other European countries.

The HC5-50, with an AF=1, was used to estimate a PNEC$_{sediment}$ of 1741 mg Cu/kg OC, for Europe in a generic context. This corresponding to 87 mg Cu/kg dry weight for a sediment with 5 % O.C.(TGD default value)

2.2.2.2.3 Terrestrial compartment

A high-quality dataset of 252 individual chronic NOEC/EC10 values from 28 different species and processes representing different trophic levels (i.e., decomposers, primary producers, primary consumers) has been retained for the PNEC derivation. The observed intra-species differences in toxicity data were related to differences in bioavailability, the latter related to differences in soil properties and to differences in ageing and application mode and rate.

The soil property best explaining the variability in toxicity for most of the endpoints was the eCEC (effective Cation Exchange Capacity).

For the normalisation of the ecotoxicity data, the respective Cu background concentrations were added on all NOEC/EC10 values which were subsequently normalised to representative EU soils using the relevant regression (bio)availability models, generating soil-type specific HC5-50 values.

Species Sensitivity Distributions were constructed using the normalised NOEC/EC10 data. HC5-50 values from log-normal distributions ranging between 13.2 and 94.4 mg Cu/kg dry weight were obtained. A total of eight single species studies were available in which the toxicity of Cu to microorganisms, invertebrates and plants in field-contaminated aged soils was investigated for a wide range of European soil types (peaty, sandy, clay). A total of five multi-species studies were available, three of which studied the effects of copper in freshly spiked soils and 2 in field contaminated aged soils. Invertebrates, plants and micro-organisms were studied. Single species and multi-species field studies indicate that effects did not occur at an exposure level at the HC5-50-value.

Normalized HC5-50 values (AF=1) were used as PNEC$_{soil}$ for the risk characterisation.

The uncertainty analysis that provides arguments for the AF=1 was based on: 1) the overall quality of the database and the end-points covered; 2) the diversity and representativeness of the taxonomic groups covered by the database; 3) corrections for differences in bioavailability (soil properties); 4) the statistical uncertainties around the 5th percentile estimate; 5) NOEC values below the HC5-50 and 6) field and mesocosm studies and comparisons of their results with the HC5-50.

To account for the observed difference between lab-spiked soils and field-contaminated soils, a conservative leaching-ageing factor of 2 was agreed based on test data from the mechanistic research on ageing and ionic strength (leaching) effects.

For the PT08 biocidal product dossiers, unlikely to the VRA, a leaching ageing “L/A” factor of 2 was not used to derive the PNECsoil but it was taken into account in the assessment of the PEC soil (PEC divided by 2). Indeed it was stated that decrease of Cu toxicity with ageing has to be taken into account but rather in the exposure assessment than in the hazard assessment. Since this factor was determined over a period of 18 months, it can be applied for PEC calculation over the same amount of time (i.e. TIME 2 only in the PT08). The L/A factor of 2 was used in the PEC (PEC/2), while for VRA, the L/A factor was used in the PNEC (PNEC/2). In the VRA, the NOEC added were fisrt multiplied by the L/A factor (2). The background concentrations from corresponding control soil were then added. All the individual aged NOECtotal were then normalized and finally the HC5-50 was derived; The AF of 1 was applied on the HC5-50. More explanations are given in the environmental exposure assessment chapter.

The HC5-50, with an AF=1, was used to derive a PNEC$_{soil}$ of 45.6 mg Cu/kg dry weight for Europe in absence of site-specific information on soil properties.

2.2.2.2.4 STP compartment

For the STP compartment, high-quality NOECs from respiration or nitrification inhibition studies, relevant to the functioning of a Sewage Treatment Plant (STP), resulted from biodegradation/removal studies and NOECs for ciliated protozoa were used to derive the PNEC for STP micro-organisms.

The lowest reliable observed NOEC value was noted for the inhibition of respiration (AF=1) of 0.23 mg/l expressed as dissolved copper and carried forward as PNEC$_{STP}$ to the risk characterisation.

2.2.2.2.5 Summary of PNECS

Compartment	PNEC	Unit
STP	0.23	[mg.L-1]
Freshwater	7.8	[µg.L-1]
Sediment	87 18.9	[mg.kg$_{dwt}$-1] [mg.kg$_{wwt}$-1]
Soil	45.6 40.35	[mg.kg$_{dwt}$-1] [mg.kg$_{wwt}$-1]

2.2.2.3 Risk characterisation for the environment

General introduction

No quantitative exposure assessment has been carried out for the life cycle stages “production” and “formulation of the biocidal product” since environmental exposure due to manufacturing of the active substance is covered by other legislation and will therefore not be considered here.

No exposure assessment has been performed for the life cycle stage “service life of the treated wood” intended for use classes 1 and 2 (indoor use) assuming negligible emissions to the environment.

The concentrations of copper in the environment were estimated following the recommendations given in the currently available Guidance Documents. Stages of the wood life considered for the exposure assessment are industrial wood treatment, storage of treated wood and wood in-service for use class 3 and use class 4.

As cooper is a natural endogenous compound, the releases due to its use as wood preservative have been added to the background environmental concentration. In a first step, the added predicted concentrations of copper were calculated, in line with the equation given by the ESD. In a second step, the added values were corrected in order to integrate the natural/pristine or the regional background concentrations in copper (as agreed under the Council Regulation (EEC) 793/93 on Existing Substances - EU-RAR):

- Natural/pristine background Cu concentrations in water, sediment and soil were taken from the FOREGS Geochemical Baseline Programme (FGBP) database published in March 2004 (http://www.gsf.fi/foregs/geochem/),
- Regional background Cu concentrations in water, sediment and soil were taken from the EU Existing Chemical Regulation.

Compartment	Natural/pristine background concentration	Regional background concentration	Unit
Surface water	0.88	2.9	[µg.L^{-1}]
Ground water	0.88	2.9	[µg.L^{-1}]
Soil	12 10.6	24.4 21.6	[mg kg$_{dwt}^{-1}$] [mg kg$_{wwt}^{-1}$]
Sediment	21 4.56	67.5 14.7	[mg kg$_{dwt}^{-1}$] [mg kg$_{wwt}^{-1}$]

In the specific case of copper release to soil, the applicant presented studies on copper toxicity in aged contaminated soils. Results from these studies have been reviewed by RMS. They show that, after 18 months ageing, NOECs increased for plants and invertebrates corresponding to a decrease of copper toxicity threshold. For micro-organisms, NOECS increased also but this is also probably due to an adaptation to copper. 18 months ageing tests were however not long enough to show a total remove of toxicity.

The applicant used these data to derive a lab to field factor reflecting the decrease in bioavailability of copper after 18 months, and proposed to apply this factor for the PNEC derivation. Possible underlying mechanisms were detailed by the applicant and RMS considers that decrease of Cu toxicity with ageing has to be taken into account, but rather in the exposure assessment than in the hazard assessment. Since this factor was determined over a period of 18 months, it can be applied for PEC calculation over the same amount of time or higher (*i.e.* TIME 2 only).

Therefore, an ageing factor of 2 was applied on the total copper concentrations in soil for the values calculated in TIME 2, in order to consider the phenomenon of copper ageing in soil. This strategy was validated at TMIII08.

Intended uses

The intended uses of the representative biocidal product **SPU 01840 F (Spiess Urania)** are industrial treatments of wood by dipping/immersion and vacuum pressure impregnation for use classes 1 – 3 (dipping/immersion) and use classes 1 – 4-1 (vacuum pressure impregnation).

The intended use of the representative biocidal product **ACQ-C2D (WPCTF)** is only industrial treatment by vacuum pressure impregnation for use classes 1 – 4.

Leaching rates evaluation

SPU 01840 F (SU)

For Spiess Urania dossier the emissions to the environment from the stages of storage and wood in-service were calculated on the basis of the results of leaching tests with treated wood in contact with water.

ACQ-C2D (WPCTF)

For the dossier from the WPCTF, the emissions to the environment from the stages of storage and wood in-service were also calculated on the basis of the results of leaching tests with treated wood in contact with water. Nevertheless, none of the studies submitted by the applicant for the determination of the leaching rates completely comply with the current requirements for this type of test. As a first Tier, calculations are also made assuming a 100% leaching of copper from treated wood over the life service of the vacuum pressure impregnation treatment (20 years).

2.2.2.3.1 Aquatic compartment (including sediment)

SPU 01840 F (SU)

Dipping/immersion

Estimated risks from **industrial treatment by dipping/immersion process** indicate an unacceptable risk to surface water and sediment considering a natural and a regional background concentration. Therefore, during the application process, the product must be re-cycled within the facility or collected and disposed of according to local authority regulations in order to minimise the release to the environment.

Estimated risks from **storage** of wood treated by dipping/immersion indicate an unacceptable risk to surface water and sediment considering a natural background concentration and to surface water and sediment considering a regional background concentration. All timbers treated by industrial process will have to be stored on impermeable hard standing to prevent direct losses surface water and to allow losses to be collected for disposal.

Concerning **wood-in-service** releases for use class 3, the noise barrier and the bridge over the pond are the only scenarios that foresee emissions to the aquatic compartment. These scenarios indicate an acceptable risk for surface water and sediment when releases from wood treated by dipping/immersion are directed to a sewage treatment plant (noise barrier scenario) but show unacceptable risk when surface treated wood is located above a water body (bridge scenario) even when removal processes are considered (adsorption onto suspended matter and sediment and time-weighted averaging of concentrations). Since an unacceptable risk is identified where direct loses to water are possible there should be a labelling against applications where direct losses to water are possible, thereby preventing use in these situations.

Vacuum pressure impregnation

Estimated risks from **industrial treatment by vacuum pressure impregnation** indicate an unacceptable risk to sediment considering a regional background concentration. Therefore, during the application process, the product must be re-cycled within the facility or collected and disposed of according to local authority regulations in order to minimise the release to the environment.

Estimated risks from **storage** of wood treated by vacuum pressure impregnation indicate an unacceptable risk to sediment considering a regional background concentration. All timbers treated by industrial process will have to be stored on impermeable hard standing to prevent direct losses surface water and to allow losses to be collected for disposal.

Concerning **wood-in-service** releases for use class 3, the noise barrier and the bridge over the pond are the only scenarios that foresee emissions to the aquatic compartment. These scenarios indicate an acceptable risk for surface water and sediment when releases from wood treated by vacuum pressure impregnation are directed to a sewage treatment plant (noise barrier scenario) but show unacceptable risk when surface treated wood is located above a water body (bridge scenario) when removal processes are not considered (adsorption onto suspended matter and sediment and time-weighted averaging of concentrations). The risk to sediment is unacceptable whatever the conditions. Since an unacceptable risk is identified where direct loses to water are possible there should be a labelling against applications where direct losses to water are possible, thereby preventing use in these situations.

ACQ-C2D (WPCTF)

Vacuum pressure impregnation

Estimated risks from **industrial treatment by vacuum pressure impregnation** indicate an unacceptable risk to surface water and sediment when results are expressed as total concentration, either considering a natural or a regional background concentration. Therefore, during the application process, the product must be re-cycled within the facility or collected and disposed of according to local authority regulations in order to minimise the release to the environment.

Estimated risks from **storage** of wood treated by vacuum pressure impregnation indicate an unacceptable risk to the aquatic environment whatever the background considered. All timbers treated by industrial process will have to be stored on impermeable hard standing to prevent direct losses surface water and to allow losses to be collected for disposal.

Concerning **wood-in-service,** the relevant scenarios tested for uses in hazard classes 3 and 4-2 indicate an acceptable risk for surface water and sediment when releases from wood treated by vacuum pressure impregnation are directed to a sewage treatment plant (noise barrier scenario – class 3) but show unacceptable risk when surface treated wood is located above or in a water body (bridge scenario – class 3, sheet pilling scenario – class 4-2) even when removal processes are considered (adsorption onto suspended matter and sediment and time-weighted averaging of concentrations). For the scenario water jetty (class 4-2), release to fresh water is acceptable for the aquatic organisms when removal processes are taken into account even in considering a worst case situation of 100% leaching rate of applied copper during TIME2 and whatever the background used. But for this same scenario, risks are expected for sediment even in considering a Tier 2 approach and whatever the background used. Since an unacceptable risk is identified where direct loses to water are foreseen there should be a labelling against applications where direct losses to water are possible, thereby preventing use in these situations. The uses in class 4-2 should not be allowed.

2.2.2.3.2 Sewage treatment plant organism

Considering the two products SPU 01840 F (Spiess Urania) and ACQ-C2D (WPCTF), PEC/PNEC ratios indicate acceptable risks to sewage treatment plant either from industrial treatments, or from wood-in-service releases (noise barrier scenario).

2.2.2.3.3 Atmosphere

Considering the two products SPU 01840 F (Spiess Urania) and ACQ-C2D (WPCTF), there would be no exposure from copper-treated wood via the atmosphere due to the very low vapour pressure of copper and copper compounds. Therefore, copper-treated wood would not pose an unacceptable risk to the air compartment.

2.2.2.3.4 Terrestrial compartment

SPU 01840 F (SU)

Dipping/immersion

The **industrial treatment by dipping** scenario considers the exposure of the soil compartment via the application of contaminated sludge to soil. No risk to terrestrial organisms is expected. However, due to the risk identified for sediment during the industrial application phase, releases via STP during industrial application should not be allowed.

The outdoor **storage of treated wood** (class 3) following dipping industrial treatment on bare soil is expected to pose a long-term risk to soil organisms whatever the background considered. Storage on bare soil should not be allowed. The emissions from treated wood to soil should be substantially reduced by covering the storage area with protective roof or covering the soil with impermeable coating e.g. concrete. Leachates should be collected and treated appropriately (e.g. incineration).

Concerning the use class 3, the PEC/PNEC ratios calculated for **wood in service** treated by dipping industrial treatment are below 1 for all the corresponding scenarios (house, fence, noise barrier) considering a natural or a regional background concentration, which indicates an acceptable risk for terrestrial organisms. The wood treated by dipping/immersion should be allowed for a use in class 3.

Vacuum pressure impregnation

As for dipping/immersion, the **industrial treatment by vacuum pressure impregnation** scenario considers the exposure of the soil compartment via the application of contaminated sludge to soil. No risk to terrestrial organisms is expected. However, due to the risk identified for sediment in this scenario (considering a regional background concentration), releases via STP during industrial application should not be allowed.

The outdoor **storage of treated wood** on bare soil (class 3) following the industrial vacuum pressure impregnation is expected to pose a risk to soil organisms, even in considering an ageing factor of 2. Storage on bare soil should not be allowed. The emissions from treated wood to soil should be substantially reduced by covering the storage area with protective roof or covering the soil with impermeable coating e.g. concrete. Leachates should be collected and treated appropriately (e.g. incineration).

Concerning the use class 3 and 4-1, the PEC/PNEC ratios calculated for **wood in service** treated by industrial vacuum pressure impregnation are below 1 for all the corresponding scenarios (house, fence, noise barrier, fence post and transmission pole) considering a natural or a regional background concentration, which indicates an acceptable risk for terrestrial organisms. The wood treated by vacuum pressure impregnation should be allowed for a use in class 3 and 4-1.

ACQ-C2D (WPCTF)

Vacuum pressure impregnation

The **vacuum pressure impregnation application** scenario considers the exposure of the soil compartment via the application of contaminated sludge to soil. No risk to terrestrial organisms is expected. However, due to the risk identified for sediment in this scenario (considering a natural or a regional background concentration), releases via STP during industrial application should not be allowed.

The outdoor **storage** of treated wood on bare soil (class 3) following the industrial vacuum pressure impregnation is expected to pose a risk to soil organisms, even in considering an ageing factor of 2. Storage on bare soil should not be allowed. The emissions from treated wood to soil should be substantially reduced by covering the storage area with protective roof or covering the soil with impermeable coating e.g. concrete. Leachates should be collected and treated appropriately (e.g. incineration).

Concerning the use class 3 and 4-1, the PEC/PNEC ratios calculated for **wood in service** treated by industrial vacuum pressure impregnation are below 1 for all the corresponding scenarios (house, fence, noise barrier, fence post and transmission pole) considering a natural or a regional background concentration and a Tier 2 approach for House scenario. For this last scenario, the risk in Time 2 was considered acceptable seeing that PEC/PNEC ratios are equal or only slightly above the trigger value of 1 and that leaching rates from treated wood were probable overestimated. Therefore, these results were considered to show an acceptable risk for terrestrial organisms. The wood treated by vacuum pressure impregnation should be allowed for a use in class 3 and 4-1.

2.2.2.3.5 Ground water

Considering the two products SPU 01840 F (Spiess Urania) and ACQ-C2D (WPCTF), copper is strongly absorbed and immobile in soil. Therefore, no copper is expected to reach groundwater, and copper carbonate as a wood preservative is not expected to pose a risk for groundwater contamination following the use of the two products SPU 01840 F (Spiess Urania) and ACQ-C2D (WPCTF) as PT08.

2.2.2.3.6 Secondary poisoning

Copper is an essential micronutrient, needed for optimal growth and development of micro-organisms, plants, animals and humans. Copper acts as an active cofactor in over 20 enzymes and proteins. To ensure appropriate copper tissue levels without causing toxicity from copper excess, internal copper levels are homeostatically regulated by all living organisms. Homeostatic regulation of copper allows organisms, within certain limits, to maintain their total body copper level and to maintain physiologically required levels of copper in their various tissues, both at low and high copper intakes.

In the aquatic environment, homeostatic regulation of invertebrates and fish resulted in an inverse relationship between copper BCFs and concentrations in the water. The importance of such homeostasis regulation was recognised in the regulatory framework of aquatic hazard classification (OECD, 2001). Similarly, in terrestrial plants, copper BCFs were inversely related to copper levels in soils.

The molecular mechanism of copper homeostasis, is related to 2 key elements: P-type ATPases that can pump copper across biological membranes in either direction and copper chaperones, important for the intracellular copper homeostasis. This cellular copper homeostasis mechanism is considered as being universal as the sequences of copper chaperones are highly conserved between species.

Besides these active regulation mechanisms, some groups of organisms have developed additional internal regulation mechanism (molecular binding and sequestration) as a strategy to cope against copper excess.

In higher organisms, dietary copper exposure studies in mammals and humans have shown that the intestinal adsorption / biliary excretion of copper is regulated with varying dietary intakes. Research indeed demonstrated that copper adsorption in humans can vary between 11 and 75 %, depending on the dietary intake. Similarly, mammals and birds, can rely on intestinal adsorption and biliary excretion to maintain internal copper levels with large variation in dietary intakes.

Based on the above information, bioaccumulation and biomagnification phenomenons are considered as not applicable for copper.

2.2.2.4 PBT assessment

Being an inorganic compound, the persistence criteria of DT90, field < 1 year and DT50 at 20°C < 6 months that are laid down in paragraph 85 of Annex VI to the Biocides Directive and in the TNsG on Annex I inclusion are not applicable to basic copper carbonate. According to the latter, the degradation triggers do not necessarily apply if the active substance is included in Annex I with regard to areas of use where a long lasting service-life of the treated material is essential and it is scientifically demonstrated that under field conditions there is no unacceptable accumulation in soil (e.g. that the PEC/PNEC < 1 in soil during storage and the service-life of the treated article).

The application as a wood preservative can be considered as such. It was shown above that for storage the PEC/PNEC ratio is above 1. Copper carbonate meets the criteria for persistence in soil, and can be therefore considered as persistent.

Due to the homeostatic regulation process of invertebrates and fish of copper, bioaccumulation and biomagnification of cooper are considered as not applicable for copper.

Considering the HC5-50 value of 7.8 µg/L for the aquatic compartment, Basic Copper Carbonate fulfils the T criterion.

Copper carbonate does not fulfil the PBT-criteria. Therefore inclusion in Annex I is not restricted by these criteria.

2.2.3 Overall summary

SCENARIO		Human primary exposure		Human secondary exposure		Aquatic compartment	STP	Terrestrial compartment	Ground water	Air	Secondary poisoning
		Professional	Non professional	Worker	Consumer						
INDUSTRIAL APPLICATION : DIPPING/IMMERSION (SPIESS URANIA ONLY)											
Application		**Not acceptable***	NR	Acceptable	Acceptable	**Not acceptable**	Acceptable	Acceptable	NR	NR	NR
Storage						**Not acceptable**	NR	**Not acceptable**	NR	NR	NR
Wood in-service	Classes 1-2	NR	NR	Acceptable	Acceptable	NR	NR	NR	NR	NR	NR
	Class 3 **without** direct release to water					Acceptable	Acceptable	Acceptable	NR	NR	NR
	Class 3 **with** direct release to water					**Not Acceptable**	NR	NR	NR	NR	NR
Overall conclusions: Dipping process should not be allowed because of the unacceptable risks for industrial workers (short-term and long-term exposure), even if PPE are worn.											
INDUSTRIAL APPLICATION : VACUUM PRESSURE IMPREGNATION											
Application		Acceptable*	NR	Acceptable	Acceptable	**Not acceptable**	Acceptable	Acceptable	NR	NR	NR
Storage						**Not acceptable**	NR	**Not acceptable**	NR	NR	NR
Wood in-service	Classes 1-2	NR	NR	Acceptable	Acceptable	NR	NR	NR	NR	NR	NR
	Class 3 **without** direct release to water					Acceptable	Acceptable	Acceptable	NR	NR	NR
	Class 3 **with** direct release to water					**Not acceptable**	NR	NR	NR	NR	NR
	Class 4-1					NR	NR	Acceptable	NR	NR	NR
	Class 4-2 **(WPCTF only)**					**Not acceptable**	NR	NR	NR	NR	NR
Overall conclusions: Vacuum pressure impregnation process should be allowed due to acceptable risk for uses in class 1 to 4-1 with the following mitigation measures: • During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments. • During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed. • All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration) • Pre-treated timber must not be in contact with or above surface water. A use in class 4-2 should not be allowed unless data is submitted to demonstrate that the product will meet the requirements of Article 5 and Annex VI, if necessary by the application of appropriate mitigation measures.											

NR: Non relevant

* Considering the wearing of PPE

3 – PROPOSAL FOR DECISION

3.1 Background to the proposed decision

The Copper (II) carbonate – Copper hydroxide (1:1)[7] dossier has been submitted by the Wood Preservative Copper Task Force (WPCTF) and by Spiess-Urania for its use as a wood preservative. The reference biocidal products that will contain copper carbonate are limited to a professional use for treating timbers.

The applicant is not currently placing nano forms of basic copper carbonate on the market. Therefore, the submitted dossier and the finalised assessment report don't cover potential nanoforms of this copper compound, should such forms exist.

Use class 1 to 3 is claimed for wood treated by dipping by Spiess-Urania.
Use class 1 to 4-1 is claimed for wood treated by vacuum pressure by Spiess-Urania.
Use class 1 to 4-2 is claimed for wood treated by vacuum pressure by the Wood Preservative Copper Task Force.

The physicochemical properties of basic copper carbonate are deemed acceptable for the appropriate use, storage and transportation of the biocidal product.

The submitted information on basic copper carbonate proves a sufficient efficacy against wood destroying fungi (wood rotting basidiomycetes and soft rot fungi and insects (wood boring beetles and termites for the wood preservatives copper task force)).

The health effects of basic copper carbonate are well documented for acute and irritation endpoints. In contrast, all the chronic data are based on copper sulphate. However, considering that basic copper carbonate is a precursor releasing cupric ion, which is the actual active element, it was accepted to base the risk assessment on the provided studies. Toxicological profile in the light of exposure resulting from the use of this substance is of no concern. The conclusion of the toxicological assessment is that the risk for professional users is negligible when safe operational procedures are established and appropriate PPE are used, only when wood is treated by a simple vacuum pressure process. Risks to indirectly exposed persons (including infants) is also negligible.

With regard to environmental exposure and effects, based on the risk assessments conducted for the industrial application phases, it is considered that safe uses can only be identified if the possibility of STP exposure during treatment (dipping and vacuum pressure impregnation) is excluded. It is recommended that this should be a condition of Annex I inclusion. The environmental risk assessment indicates that all mode of industrial application result in an unacceptable risk to the aquatic and terrestrial environment during storage (class 3 and class 4). The environmental risk assessment indicates that all scenarios investigated for wood in service used in class 3 for dipping treatment and in classes 3 and 4 for vacuum pressure impregnation result in acceptable risk to the terrestrial environment. Nevertheless, it is considered that safe uses can only be identified if the possibility of a direct release to surface water is excluded. It is recommended that this should be a condition of Annex I inclusion. All uses in class 4-2 should therefore not be allowed.

3.2 Proposed decision regarding the inclusion in Annex I

On the basis of the proposed and supported uses and the evaluation conducted as summarised in chapter 2 of this document, it can be concluded that basic copper carbonate fulfils under the conditions listed in 3.2 the requirements laid down in Article 5(1) (b), (c), and (d) of Directive 98/8/EC.

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[7] Also mentioned as basic copper carbonate or copper carbonate, which is a shorter although less accurate name.

It is proposed that basic copper carbonate (CAS no. 12069-69-1) be included in Annex I of Council Directive 98/8/EC as an active substance in wood preservative products (product type 8), subject to the following specific provisions:

1. The active substance copper carbonate shall have a minimum purity ≥ 95.7% w/w equivalent to 55.0 % w/w copper.
2. The identity and the maximum content of impurities have to comply with the confidential part of the dossier.
3. In view of the risks identified for industrial workers during dipping treatment, products shall be authorised only for industrial use by vacuum pressure impregnation, unless it is demonstrated in the application for product authorisation that risks to human and environment demonstrate acceptable levels for other types of application in accordance with Article 5 and Annex VI.

4. In view of the assumptions made during the risk assessment, products authorised for industrial use must be applied with appropriate personal protective equipment and safe operational procedures should also be established, unless it can be demonstrated in the application for product authorisation that risks to industrial users can be reduced to an acceptable level by other means.

5. In view of the risks identified for the aquatic and soil compartments, appropriate risk mitigation measures must be taken to protect those compartments. In particular, labels and/ or safety data sheets of products authorised for industrial use shall indicate that freshly treated timber must be stored after treatment under shelter or on impermeable hard standing to prevent direct losses to soil or water and that any losses must be collected for reuse or disposal.

6. In view of the risks identified for the aquatic compartments, products shall not be authorised for treatment of wood that will be used in outdoor constructions near or above water, and for the treatment of wood in direct surface water contact, unless data is submitted to demonstrate that the product will meet the requirements of Article 5 and Annex VI, if necessary by the application of appropriate mitigation measures.

Specific provisions n°3 and 4 are necessary due to risks identified for industrial users (see section 2.2.1.3).
Specific provision n°5 is necessary due to risks identified for the aquatic and soil compartments, during the industrial treatment phase (see section 2.2.2.3.1 and 2.2.2.3.4).
Specific provision n°6 is necessary due to risks identified for the aquatic compartment, during service-life of wood continuously exposed to water (see section 2.2.2.3.1).

3.3 Factor to be taken into account by Member States when authorising products

1. The assessment was made for products containing Copper carbonate only for dipping/immersion treatment and industrial treatments by vacuum pressure impregnation for uses in hazard classes 1 to 4-1. Other uses will have to be considered at the product authorisation stage.

2. Studies provided regarding efficacy were done with tests on Cu^{2+} delivered as copper sulphate or copper carbonate. However, a full complete efficacy data package will be required to support authorisation of products for all claimed organisms.

3. No repeated-dose inhalation study was submitted due to the negligible exposure by this route. A negligible inhalation exposure must therefore be checked when authorising products. Otherwise adequate inhalation data will have to be submitted.

4. Concerning environmental risk assessment, Biotic Ligand Modelling (BLM)-calculated HC5-50 values were used as PNEC for risk characterization. Under product authorization, Member States will have to investigate if the BLMs can be applied under their specific conditions. Moreover, the national natural background should be compared to the background level used for the risk assessment.

3.4 Demand for further information

The submitted dossier satisfies the requirements of Annexes IIA, IIIA, IIB and IIIB of Directive 98/8/CE and is sufficient to recommend Annex I inclusion for copper carbonate as wood preservative.

Nevertheless, some information or studies, that are not expected to change the conclusion on the inclusion into Annex I, are needed as confirmatory data. They should preferably be submitted to the original Rapporteur Member State (France) at the latest 6 months before the date of inclusion of the active substance into Annex I :

> A new 5-batch analysis is required to support each source and to ensure compliance of current production of each source of basic copper carbonate to the specifications. This must include the analysis of all relevant and significant impurities using validated methods of analysis. Nickel should be determined in the 5-batch analysis as it is a relevant impurity. Besides, a method of analysis of Nickel should therefore be provided as well.

- Spiess Urania shall submit :
    - Methods of analysis for the impurities arsenic, cadmium, lead and nickel.
    - Validation data for the methods of analysis copper in soil and water.
    - Further data must be provided to fully validate the analytical method for the determination of the active substance in the biocidal product
- The WPCTF shall submit :
    - The process of manufacture of three sources of the WPCTF (Alchema, and the two sources of Adchem) should be provided, and the manufacturing site(s) should clearly identified for the two sources of Adchem
    - Validation data must be provided for the determination on copper in basic copper carbonate by the WPCTF
    - A method of analysis for one impurity > 0.1% was not provided by the WPCTF (see detail in the confidential part of the CAR)
    - A validated analytical method for the determination of copper in the biocidal product must be provided.
    - If a demand of authorization is submitted for the reference product of the annex I dossier, surface tension and compatibility with other products have to be provided.

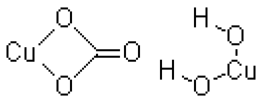
Appendix 1 – Listing of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	Basic Copper carbonate (Copper carbonate should be understood as basic copper carbonate in this document)
Function (*e.g.* fungicide)	Fungicide, insecticide

Rapporteur Member State	France

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Copper(II) carbonate-copper(II) hydroxide (1:1)
Chemical name (CA)	Copper (II) carbonate, basic
CAS No	12069-69-1
EC No	235-113-6
Other substance No.	The CIPAC code number for copper compounds is 44
Minimum purity of the active substance as manufactured (g/kg or g/l)	957g/kg equivalent to 550 g/kg as copper. (SU) Min. 957 g/kg as basic copper carbonate equivalent to,550 g/kg as copper, in dry weight. Up to 20 % of water in wet technical grade material. (WPCTF)
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Lead : max 0.02% Cadmium : max 0.0001% Arsenic : max 0.009% Nickel : max 0.003% (see detail in the confidential part of the CAR)
Molecular formula	$CH_2Cu_2O_5$
Molecular mass	221.1 g/mol
Structural formula	

Physical and chemical properties (Annex IIA, point III., unless otherwise indicated)

Melting point (state purity)	No melting point – decomposes before melting (ca. 96%) (SU) No melting point – decomposes before melting (ca. 83%) (WPCTF)
Boiling point (state purity)	No boiling point – decomposes before boiling (ca. 96%) (SU) No boiling point – decomposes before melting (WPCTF)
Temperature of decomposition	> 200°C (SU) 206°C (WPCTF)
Appearance (state purity)	Solid green powder, odourless (ca. 96%) (SU) Moist, green powder, no odour readily detectable at 21°C (ca. 83%) (WPCTF)
Relative density (state purity)	$D^{20}_{4\,0}$ = 3.761 (ca. 96%) (SU) 3.48 at 21°C (ca. 83%) (WPCTF)
Surface tension	Not surface active (SU) Not required for substances with water solubility <1mg/L (WPCTF)
Vapour pressure (in Pa, state temperature)	< 10^{-5} Pa theoretically assessed (SU) Not measurable. (WPCTF)
Henry's law constant (Pa m^3 mol^{-1})	Not applicable (SU) Not applicable (WPCTF)
Solubility in water (g/l or mg/l, state temperature)	pH: 5.80 - 6.08; pure water, T = 20 °C: 1.237 mg/l (SU)
	in water; pH results from by the active substance itself (basic Copper carbonate) (SU) Solubilities at acidic and alkaline pH cannot be determined due to interferences (SU) pH 5.6 – 5.8 (buffered solution): >1.16 g/l at 20^{o}C +/- 0.5^{o}C.(dependant on acid availability pH increased during solubilisation) (WPCTF) pH 6.2-6.8 (deionised water): 4.68 x 10^{-3} to 1.59 x 10^{-3} g/l at 20^{o}C +/- 0.5^{o}C (decreasing against time) (WPCTF) pH 8.7 to 8.8 (buffered solution): < 1.0 x 10^{-5} g/l at 20^{o}C +/- 0.5^{o}C (WPCTF)
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	In n-heptane and methanol
	< 10 g/l at T = 20°C (for n-heptane) and 30 °C (for methanol) (SU) Not determined, as basic copper carbonate will be used only in aqueous formulations. (WPCTF)
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not determined, as basic copper carbonate will be used only in aqueous formulations. (SU)

	Not determined, as basic copper carbonate will be used only in aqueous formulations. (WPCTF)
Partition coefficient (log P_{OW}) (state temperature)	Not appropriate, due to the nature of the active substance (inorganic salt) Partition coefficients in water, sediments and soils are used instead. (SU) Due to the nature of the active substance (inorganic salt), log Pow is not relevant information. Partition coefficients in water, sediments and soils are used instead. (WPCTF)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	Not appropriate, due to the nature of the active substance (inorganic salt) (SU) Not applicable. (WPCTF)
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not available: only required if water solubility cannot be measured. (SU) Not available: only required if water solubility cannot be measured. (WPCTF)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Not appropriate, due to the nature of the active substance (inorganic salt) (SU) Molar absorption coefficient ($dm^3.mol^{-1}.cm^{-1}$): 294 Medium: Acidic (pH 1.2) Wavelength: 245 nm (WPCTF)
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	Not appropriate, due to the nature of the active substance (inorganic salt) (SU) Not applicable. (WPCTF)
Quantum yield of direct phototransformation in water at $\Sigma > 290$ nm (point VII.7.6.2.2)	Not appropriate, due to the nature of the active substance (inorganic salt) (SU) Not applicable. (WPCTF)
Flammability	Not highly flammable (SU) Not highly flammable. (WPCTF)
Explosive properties	No explosive groups contained: not explosive. (SU) Not explosive. (WPCTF)

Classification and proposed labelling (Annex IIA, point IX.)

	Directive 67/548/EEC	**Regulation 1272/2008**
With regard to physical/chemical data	Not required	
With regard to toxicological data	Xn, Harmful R20, Harmful by inhalation R22, Harmful if swallowed Safety phrases: S37/38: Wear suitable gloves and eye/face protection	Acute Tox. 4 /H332 – Harmful if inhaled Acute Tox. 4/H302 – Harmful if swallowed
With regard to fate and behaviour data	N, dangerous for environment R53, May cause long-term adverse effects in the aquatic environment	Aquatic chronic/H410 - Very toxic to aquatic organisms and may cause long lasting effects in the aquatic environment
With regard to ecotoxicological data	N Dangerous for the environment R50, Very toxic to aquatic organisms Safety phrases: S60: this material and its container must be disposed as hazardous waste S61 : Avoid release to the environment Refer to special instructions/safety data sheets	Aquatic chronic/H410 - Very toxic to aquatic organisms and may cause long lasting effects in the aquatic environment

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	Electrogravimetric Method : CIPAC 44/TC/M/3.1 (Methods for total copper determination, not specific to copper (II) hydroxide). Purity can be calculated from the total copper content because other copper forms (i.e. metallic and cuprous) are not expected to be present in the technical material (SU) Volumetric Thiosulphate Method : CIPAC 44/TC/M/3.2 Electrogravimetric Method : CIPAC 44/TC/M/3.1 Purity is not directly determined but calculated from total copper content. This is possible because other copper forms (i.e. metallic and cuprous) are not expected to be present in the technical materials.Total copper content can be determined by various well-known methods such as volumetric thiosulphate method (CIPAC E Copper 44/TC/M/3.2), electrogravimetric method (CIPAC E Copper 44/TC/M/3.1, ASTM E53-98). A validation study is required (WPCTF)
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	DIN 18121-1 (1998), DIN EN 13137:2001, (SU) Methods for arsenic, cadmium, lead and nickel must be provided (SU) Trace metals, including those of toxicological significance can be determined by AAS. Before analysis, the sample is dissolved in an acid mixture and placed on a hotplate until digestion is complete. The AAS methods used to obtain five batch analysis data of impurities in basic copper carbonate are variations on internationally accepted guidelines such as ASTM E53-98 and US EPA methods 206.2, 213.1 and 239.1. Other suitable methods include: Inductively Coupled plasma – Mass Spectroscopy (ICP-MS) (e.g. US EPA method 6020). ICP-MS is applicable to the determination of sub-µg/l concentrations of a large number of elements in water samples and in waste extracts or digests. No digestion is required prior to analysis for dissolved elements in water samples. Acid digestion prior to filtration and analysis is required for samples for which total (acid-leachable) elements are required. The method measures ions produced by a radio-frequency inductively coupled plasma. Analyte species originating in a liquid are nebulised and the resulting aerosol transported by argon gas into the plasma torch. The ions produced are entrained in the plasma gas and introduced into a mass spectrometer. The ions are then sorted according to their mass-to-charge ratios and quantified with a channel electron multiplier. Inductively Coupled Plasma – Atomic Absorption

	^{2}Spectroscopy (ICP-AES), (e.g. US EPA method 200.7). Prior to analysis, samples must be solubilised or digested using an appropriate method. Samples are nebulised and the resulting aerosol is transported to the plasma torch. Element-specific emission spectra are produced by a fadio-frequency inductively coupled plasma. The spectra are dispersed by a grating spectrometer, and the intensities of the emission lines are monitored by photosensitive devices. (WPCTF) Method for one impurity > 0.1% must be provided (WPCTF)

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Flame Atomic Absorption (EPA 7210, 220.1) Validation data must be provided (SU) Residues of copper may be determined in soils using ICP-AES methods (e.g. AOAC official method 990.8). The estimated instrumental limit of detection (LOD) is 6 µg Cu/l. (LOQ not determined). Another suitable method is AAS (e.g. US EPA method 7210), with an LOQ of 0.2 mg/L. For both methods of analysis, the sample must first be digested. (WPCTF)
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Not available for lack of volatility and no exposition via the respiratory system when used in wood preservatives (SU) Residues of copper may be determined in air using Flame-AAS or ICP-AES methods (e.g. NIOSH methods 7029 or 7300 respectively). The estimated instrumental limits of determination (LOD) are 0.05 and 0.07 µg Cu/filter (LOQ not determined). (WPCTF)
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Furnace Atomic Absorption (EPA 220.2, 7211) Validation data muste be provided (SU) In water, trace elements may be determined by Inductively Coupled Plasma – Mass Spectroscopy (ICP-MS) (e.g. US EPA method 220.7). The LOD for this method was estimated at 3 µg Cu/l and the LOQ was determined at 20 µg Cu/l. Other suitable methods include AAS with direct aspiration (LOD 20 µg/l, LOQ 200 µg/l) (e.g. US EPA method 220.1) and AAS with graphite furnace (LOD 1 µg/l, LOQ 5 µg/l) (e.g. US EPA method 220.2). For all three methods of analysis, the sample must first be digested.(WPCTF)
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not relevant as not toxic (SU) ICP-AES may also be used for analysing elements in body fluids and tissues following acid digestion of the sample. LOQs are 10 µg/100 g blood, 2 µg/g tissue (e.g. NIOSH method 8005) and 0.25 µ/sample of urine (NIOSH method 8310). (WPCTF)
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not available for lack of exposure (SU) Not applicable (WPCTF)

Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not available for lack of exposure (SU) Not applicable (WPCTF)

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	It was agreed during the TMIII09 that an oral absorption of 36% for humans and 25% for animals have to be used.
Rate and extent of dermal absorption:	It was agreed during the TMIII09 that a dermal absorption of 5% has to be used for diluted solutions and 100% for the concentrated product.
Distribution:	Once absorbed by oral route, copper is bound to albumin and transcuprein and then rapidly transported to the liver where it is incorporated to ceruloplasmin, a transport protein that circulates in the organism and deliver the copper to other organs. The liver is the main organ involved in copper distribution and plays a crucial role in copper homeostasis by regulating its release. It should be however noted that a minor fraction of the absorbed dose can directly be distributed to peripheral organs. In both humans and animals, copper is tightly regulated at a cellular level, involving metallothionein and metallochaperones. These regulating molecules prevent from the accumulation of potentially toxic, free copper ions within the cell. In addition to the liver, the brain is another organ which contains relatively high concentrations of copper.
Potential for accumulation:	All mammals have metabolic mechanisms that maintain homeostasis (a balance between metabolic requirements and prevention against toxic accumulation). Because of this regulation of body copper, indices of copper status remain stable except under extreme dietary conditions. This stability was demonstrated in a study in which human volunteers received a diet containing total copper in the range 0.8 to 7.5 mg/d. Under these conditions, there were no significant changes in commonly used indices of copper status, including plasma copper, ceruloplasmin, erythrocyte superoxide dismutase and urinary copper..
Rate and extent of excretion:	Biliary excretion is quantitatively the most important route, with a mean copper excretion estimated to be in the order of 1.7 mg Cu/day (24.6 ± 12.8 µg Cu/kg bodyweight). A small amount of copper is also lost in urine and in sweat. Excretion of endogenous copper is influenced by dietary copper intake. When the copper intake is low, turnover is slow and little endogenous copper is excreted and vice versa. Faecal copper losses reflect dietary copper intake with some delay as intake changes and copper balance is achieved. Urinary losses do not contribute to the regulation of copper stores and contribute very little to the overall balance.

Toxicologically significant metabolite	None

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	between 500 and 2000 mg/kg (WPCTF) Males: 1350 mg/kg bw (SU) Females: 1495 mg/kg bw (SU)
Rat LD_{50} dermal	> 2000 mg/kg bw (both sexes)
Rat LC_{50} inhalation	$1.03 < LC_{50} < 5.20$ mg/L air (SU)
Skin irritation	Not irritating
Eye irritation	Moderately irritating (reversible after 7 and 14 days): does not require classification.
Skin sensitization (test method used and result)	Not sensitising

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	The test substance used the following study was copper (II) sulphate. Rat/ liver/ inflammation Rat/ kidney/ cytoplasmic droplets Rat, mouse/ forestomach/ minimal to moderate hyperplasia of the squamous mucosa
Lowest relevant oral NOAEL / LOAEL	16.3 mgCu/mg kg/d
Lowest relevant dermal NOAEL / LOAEL	Not available
Lowest relevant inhalation NOAEL / LOAEL	Not available

Genotoxicity (Annex IIA, point 6.6)	The test substance used in each of the following studies was copper (II) sulphate pentahydrate. 1. Ames test in Salmonella typhimurium - negative in both the presence and absence of S9 mix. 2. Bone marrow micronucleus study in the mouse – negative at a dose of 447 mg/kg bw. 3. *In vivo/in vitro* unscheduled DNA synthesis study in the livers of orally dosed male rats – negative, following treatment with doses of 632.5 or 2000 mg/kg bw. These studies demonstrate that copper is not mutagenic in the in vitro and in vivo test systems used.

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Available studies of the carcinogenicity of copper compounds in rats and mice, although not fully reliable, have given no indication that copper salts are carcinogenic.
lowest dose with tumours	Not applicable

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target / critical effect	The test substance used in the following study was copper (II) sulphate pentahydrate. Rat/Two-generation study/No evidence of effects on the fertility potential of either male or female rats.
Lowest relevant reproductive NOAEL / LOAEL	Copper sulphate cannot be regarded as having adverse effects on fertility in the animals tested. 1500 ppm NOAEL in rat two-generation study = 23.6-43.8 mgCu/kg bw/d (maximal dose tested)
Species/Developmental target / critical effect	Mouse/ Developmental toxicity/ malformations (study with major methodological deficiencies)
Lowest relevant developmental NOAEL / LOAEL	6 mg Cu/kg bw/d (NOAEL maternal toxicity = 6 mg Cu/kg bw/d) **However rat two-generation study with copper sulphate pentahydrate does not raise any particular teratogenic concern.**

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect Lowest relevant developmental NOAEL / LOAEL.	No evidence for neurotoxic potential from other studies

Other toxicological studies (Annex IIIA, VI/XI)

	None

Medical data (Annex IIA, point 6.9)

Direct observation, eg clinical cases, poisoning incidents if available; data point 6.12.2.	Acute symptoms resulted in metallic taste, salivation, epigastric pain, nausea, vomiting and diarrhoea. Anatomo-pathological examinations after self-poisoning (ingestion varying between 1 and 100 g of copper dissolved in water) revealed ulcerations of gastro-intestinal mucosa, hepatic damages (dilatation of central vein, cell necrosis and bile thrombi) and kidney lesions (congestion of glomeruli, swelling or necrosis of tubular cells and sometimes haemoglobin casts). Chronic symptoms, occurred in a voluntary intoxication by daily ingestion of 30 mg of copper for 2 years and 60 mg during the third year, were malaise, jaundice, hepatomegaly and splenomegaly. Liver examination revealed micronodular cirrhosis. In the particular case of vineyard sprayers intoxication by the Bordeaux mixture

	(unknown doses), lung lesions with focal distribution were observed: alveoli filled with desquamated macrophages, granuloma in the alveoli septa and fibro-hyaline nodules.

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
ADI (if residues in food or feed)	0.15 mgCu/kg bw/day	EFSA (2008)	Not applicable.
AEL short and medium term	0.082 mg/kg bw/d	90d in rats	MOE ref = 50
AEL long-term	0.041 mg/kg bw/d	90d in rats	MOE ref = 100
Drinking water limit	No data reported		
ARfD (acute reference dose)	Not applicable		

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	Not applicable to metals.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Not applicable to metals.
Readily biodegradable (yes/no)	Not applicable to metals.
Biodegradation in seawater	Not applicable to metals.
Non-extractable residues	Not applicable to metals.
Distribution in water / sediment systems (active substance)	The distribution of metals between aqueous phase and soil/sediment/suspended matter should preferentially be described on the basis of measured soil/water, sediment/water and suspended matter/water equilibrium distribution coefficient (TECHNICAL GUIDANCE DOCUMENT on Risk Assessment Part II Appendix VIII, 2003; TECHNICAL GUIDANCE DOCUMENT Annex 4-VIII Environmental risk assessment for metals and metal compounds (RIP 3.2-2). From the literature overview, the following partitioning coefficients have thus been derived for Cu metal and Cu compounds: **Partition coefficient in suspended matter** Kp_{susp} = 30,246 l/kg (log Kp (pm/w) = 4.48) (50th percentile) (Heijerick *et al,* 2005) **Partition coefficient in sediment** Kpsed = 24,409 l/kg (log Kp(sed/w) = 4.39) (50th percentile) (Heijerick *et al.,* 2005)
Distribution in water / sediment systems (metabolites)	Not applicable to metals.

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	Not Relevant for the nature of the active substance which an inorganic metal salt
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): Not applicable to metals.
	DT_{90lab} (20°C, aerobic): Not applicable to metals.
	DT_{50lab} (10°C, aerobic): Not applicable to metals.
	DT_{50lab} (20°C, anaerobic): Not applicable to metals.
Field studies (state location, range or median with number of measurements)	DT_{50f}: Not applicable to metals.
	DT_{90f}: Not applicable to metals.
Anaerobic degradation	Not applicable to metals.

Soil photolysis	Not applicable to metals.
Non-extractable residues	Not applicable to metals.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not applicable to metals.
Soil accumulation and plateau concentration	Although unable to degrade, the affect of ageing on the distribution of copper in soil results in increased immobilisation by long term adsorption and complexation reactions in the soil.

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	The distribution of metals between aqueous phase and soil/sediment/suspended matter should preferentially be described on the basis of measured soil/water, sediment/water and suspended matter/water equilibrium distribution coefficient (TECHNICAL GUIDANCE DOCUMENT on Risk Assessment Part II Appendix VIII, 2003; TECHNICAL GUIDANCE DOCUMENT Annex 4-VIII Environmental risk assessment for metals and metal compounds (RIP 3.2-2). From the literature overview, the following partitioning coefficients have thus been derived for Cu metal and Cu compounds: **Partition coefficient in soil** Kd = 2120 l/kg (log K_p = 3.33) (50th percentile) (Sauvé *et al.* 2000)

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	Not relevant for metals
Quantum yield of direct photolysis	Not relevant for metals
Photo-oxidative degradation in air	Not relevant for metals)
Volatilization	Not relevant for metals

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No data submitted nor required
Surface water (indicate location and type of study)	No data submitted nor required
Ground water (indicate location and type of study)	No data submitted nor required
Air (indicate location and type of study)	No data submitted nor required

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, Point 8.2, Annex IIIA, Point 10.2)

Acute toxicity to aquatic organisms	No acute toxicity data are presented as the toxicity was evaluated using a SSD based on chronic toxicity data.
Chronic toxicity to aquatic organisms in the FRESHWATER COMPARTMENT	**SSD result: HC5-50 = 7.8 µg Cu / l as reasonable worst case** **Freshwater algae and higher plants:** Lowest NOEC used in the SSD = 15.7 µg Cu /L (growth of *Pseudokirchneriella subcapitata*) Highest NOEC used in the SSD = 510.2 µg Cu /L (growth of *Chlorella vulgaris*) **Freshwater Invertebrates:** Lowest NOEC used in the SSD = 4 µg Cu /L (mortality and reproduction of *Ceriodaphnia dubia*) Highest NOEC used in the SSD = 181 µg Cu /L (reproduction of *Daphnia magna)* **Freshwater Fishes:** Lowest NOEC used in the SSD = 2.2 µg Cu /L (growth of *Oncorhynchus mykiss***)** Highest NOEC used in the SSD = 188 µg Cu /L (mortality of *Perca fluviatilis)*
Chronic toxicity to aquatic organisms in the SEDIMENT COMPARTMENT	**SSD result: HC5-50 = 1741 mg Cu/kg OC,** corresponding to **87 mg Cu/kg dry weight for a sediment with 5 % O.C**.(TGD default value) **Sediment organisms:** Lowest NOEC used in the SSD = 18.3 mg Cu /kg d.w. (growth and reproduction of *Tubifex tubifex*) Highest NOEC used in the SSD = 580.9 mg Cu /kg d.w. (survival of *Tubifex tubifex*)
Chronic toxicity to Sewage microorganisms	The lowest reliable observed **NOEC** value was noted for the inhibition of respiration **= 0.23 mg/l**

Effects on earthworms or other soil non-target organisms

Acute toxicity to soil organisms (Annex IIIA, point XIII.3.2)	No acute toxicity data are presented as the toxicity was evaluated using a SSD based on chronic toxicity data.
Chronic toxicity to soil organisms in the TERRESTRIAL COMPARTMENT	**SSD result: HC5-50 = 45.6 mg Cu/kg dry weight was used as reasonable worst case value for Europe in absence of site-specific information on soil properties.** **Terrestrial higher plants:** Lowest NOEC used in the SSD = 18 mg Cu /kg d.w. (*Hordeum vulgare*) Highest NOEC used in the SSD = 698 mg Cu /kg d.w. (*Lycopersicon esculentum)*

	Terrestrial Invertebrates: Lowest NOEC used in the SSD = 8.4 mg Cu /kg d.w. (cocoon production of *Eisenia andrei*) Highest NOEC used in the SSD = 1460 mg Cu /kg d.w. (reproduction of *Falsomia candida)* **Soil micro-organisms:** Lowest NOEC used in the SSD = 30 mg Cu /kg d.w. (glucose respiration) Highest NOEC used in the SSD = 2402 mg Cu /kg d.w. (maize respiration*)*

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	No data
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	No data
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	No data
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	No data

Effects on honeybees (Annex IIIA, Point XIII.3.1)

Acute oral toxicity	No data
Acute contact toxicity	No data

Effects on other beneficial arthropods (Annex IIIA, Point XIII.3.1)

Laboratory studies	No data
Semi-field studies	No data
Field studies	No data

Bioconcentration (Annex IIA, Point 7.5)

Bioconcentration factor (BCF)	For the naturally occurring substances such as essential metals as copper, bioaccumulation is complex, and many processes are available to modulate both accumulation and potential toxic impact. Biota regulates their internal concentrations of essential metals through homeostatic control mechanisms (i.e. active regulation, storage). As a result of these processes, at low metal concentrations, organisms accumulate essential metals more actively in order to meet their metabolic requirements than when they are being exposed at higher metal concentrations. As a consequence of homeostatic processes, and unlike many organic substances, the BCF/BAF is not independent of exposure concentrations for metals and it is inversely related to exposure concentrations. Thus, the use of ratios Cbiota/Cwater or Cbiota/Csediments as an overall approach for estimating copper

	bioconcentration factors is thus not appropriate.
Depuration time(DT_{50}) **(DT_{90})**	Not applicable for metals
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable for metals

Appendix II: List of Intended Uses

Summary of intended uses[8]

Object and/or situation	**Member State or Country**	**Product name**	**Organisms controlled**	**Formulation**		**Application**			**Applied amount per treatment**			**Remarks**
(a)			(c)	Type (d-f)	Conc. of a.s. (i)	Method Kind (f-h)	Number min–max (k)	Interval between applications (min)	g a.s./l min–max	Water l/m^2 min–max	g $a.s./m^2$ min max	(m)
Fungi and insects Use Class (UC) 1, 2, 3, 4-1 and 4-2	All	ACQ-C2D	Fungi and insects	SL (soluble concentratte)	9.5%	Vacuum/pressure impregnation	one	Not applicable	See remarks	See remarks	See remarks	(1)
Fungi Use Class (UC) 1, 2, 3, 4-1	All	SPU-01840-F	Wood destroying fungi and soft rotting micro-fungi	Soluble concentrate	1% to 5% in aqueous solution 5% to 15% in aqueous solution	Vacuum pressure treatment method Dipping treatment	Single treatment	Not applicable	n.a.	n.a.	n.a.	(2)

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[8] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

Wood destroying insects Use Class (UC) 1, 2, 3, 4-1	All	SPU-01840-F	Wood destroying insects	Soluble concentrate	1% to 5% in aqueous solution 5% to 15% in aqueous solution	Vacuum pressure treatment method Dipping treatment	Single treatment	Not applicable	n.a.	n.a.	n.a.

(1) Typical concentration of product in working solution:
3.33% for use class 3 with Cu loadings of 1.9 kg/m3.
6% for use class 4 with Cu loadings of 3.42 kg/m3.
Concentration of copper as a % in the ready to use treating solution:
3.17 g Cu/l for use class 3;
5.7 g Cu/l for use class 4.

The concentrate product may contain above 9.5%w/w copper, as long as the product is suitably diluted to give the stated copper concentrations in the treatment solution

(2) A target concentration of 0.5 kg Cu/m^3 has been claimed referred to the rate that is necessary if copper is used in combination with co-biocides such as quaternary ammonium compounds contained in SPU-01840-F for example, but according to tests produced in the dossier, a target concentration of 1 kg Cu/m^3 would be needed as a substance alone (ENV807) if a product is used containing just copper and no co-biocides..

(a) *e.g.* biting and suckling insects, fungi, molds;

(b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(c) GCPF Codes – GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4);

(d) All abbreviations used must be explained

(e) g/kg or g/l;

(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;

(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;

(h) Indicate the minimum and maximum number of application possible under practical conditions of use;

(i) Remarks may include: Extent of use/economic importance/restrictions

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked “Yes” in the “Data Protection Claimed” column of the table below. Data protection is claimed under Article 12.1(c) (i) or (ii).These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 3.1.1	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF
A 3.1.3	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF
A 3.11	O'Connor, B.J. and Mullee, D.M.	2004	Copper (II) Carbonate - Copper (II) Hydroxide (1:1): Determination of General Physico-Chemical Properties. Safepharm Laboratories. Project No. 1645/007. GLP, Unpublished	Yes	WPCTF
A 3.11	O'Connor, B.J. and Mullee, D.M.	2004	Copper (II) Carbonate - Copper (II) Hydroxide (1:1): Determination of General Physico-Chemical Properties. Safepharm Laboratories. Project No. 1645/007. GLP, Unpublished	Yes	WPCTF
A 3.16	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF
A 3.17	O'Connor, B.J. and Mullee, D.M.	2001	Copper Carbonate (Dry Light and Wet Dense): Determination of Accelerated Storage Stability and Corrosion Characteristics. SafePharm Laboratories Ltd. Laboratory Project ID: 453/018. GLP, Unpublished.	Yes	WPCTF
A 3.3.1	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 3.3.2	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF
A 3.3.3	McKavanagh, P	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. GLP, Unpublished	Yes	WPCTF
A 3.4.1	O'Connor, B.J. and Mullee, D.M.	2004	Copper (II) Carbonate - Copper (II) Hydroxide (1:1): Determination of General Physico-Chemical Properties. Safepharm Laboratories. Project No. 1645/007. GLP, Unpublished	Yes	WPCTF
A 3.4.2	O'Connor, B.J. and Mullee, D.M.	2004	Copper (II) Carbonate - Copper (II) Hydroxide (1:1): Determination of General Physico-Chemical Properties. Safepharm Laboratories. Project No. 1645/007. GLP, Unpublished	Yes	WPCTF
A 3.5	O'Connor, B.J. and Mullee, D.M.	2004	Copper (II) Carbonate - Copper (II) Hydroxide (1:1): Determination of General Physico-Chemical Properties. Safepharm Laboratories. Project No. 1645/007. GLP, Unpublished	Yes	WPCTF
A 3.9	Pirot, F., Panisset, F., Agache, P. & Humbert, P.	1996	Simultaneous Absorption of Copper and Zinc through Human Skin in vitro. Skin Pharmacol. 9: 43-52. Not GLP, Published.	No	WPCTF
A 4.1	Anonymous	2000	Determination of iron, lead and zinc in copper carbonate. Not GLP, unpublished.	Yes	Adchem (Australia) Pty. Limited
A 4.1	S Kibble, M Reed, K Smith	2005	Analytical Method for the Determination of Iron, Lead and Zinc in Copper Oxide and Basic Copper Carbonate. , unpublished.	Yes	Adchem (Australia) Pty. Limited
A 4.1	CIPAC	-	CIPAC method for total copper 44/TC/M/3.2. Volumetric thiosulphate method. CIPAC E, Page 44. Not GLP, published.	No	Public domain
A 4.1	CIPAC	-	CIPAC method for total copper 44/TC/M/3.1. Electrolytic method (Referee method). CIPAC E, Page 42. Not GLP, published.	No	Public domain
A 4.1	O’Connor, B.J. and Mullee, D.M.	2001	Copper Carbonate (Wet Dense): Preliminary Analysis. Safepharm Laboratories Limited, Project ID: 453/021. GLP, Unpublished.	Yes	William Blythe Limited

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 4.2	AOAC	1993	AOAC Official Method 990.08,. Metals in Solid Wastes; Inductively Coupled Plasma Atomic Emission Method. AOAC Official Methods of Analysis; Metals and Other Elements, Chapter 9, page 31. Not GLP, published.	No	Public domain
A 4.2	EPA	1983	Methods for Chemical Analysis of Water and Wastes. Method 220.2 (Copper. Atomic Absorption, furnace technique). Washington, DC; U.S. Environmental Protection Agency. Not GLP, published.	No	Public domain
A 4.2	EPA	1983	Inductively Coupled Plasma – Atomic Emission Spectrometric Method for Trace Element Analysis of Water and Wastes – Method 200.7. Washington, DC; U.S. Environmental Protection Agency. Not GLP, published.	No	Public domain
A 4.2	EPA	1986	Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (SW-846). Method 7210 (Copper. Atomic Absorption, direct aspiration). Washington, DC; U.S. Environmental Protection Agency. Not GLP, published. And appended: EPA, 1986. Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (SW-846). Method 3050B (Acid digestion of sediments, sludges and soils). Washington, DC; U.S. Environmental Protection Agency. (published).	No	Public domain
A 4.2	EPA	1986	Methods for Chemical Analysis of Water and Wastes. Method 220.1 (Copper. Atomic Absorption, direct aspiration). Washington, DC; U.S. Environmental Protection Agency. Not GLP, published.	No	Public domain
A 4.2	NIOSH	1987	Method 8005. NIOSH Manual of Analytical Methods, Fourth Edition, 8/15/94. Not GLP, published.	No	Public domain
A 4.2	NIOSH	1987	Method 8310. NIOSH Manual of Analytical Methods, Fourth Edition, 8/15/94. Not GLP, published.	No	Public domain
A 4.2	NIOSH	N/A	Method 7029. NIOSH Manual of Analytical Methods, Fourth Edition, 8/15/94. No GLP, published.	No	Public domain
A 5	Cockcroft, R.	1981	Wood Destroying Basidomyctest Vol. 1. IRG 81/1121	No	Public domain
A 5	Connell M, Cornfield J A and Williams G R	1993	A New Timber Preservative. Rec of the Annual Convention of the British Wood Preserving and Damp-proofing Association pp 28-36	No	Public domain
A 5	Eaton, R.A. & Hale, M.D.C.	1993	Wood: Decay Pests and Protection'. Chapman and Hall	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 5	Fox R F , Pasek E A , Patel J	2000	Laboratory Termite testing of Copper/Boron / Tebuconazole . International Research Group on Wood Preservation. Document No. IRG/WP 00-20192	No	Public domain
A 5	Greaves H	1977	Potential toxicants for controlling soft rot in hardwoods 1. Laboratory screening tests using a filter paper technique Material und Organismen 12 Bd 1997 Heft	No	Public domain
A 5	Pohleven, F., Miha, H., Sam, A & Jaka, B.	2002	Tolerance of wood decay fungi to commercial copper based wood preservatives. IRG Document No. 02-30291.	No	Public domain
A 5	Preston A, Walcheski P, Archer K, Zahora A and Jin L	2000	The Ground Proximity Decay Test Method, International Research Group on Wood Preservation Doc No. 00-20205	No	Public domain
A 5	Price E.A.S and Watson, R.W.	1962	Review of water-borne preservatives Rec. of 12th Annual Convention of the British Wood Preserving and Damp-proofing Association, London	No	Public domain
A 5	Thornton J D	1977	Potential toxicants for controlling soft rot in hardwoods II Laboratory tests using sawdust Material und Organismen 12 Bd 1997 Heft 3	No	Public domain
A 6.1.1	Glaza, S.M.	2001	Acute Oral Toxicity Study of Copper Carbonate Dry Light in Rats. Covance Laboratories, Inc. Report No. 7180-100. GLP, Unpublished	Yes	WPCTF
A 6.1.1	Lheritier, M.	1994	Test to Evaluate the Acute Toxicity Following a Single Oral Administration (LD50) in the Rat. Pharmakon Europe. Report No. 44193. GLP, Unpublished	Yes	WPCTF
A 6.1.1	Lindena, J	1990	Acute Oral Toxicity Test of 'Kupferkarbonat Griin Gefallt 54/56% Cu' in Rats. International Bio Research. Report No. 10-04-0714-90. GLP, Unpublished	Yes	
A 6.1.1	Sanders, A	2002	Acute Oral Toxicity Study in the Rat - Acute Toxic Class Method. Safepharm Laboratories. Project No. 1645/001. GLP, Unpublished	Yes	WPCTF
A 6.1.2	Driscoll, R	2001	Copper Carbonate: Acute Dermal Toxicity (Limit Test) in the Rat. SafePharm Laboratories. Project No. 453/008R. GLP, Unpublished.	Yes	WPCTF
A 6.1.4	Driscoll, R	2001	Copper Carbonate: Acute Dermal Irritation in the Rabbit. SafePharm Laboratories. Report No. 453/009R. GLP, Unpublished	Yes	WPCTF
A 6.1.4	Driscoll, R.	2001	Copper Carbonate: Acute Eye Irritation in the Rabbit. SafePharm Laboratories. Report No. 453/010R. GLP, Unpublished	Yes	WPCTF

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.1.5	Driscoll, R.	2001	Copper Carbonate: Skin Sensitisation in the Guinea Pig - Magnusson and Kligman Maximisation Method. SafePharm Laboratories. Report No. 453/011R. GLP, Unpublished	Yes	WPCTF
A 6.12.2	Chuttani HK, Gupta PS, Gulati S, Gupta DN.	1965	Acute Copper Sulfate Poisoning. Am J Med, 39: 849-854; Not GLP; published	No	Public domain
A 6.12.2	O'Donohue JW, Reid MA, Varghese A, Portmann B, Williams R	1993	Micronodular cirrhosis and acute liver failure due to chronic copper self-intoxication. Eur. J. Gastroenterol. 5:561-562; Not GLP; published	No	Public domain
A 6.12.2	O'Connor, J.M., Bonham, M.P., Turley, E., McKeown, A., McKelvey-Martin, V.J., Gilmore, W.S. and Strain, J.J.	2003	Copper supplementation has no effect on markers of DNA damage and liver function in healthy adults (FOODCUE Project). Ann Nutr Metab, 47: 201-206. Not GLP, Published	No	Public domain
A 6.12.2	Pimentel JC, Marques F	1969	Vineyard sprayer's lung - A new occupational disease. Thorax, 24, 678-688; Not GLP; published	No	Public domain
A 6.12.2	Pimentel JC, Menezes AP.	1977	Liver disease in vineyard sprayers. Gastroenterology 72:275-283; Not GLP; published	No	Public domain
A 6.12.2	Pimentel JC, Menezes AP.	1975	Liver granulomas containing copper in vineyard sprayer's lung - A new Etiology of Hepatic Granulomatosis. Am. Rev. Respir. Dis. 111:189-195; Not GLP; published	No	Public domain
A 6.12.2	Pratt, W.B., Omdahl, J.L. and Sorenson, R.J.,	1985	Lack of Effects of Copper Gluconate Supplementation. The American Journal of Clinical Nutrition, 42: 681 – 682. Not GLP, Published	No	Public domain
A 6.12.2	Rock, E., Mazur, A., O'Connor, J.M., Bonham, M.P., Rayssiguier, Y. & Strain, J.J	2000	The Effect of Copper Supplementation on Red Blood Cell Oxidizability and Plasma Antioxidants in Middle-Aged Healthy Volunteers. Free Radical Biology and Medicine. 28 (3); 324-329. Not GLP, Published	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.12.2	Tanner MS, Portmann B, Mowat AP, Williams R, Pandit AN, Mills CF, Bremner I.	1979	Increased hepatic copper concentration in Indian Childhood Cirrhosis. Lancet 1:1203-5; Not GLP; published	No	Public domain
A 6.12.2	Turley, E., McKeown, A., Bonham, M.P., O'Connor, J.M, Chopra, M., Harvey, L.J., Majsak-Newman, G., Fairweather-Tait, S.J., Bugel, S., Sandstrom, B. Rock, E., Mazur, A., Tayssiguier, Y. & Strain, J.J.	2000	Copper supplementation in Humans Does Not Affect the Susceptibility of Low Density Lipoprotein to In Vitro Induced Oxidation (Foodcue Project). Free Radical Biology & Medicine, 29: (11); 1129-1134. Not GLP, Published	No	Public domain
A 6.12.4	Plamenac P, Santic Z, Nikulin A, Serdarevic H.	1985	Cytologic changes of the respiratory tract in vineyard spraying workers. Eur J Respir Dis, 67: 50-55; Not GLP; published	No	Public domain
A 6.12.4	Scheinberg IH, Sternlieb I.	1994	Is non-Indian childhood cirrhosis caused by excess dietary copper? Lancet, 344: 1002-1004; Not GLP; published	No	Public domain
A 6.12.4	Tanner MS, Kantarjian AH, Bhave SA, Pandit AN.	1983	Early introduction of copper-contaminated animal milk feeds as a possible cause of Indian Childhood Cirrhosis. Lancet 2: 992-995; Not GLP; published	No	Public domain
A 6.12.5	International Programme on Chemical Safety	1990	Poisons Information Monograph (PIM G002): Copper and copper salts; Not GLP; Published	No	Public domain
A 6.12.7	International Programme on Chemical Safety	1990	Poisons Information Monograph (PIM G002): Copper and copper salts; Not GLP; Published	No	Public domain
A 6.12.8	International Programme on Chemical Safety	1990	Poisons Information Monograph (PIM G002): Copper and copper salts; Not GLP; Published	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.2	Allen, M.M., Barber, R.S., Braude, R. and Mitchell, K.G.	1961	Further studies on various aspects of the use of high-copper supplements for growing pigs. Brit. J. Nutr., **15:** 507 – 522, Not GLP Published	No	Public domain
A 6.2	Amaravadi, R., Glerum, D.M. and Tzagoloff, A.	1997	Isolation of a cDNA encoding the human homolog of COX17, a yeast gene essential for mitochondrial copper recruitment. Hum Genet. 99: 329-333. Not GLP, Published.	No	Public domain
A 6.2	Aoyagi, S. and Baker, D.H.	1993	Bioavailability of Copper in Analytical-Grade and Feed Grade Inorganic Copper Sources when Fed to Provide Copper at Levels Below the Chick’s Requirement. Poultry Science. 72: 1075-1083. Not GLP, Published	No	Public domain
A 6.2	Baker, D.H., Odle, J., Funk, M.A. and Wieland, T.M.	1991	Research Note: Bioavailability of Copper in Cupric Oxide, Cuprous Oxide, and in a Copper-Lysine Complex. Poultry Science. 70: 177-179. Not GLP, Published	No	Public domain
A 6.2	Buescher, R.G., Griffin, S.A. and Bell, M.C.	1961	Copper Availability to Swine from Cu64 Labelled Inorganic Compounds. Journal of Animal Science, 20: 529-531. Not GLP, Published	No	Public domain
A 6.2	Bunch, R.J., Speer, V.C., Hays, V.W. and McCall, J.T.	1963	Effects of High Levels of Copper and Chlortetracycline on Performance of Pigs. J. Animal Sci. 22: 56-60. Not GLP, Published	No	Public domain
A 6.2	Bunch, R.J., Speer, V.C., Hays, V.W., Hawbaker, J.H. and Catron, D.V.	1961	Effects of copper Sulfate, Copper oxide and Chlortetracycline on Baby Pig Performance. J. Animal Sci. 20: 723-726. Not GLP, Published	No	Public domain
A 6.2	Campbell, C.H., Brown, R. and Linder, M.C.	1981	Circulating Ceruloplasmin is an Important Source of Copper for Normal and Malignant Animal Cells. Biochim. Biophys. Acta. 678: 27-38. Not GLP, Published.	No	Public domain
A 6.2	Cromwell, G.L., Stahly, T.S. and Monegue, H.J.	1989	Effects of Source and Level of Copper on Performance and Liver Copper Stores in Weanling Pigs. J. Animal Sci. 67: 2996-3002. Not GLP, Published	No	Public domain
A 6.2	Culotta, V.C., Klomp, J.S., Casareno, R.L.B., Krems, B. And Gitlin, J.D	1997	The Copper Chaperone for Superoxide Dismutase. The Journal of Biological chemistry. 272 (38): 23469 – 23472. Not GLP, Published	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.2	Darwish, H.M., Cheney, J.C., Schmitt, R.C. and Ettinger, M.J.	1984	Mobilisation of copper (II) from plasma components and mechanism of hepatic copper transport. Am. J. Physiol., 246 (9):G72-G79. Not GLP, Published.	No	Public domain
A 6.2	Gunshin, H., Mackenzie, B, Berger, U.V., Gunshin, Y., Romero, M.F., Boron, W.F., Nussberger, S., Gollan, J.L. & Hediger, M.A.	1997	Cloning and Characterisation of a Mammalian Proton-Coupled Metal-Ion transporter. Nature. 388:482-488. Not GLP, Published.	No	Public domain
A 6.2	Kegley, E.B. and Spears, J.W.	1994	Bioavailability of feed-grade copper sources (oxide, sulfate, or lysine) in growing cattle. J. Animal Sci. 72: 2728-2734. Not GLP, Published	No	Public domain
A 6.2	Klomp, L.W.J., Lin, S.J., Yuan, D.S., Klausner, R.D., Culotta, V.C. and Gitlin, J.D.	1997	Identification and Functional Expression of HAH1, a Novel Human Gene Involved in Copper Homeostasis. The Journal of Biological Chemistry 272(14): 9221-9226. Not GLP, Published.	No	Public domain
A 6.2	Lee S.H., Lancey R., Montaser A., Madani N., Linder M.C.	1993	Ceruloplasmin and copper transport during the latter part of gestation in the rat. Proc Soc Exp Biol Med 203: 428-39. Not GLP, Published.	No	Public domain
A 6.2	Linder M.C., Weiss K.C. and Hai, V.M.	1987	Structure and function of transcuprein in transport of copper by mammalian blood plasma. In: Hurley L.C., Keen C.L., Lonnerdal, B. and Rucker, R.B. (eds). Trace Elements in Man and Animals (TEMA-6). New York: Plenum, 141–144. Not GLP, Published.	No	Public domain
A 6.2	McArdle, H.J., Gross S.M., Danks D.M. & Wedd, A.G.	1990	Role of Albumin's Copper Binding Site in Copper Uptake by Mouse Hepatocytes. Am. J. Physiol. 258 (Gastrointest. Liver Physiol. 21): 988-991. Not GLP, Published.	No	Public domain
A 6.2	McArdle, H.J., Gross, S.M. and Danks, D.M.	1988	Uptake of Copper by Mouse Hepatocytes. Journal of Cellular Physiology, 136: 373-378. Not GLP, Published.	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.2	Norvell, M.J., Gable, D.A. and Thomas, M.C.,	1975	Effects of feeding high levels of various copper salts to broiler chickens. In Trace Substances in Environmentsl Health – 9, (Hemphill, D.D., Ed). University of Missouri, Columbia, MO. Not GLP, Published	No	Public domain
A 6.2	Pirot, F., Millet, J., Kalia, Y.N. & Humbert, P	1996	In vitro Study of Percutaneous Absorption, Cutaneous Bioavailability and Bioequivalence of Zinc and Copper from Five Topical Formulations. Skin Pharmacol. 9: 259-269. Not GLP, Published.	No	Public domain
A 6.2	Pirot, F., Panisset, F., Agache, P. & Humbert, P.	1996	Simultaneous Absorption of Copper and Zinc through Human Skin in vitro. Skin Pharmacol. 9: 43-52. Not GLP, Published.	No	Public domain
A 6.2	Rojas, L.X., McDowell, L.R., Cousins, R.J., Martin, F.G., Wilkinson, N.S., Johnson, A.B. and Velasquez, J.B.	1996	Interaction of different organic and inorganic zinc and copper sources fed to rats. J. Trace Elements Med. Biol. 10: 139-144. Not GLP, Published	No	Public domain
A 6.2	Scott, K.C. & Turnlund, J.R.,	1994	Compartment Model of Copper Metabolism in Adult Men. J. Nutr. Biochem. 5: 342-350. Not GLP, Published.	No	Public domain
A 6.2	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.Not GlP, Published.	No	Public domain
A 6.2	Turnlund, J.R., Ketes, W.R., Peiffer, G.L. and Scott, K.C	1998	Copper absorption, excretion and retention by young men consuming low dietary copper determined using the stable isotope 65Cu. Am. J. Clin. Nutr., 67: 1219 – 1225. Not GLP, Published	No	Public domain
A 6.2	Turnlund, J.R., Keyes, W.R., Anderson, H.L. and Acord, L.L.	1989	Copper absorption and retention in young men at three levels of dietary copper by use of the stable isotope 65Cu. Am. J. Clin. Nutr. 49:870-878.Not GLP, Published.	No	Public domain
A 6.2	Turnlund, J.R., Wada, L., King, J.C., Keyes, W.R. and Lorra, L.A	1988	Copper Absorption in Young Men Fed Adequate and Low Zinc Diets. Biological and Trace Element Research, 17: 31 – 41. Not GLP, Published	No	Public domain

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A 6.2	van Berge Henegouwen, G.P., Tangedahl, T.N., Hofmann, A.F., Northfield, T.C. La Russo, N.F. and McCall, J.T.,	1977	Biliary Secretion of Copper in Healthy Man. Quantitation by an intestinal perfusion technique. Gastroenterology, 72:1228-1231. Not Published.	No	Public domain
A 6.2	Van den Berg, G.J., Van Wouwe, J.P and Beynen, A.C.,	1990	Ascorbic Acid Supplementation and Copper Status in Rats. Biological Trace Element Research, 23: 165-172. Not GLP, Published	No	Public domain
A 6.2	Walker, R.W.	1982	The Result of a Copper Bracelet Clinical Trial and Subsequent Studies. P 469 – 478. In: J. R. J. Sorenson (ed) Inflammatory Diseases and Copper: The Metabolic and Therapeutic Roles of Copper and Other Essential Metalloelements in Humans; Humana Press; Clifton N.J., USA. Not GLP, Published.	No	Public domain
A 6.2	Weiss K.C. & Linder M.C.	1985	Copper transport in rats involving a new plasma protein. Am. J. Physiol. 249: E77-88. Not GLP, Published.	No	Public domain
A 6.2	Whitaker, P. & McArdle, H.J.	1997	Iron Inhibits Copper Uptake by Rat Hepatocytes by Down-Regulating the Plasma Membrane NADH Oxidase. In. Fisher, P.W., L'Abbe, M.R., Cockell, K.A. et al. (Eds). Trace Elements in Man and Animals. (TEMA9). NRC Research Press, Ottowa, pp 237-239	No	Public domain
A 6.2	Wirth, W.L. and Linder, M.M.	1985	Distribution of Copper Among Components of Human Serum. JNCI. 75: 277-284. Not GLP, Published.	No	Public domain
A 6.2	Xin, Z., Waterman, D.F., Hemken, R.W., Harmon, R.J. and Jackson, J.A	1991	Effects of copper sources and dietary cation-anion balance on copper availability and acid-base status in dietary calves. J. Dairy Sci. 74: 3167-3173. Not GLP, Published	No	Public domain
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A 7.5.1.2/ 7.5.6/ 7.5.2.1	Spurgeon, D.J. & Hopkin, S.P.*	1995	Extrapolation of the Laboratory-Based OECD Earthworm Toxicity Test to Metal-Contaminated Field Sites. Ecotoxicity. 4; 190-205	No	Public domain
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B 4.1	Warncke, U.	2004	Validated method of analysis for the determination of N,N- Didecyl-N-methyl-poly(oxyetyl)ammoniumpropionate (DMPAP) and copper in SPU-01840-F-0-SL Laboratory: Spiess-Urania Chemicals GmbH - Versuchsstation Christinenthal Doc. No.: Wa-26-01-04-1840 Date: 26.01.2004; not published	Yes	SPU

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B 5.10.2 /01	Kirk, H.	1996	Determination of the protective effectiveness against wood destroying basidiomycetes according to EN 113 (04/90) - after leaching procedure according to EN 84 (04/90) - VP 3148 Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 32/691/1 Date: 20.01.1996; not published	Yes	OBM
B 5.10.2 /02	Unger, W.	1997	Determination of the toxic values against larvae of Hylotrupes bajulus (L) according to EN 47 (04/90) after leaching procedure according to EN 84 (04/90) - Korasit KS Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 32/7107 Date: 30.07.1997; not published	Yes	OBM
B 5.10.2 /03	Kirk, H.	1995	Determination of the protective effectiveness against soft rotting microfungi and other soil-inhabiting micro-organisms according to ENV 807 (05/94) - after leaching procedure according to EN 84 (04/90) - using vermiculite method - VP 3148 Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 32/691/2 Date: 15.12.1995; not published	Yes	OBM
B 6.1.1	Kuszewski, B.	1996	Acute Oral Toxicity Test of "Korasit KS" in Rats Laboratory: medcon Kontraktlabor GmbH Doc. No.: 10-04-0136/00-96 Date: 19.08.1996 GLP: yes; not published	Yes	OBM
B 6.1.2	Kuszewski, B.	1996	Acute Dermal Toxicity Test of "Korasit KS" in Rats Laboratory: medcon Kontraktlabor GmbH Doc. No.: 10-04-0135/00-96 Date: 19.08.1996 GLP: yes; not published	Yes	OBM
B 6.2 /01	Leuschner, J.	2003	Acute Skin Irritation Test (Patch Test) of SPU-01840-F-0-SL in Rabbits Laboratory: LPT Laboratory of Pharmacology and Toxicology KG Doc. No.: 16754/03 Date: 13.10.2003 GLP: yes; not published	Yes	SPU

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B 6.2 /02	Leuschner, J.	2003	Acute Eye Irritation Study of SPU-01840-F-0-SL by Instillation into the Conjunctival Sac of Rabbits Laboratory: LPT Laboratory of Pharmacology and Toxicology KG Doc. No.: 16755/03 Date: 13.10.2003 GLP: yes; not published	Yes	SPU
B 6.3	Chevalier, F.	2003	Examination of SPU-01840-F-0-SL in the Skin Sensitisation Test in Guinea Pigs According to Magnusson and Kligman (Maximisation Test) Laboratory: LPT Laboratory of Pharmacology and Toxicology KG Doc. No.: 16756/03 Date: 24.10.2003 GLP: yes; not published	Yes	SPU
B 7.1 /01	Schumacher, P., Wegner, R.	2005	OECD guideline I: “Estimation of emission from preservative-treated wood to the environment: laboratory method for wood held in storage after treatment and for wood commodities that are not covered, and are not in contact with ground” (proposal, version 17.02.2003) Laboratory: Materialprüfungsamt des Landes Brandenburg, Eberswalde, Germany Report no. 31/05/7668/01. Date: September 4, 2006; not published	Yes	SPU
B 7.1 /02	Schumacher, P., Wegner, R.	2006	OECD guideline II: “Estimation of emission from preservative-treated wood to the environment: Laboratory method for wooden commodities that are not covered and are in contact with ground, fresh water or seawater (proposal, version 17.02.2003). Laboratory: Materialprüfungsamt des Landes Brandenburg, Eberswalde, Germany Report no. 31/05/7668/02. Date: September 4, 2006; not published	Yes	SPU
B 7.7.1.1.1	Scheerbaum, D.	2004	Fish (Rainbow trout), Acute Toxicity Test, Static, 96 h (Draft report) Laboratory: Dr.U.Noack-Laboratorien Doc. No.: FAR93142 Date: 00.03.2004 GLP: yes; not published	Yes	SPU

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B 7.7.1.1.2	Noack, M.	2004	Acute Immobilisation Test (static, 48 h) to Daphnia magna STRAUS, SPU-01840-F-0-SL (Draft report) Laboratory: Dr.U.Noack-Laboratorien Doc. No.: DAI93142 Date: 00.03.2004 GLP: yes; not published	Yes	SPU
B 7.7.1.1.3	Scheerbaum, D.	2004	Alga, Growth Inhibition Test with Desmodesmus subspicatus, 72 h (formerly Scenedesmus subspicatus) - SPU-01840-F-0-SL (Draft report) Laboratory: Dr.U.Noack-Laboratorien Doc. No.: SSO93141 Date: 00.03.2004 GLP: yes; not published	Yes	SPU
B.6.1.3	Blagden S.M.	1994	Acute Inhalation Toxicity Study Four-Hour Exposure (Nose Only) in the Rat. Safepharm Laboratories Limited. Project Number 577/19. (Unpublished).	Yes	WPCTF
B.6.2	Allen D.J.	1994	Allen, D.J. (1994). Acute Dermal Irritation Test in the Rabbit. Safepharm Laboratories Limited. Project Number 577/20. (Unpublished).	Yes	WPCTF
B.6.3	Allen D.J.	1994	Buehler Delayed Contact Hypersensitivity Study in the Guinea Pig. Safepharm Laboratories Limited. Project Number 577/22. (Unpublished).	Yes	WPCTF
B6.1.1	Allen D.J.	1994	Acute Oral Toxicity Test in the Rat. Safepharm Laboratories Limited, Project Number 577/17. (Unpublished)	Yes	WPCTF
B6.1.2	Allen D.J.	1994	Acute Dermal Toxicity (Limit Test) in the Rat. Safepharm Laboratories Limited. Project Number 577/18. (Unpublished)	Yes	WPCTF
B7.1/01	van der Zee, M.E.	2001	Submersion tests (NEN 7345) of Tanalith 3494 treated timber. Foundation for Timber Research SHR. Report number 98.214; not GLP; Not published.	Yes	Arch Timber Protection
B7.1/02	Caswell S	2000	Determination of the Emission Profile from Tanalith E Treated Timber. Laboratory Metho to Simulate Exposure from Tanalith E (3491) Treated Timber in an Above Ground (Hazard Class 3) Environment. Hickson Timber Products Limited, Technical Centre. Report No. W20/001a; not GLP; Not published.	Yes	Arch Timber Protection
B7.1/03	Hohman W.J.	1993	Assessing the losses of copper and boron from Tanalith 3485 treated timber with the shower test. Foundation for Timber Research SHR. Report number 92.040 ; not GLP; Not published.	Yes	Arch Timber Protection

Reference No.	Author(s)	Year	Title.Source (where different from company), Company, Report No.GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B7.1/04	Lindegaard, B.	2003	Test Methods to Evaluate the leaching of Wood Preservatives from Preservative Treated Wood. Phase II Laboratory Tests. Status Report after 1st Test Round. Danish Technological Institute, Timber. Report No. 1175742-02 ; not GLP; not published.	Yes	Arch Timber Protection
B7.1/05	Caswell S	2000	Determination of the emission profile from TANALITH® E treated timber: Laboratory Method to Simulate Exposure of TANALITH® E (3491) Treated Timber in a Water Contact (Hazard Class 4) Environment. Hickson Timber Products Limited – Technical Centre (Unpublished)	Yes	ECI
	Ralph A. & McArdle H.	2001	Copper metabolism and copper requirements in the pregnant mother, her fetus and children.	No	Public domain