Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

Copper(II) oxide

EC number: 215-269-1
CAS number: 1317-38-0

CLH-O-0000001412-86-45/F

Adopted

04 December 2014

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.
All attachments including confidential documents received during the public consultation have been provided in full to the dossier submitter, to RAC members and to the Commission (after adoption of the RAC opinion). Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website.

Substance name: Copper (II) oxide
CAS number: 1317-38-0
EC number: 215-269-1
Dossier submitter: France

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	Germany		MemberState	1
Comment received				
The DE CA does not support the proposal for classification as Acute Tox 2 – H330. In addition the DE CA has general problems with some methodologies referring to the environmental classification used in the CLH-proposal. In table 9, Part B, chapter 1.3. "Physicochemical properties", the relative density is given as 1.018g/cm3. Literature states a much higher value of 6.315 g/cm3 ("Hazardous Substances Data Bank" data from the National Library of Medicine (US)) or ~6.4 g/cm3 (J. Non-Cryst. Solids 1997, 215, 271-282).				
Dossier Submitter's Response				
Human health hazard: Based on the information provided during consultation by member states and other organisation, agree to delete the proposal classification of Acute tox 2 –H330. Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation. There is also no evidence that it is implicated in metal fume fever in industry. **Environmental hazard:** see response to detailed comment below.				
RAC's response				
Human health hazard: see RAC's response to comment no. 7. **Environmental hazard:** see response to comment no. 8.				

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom	CLEAPSS	BehalfOfAnOrganisation	2
Comment received				
1 The data provided (via read-across to copper(II) hydroxide) does not seem to place CuO well within the criteria for classification as Acute Toxicity 2 by inhalation. 2 No other data supports its toxicity via inhalation in humans. The detailed report in				

‘Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate’ (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation.
3 There is also no evidence that it is implicated in metal fume fever in industry - all studies were critiqued in the 2006 report mentioned above, because other factors were involved in the studies.
4 This classification would be a major step up from the current self-classifications, which appear to be as ‘only’ R20/H332 Harmful by inhalation.
5 The data presented in the proposal for this classification is not new (the relevant studies are dated 1992 and 2003).
6 Copper(II) oxide is not soluble, as is incorrectly stated in the proposal (section 2.2). Therefore any conclusion based on this assumption is questionable.

Dossier Submitter’s Response

Human health hazard:
Based on the information provided during consultation by member states and other organisations, agree to delete the proposal classification of Acute tox 2 –H330.
Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in ‘Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate’ (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation.
There is also no evidence that it is implicated in metal fume fever in industry.

RAC’s response

See RAC’s response to comment no. 7, for points 1 to 5.

6. CuO is considered as readily soluble metal compound from the point of view of classification (CLP), according to the following definition: a metal compound is considered as readily soluble if its water solubility is greater or equal to the acute ERV of the dissolved metal ion concentration. The water solubility of copper(II) oxide is equal to 0.394 mg/L and 0.01 mg/L at pH 6 and 9 respectively, the acute ERV is 0.01 mg/L. Therefore, this compound is considered as ready soluble metal compound for classification purposes.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom	Regulatory Compliance Limited	BehalfOfAnOrganisation	3

Comment received

We acknowledge and appreciate the alignment with the copper risk assessment dossier as well as the incorporation of some post risk assessment data.

For most endpoints, the data used and interpretation of the data reflect the hazard profiles agreed in the copper risk assessment report (RAR) and used for the CuO REACH dossier.

For some endpoints, we noted some differences in data-interpretation between the copper oxide CLH report and REACH dossier. We have therefore focussed the review on these endpoints and propose to revise the classification to:

No classification warranted for acute inhalation
Environmental hazard Acute category 1. M factor = 1.
Environmental hazard Chronic category 2.

See non-confidential attachment.

Dossier Submitter's Response
Human health hazard: Based on the information provided during consultation by member states and other organisations, agree to delete the proposal classification of Acute tox 2 –H330. Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation. There is also no evidence that it is implicated in metal fume fever in industry. **Environmental hazard:** see response to detailed comment no 12 below.
RAC's response
Human health hazard: see RAC's response to comment no. 7. **Environmental hazard:** see response to detailed comment no. 12 below.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	Germany		MemberState	4
Comment received				
No acute inhalation study is available for classification. Additional justification is needed for the proposal H330.				
Dossier Submitter's Response				
Human health hazard: Based on the information provided during consultation by member states and other organisations, agree to delete the proposal classification of Acute tox 2 –H330. Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation. There is also no evidence that it is implicated in metal fume fever in industry.				
RAC's response				
See RAC's response to comment no. 7.				

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom		MemberState	5
Comment received				
Read-across to copper hydroxide (Cu(OH)2) is proposed based on the similarity of the solubilities at pH 6 and 9 and of the molecular mass. However, we note that the acute oral toxicity of Cu(OH)2 is higher than that of Cu(II)O. From three acute oral toxicity studies with Cu(OH)2, LD50s between 489 and 1280 mg/kg were obtained, leading to a proposed classification of Acute Tox. 4 – H302. Therefore the acute oral toxicity of Cu(OH)2 is clearly higher than that of Cu(II)O, which has an acute oral LD50 > 2000 mg/kg. This calls into question the validity of reading across the acute inhalation toxicity, and suggests that applying Acute Tox. 2 – H330 to Cu(II)O is over conservative. Overall, the read-across to Cu(OH)2 has not been adequately justified in the CLH report. Strength of evidence of acute inhalation toxicity of copper (II) hydroxide				

We also have doubts about the classification proposed for Cu(OH)2, to which Cu(II)O has been read-across. In a study that used whole-body exposure, the LC50 was 0.5 mg/L for males and 0.61 mg/L for females, giving a combined LC50 of 0.56 mg/L. Considering that oral exposure from coat grooming would have been possible in this study, that Cu(OH)2 meets the criteria for classification for acute oral toxicity category 4 and that the inhalation results are at or above the cut-off values for Acute Tox. 2, we would consider that Acute Tox. 3 – H331 is more appropriate based on this data. A nose-only exposure gave a result of 0.205<LC50<1.08 mg/L. It would be helpful if a more precise LC50 value could be provided. Nevertheless, only 1/10 animals died at 0.205 mg/L, whereas 8/10 died at 1.08 mg/L. It therefore seems likely that the LC50 is closer to 1.08 mg/L than it is to 0.205 mg/L, which supports a classification for Acute Tox. 3 – H331.

Dossier Submitter's Response

Human health hazard:
Based on the information provided during consultation by member states and other organisation, agree to delete the proposal classification of Acute tox 2 –H330.
Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation.
There is also no evidence that it is implicated in metal fume fever in industry.

For copper hydroxide, see RCOM of this substance.

RAC's response

As to the read-across, see RAC's response to comment no. 7.
As to copper dihydroxide, see RCOM of that substance.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom	CLEAPSS	BehalfOfAnOrganisation	6

Comment received

1 The data provided (via read-across to copper(II) hydroxide) does not seem to place CuO well within the criteria for classification as Acute Tox 2 by inhalation.
3 No other data supports its toxicity via inhalation in humans. The detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation.
3 There is also no evidence that it is implicated in metal fume fever in industry - all studies were critiqued in the 2006 report mentioned above, because other factors were involved in the studies.
4 This classification would be a major step up from the current self-classifications, which appear to be as 'only' R20/H332 Harmful by inhalation.
5 The data presented in the proposal for this classification is not new (the relevant studies are dated 1992 and 2003).

ECHA note: The information below was provided in ECHA consultation on proposed harmonised classifications for some copper compounds.docx [attachment no.1]

ECHA consultation on proposed harmonised classifications for some copper compounds (19/12/13-03/02/14)
CLEAPSS points re proposal for Acute Toxicity (inhalation) 2 for copper(II) oxide

http://www.echa.europa.eu/harmonised-classification-and-labelling-consultation

The proposed harmonised classification: Copper(II) oxide

> H statements: H330 Fatal if inhaled (CLEAPSS highlighting), H410 (environmental hazards)
> Pictograms: GHS06 ('skull & crossbones), GHS09 (environmental hazard)
> Signal word: Danger.

http://www.echa.europa.eu/documents/10162/64402c74-1625-47e8-9cf9-553e12b07f7b

Several reports and other documents are available via the ECHA website.

In 2006, ***Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate*** was published. This details the properties of the forms and compounds of copper, including solubility, airborne particle size and toxicokinetics. The paper makes a case for derogating copper(II) oxide from the requirement for animal testing and also from classification for acute toxicity by inhalation. Under section ***7 Derogation and classification proposals/7.1 Copper(II) oxide***:

> The following conclusions are drawn from the data presented in this document:
> - Copper (II) oxide has a moderate (but not negligible) tendency to become airborne,
> - however, based on particle size considerations (MMAD > 60 µm), more than 95% of the material deposited in the respiratory tract will be translocated to the GI tract shortly after inhalation, so that the acute toxicity will be determined by that of the oral route,
> - Copper (II) oxide is assumed to have a low bioavailability, based on water solubility and on indicative data from animal feeding studies,
> - it has an established low oral toxicity (LD50 > 2000 mg/kg bw).
>
> It can therefore be concluded that the inhalation hazard of Copper (II) oxide is very low. It is therefore proposed to derogate from animal testing. In consideration of the arguments set forth above, a classification for acute inhalation toxicity is not required. (CLEAPSS highlighting)

In 2007, ***European Union Risk Assessment Report: COPPER, COPPER II SULPHATE PENTAHYDRATE, COPPER(I)OXIDE, COPPER(II)OXIDE, DICOPPER CHLORIDE TRIHYDROXIDE: CAS No: 7440-50-8, 7758-99-8, 1317-39-1, 1317–38–0, 1332-65-6; EINECS No: 231–159–6, 231–847–6, 215-270-7, 215–269–1, 215-572-9: VOLUNTARY RISK ASSESSMENT* (distribution date 1 June 2007),** collated data and information from a wide range of sources is presented. Much of the data and conclusions quoted in the harmonised proposal are detailed in this document. However, for Acute toxicity (inhalation) for copper(II) oxide/copper(II) hydroxide, none of the rat studies quoted in the proposals for harmonised classification (see overpage) are mentioned. Under ***Absorption in animals/inhalation*** (page 7), one animal study is described and it states:

> This study demonstrates the potential for systemic absorption of copper following inhalation of dust containing an unspecified amount of copper, but provides no reliable quantitative data which are relevant to human risk assessment.

In the absence of human data, MPPD modelling was carried out. The conclusions are that exposure of workers in a range of industrial contexts are not of concern so long as suitable respiratory protection is employed. On page 45:

> … Consideration of the available information against EU classification criteria leads to the conclusion that copper (II) oxide and copper powder do not require classification for acute inhalation effects. (CLEAPSS highlighting)

Comments were published by the European Copper Institute in 2008: ***Opinion of the TC NES on the Human Health Part of Industry Voluntary Risk Assessments on Copper and Copper compounds*** **(08/02/2008)**

In this document:

> UK expressed concerns linked to evidence of irritation as a local effect for some copper compounds since all the human data is based on oral exposure and there are uncertainties about effects following exposure by inhalation.

In the current proposal, other research seems to be presented. ***CLH report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 Substance Name: Copper (II) oxide or cupric oxide or copper oxide*** **(12/07/2013)** http://www.echa.europa.eu/documents/10162/64402c74-1625-47e8-9cf9-553e12b07f7b

explains how the assessment of the acute toxicity (inhalation) risk was derived for this proposal. A comparison with copper(II) hydroxide is made in the section on inhalation studies, and a decision to employ read-across to studies on that compound is recorded:

> ***Inhalation studies*****:**
> No data are available on acute inhalation toxicity of copper (II) oxide in animals. But several salts of copper are classified for acute inhalation endpoint. In this context, a read across with an other salt was proposed. It was stated in VRA that acute inhalation toxicity of a substance could be determined to a large extent by solubility. Other physico/chemical properties may also be involved. …
> It was observed that Cu(II)O has a solubility very closed of CuOH at different pH. Moreover, CuOH and Cu(II)O have molecular mass roughly similar. And the two salts are made up of copper under the same state of oxidation (Cu2+). In this context, a read across between CuOH and Cu(II)O for acute inhalation endpoint was proposed .
> Copper Hydroxide requires a classification Acute Tox.2-H330 under CLP regulation.
> In this context, a classification Acute Tox.2-H330 under CLP regulation is also proposed for copper (II) oxide.

However, the data upon which the inhalation hazard classification for copper(II) hydroxide of H330 does not appear (to us at CLEAPSS) to be overwhelmingly strong. The proposal document for copper(II) hydroxide**: *CLH report: Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 Substance Name: Copper (II) Hydroxide or Copper Hydroxide or Copper Dihydroxide or Cupric Hydroxide* (12/07/2013)**
http://www.echa.europa.eu/documents/10162/c14572c9-08bb-44ee-b807-c2d480ced8a4

discusses the evidence for copper and its compounds to provoke metal fume fever (page 23):

> The conclusion of Borak et al was that, based on the seven studies identified in the literature search, there is insufficient evidence to conclude that exposure to copper dust or fume causes MFF. Based on data which are currently available, this conclusion would appear to be justified.

The proposal paper also presents data for 3 studies on rats, one which was not standard or totally reliable. The other 2 studies yielded the following results:

Chevalier (2003):	~$0.205<LC_{50}<1.08$ mg/L air
Rush (1992):	LC_{50} (male) = 0.5 mg/L air
	LC_{50} (female) = 0.61 mg/L air

Section ***4.2.4 Comparison with criteria*** states:

> The inhalation LC_{50} lies within the range (0.05-0.5 mg/l) for classification as Acute Tox. 2 (H330: Fatal if inhaled) under regulation (EC) 1272/2008. (page 33)

The inhalation LC_{50} range for classification as Acute Tox. 3 (H331: Toxic if inhaled) is (0.5-1.0 mg/l). The data appear to fall closer within this range, though considering the other data presented, we wonder whether even this classification can be justified.

CLEAPSS comments

The above data appear to fall towards, and some even above, the higher end of the classification bracket for classification as Acute Toxicity 2 for inhalation.
In view of this, as well as the sparsity of evidence of inhalation risk in mammals, the lack of human data and conclusions in the other references above, CLEAPSS does not agree that such a classification is justified. We suggest that even a classification of Acute Tox. 3 may not be fully justified.

CLEAPSS comments of the proposal for a harmonised classification for copper(II) oxide for Acute toxicity (inhalation) category 2 (H330 Fatal by inhalation) 03/02/2014

Dossier Submitter's Response

Human health hazard:
Based on the information provided during consultation by member states and other organisations, agree to delete the proposal classification of Acute tox 2 –H330.

Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation. There is also no evidence that it is implicated in metal fume fever in industry.
RAC's response
See RAC's response to comment no. 7.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom	Regulatory Compliance Limited	BehalfOfAnOrganisation	7

Comment received

It can be concluded that the reference substance, copper dihydroxide, is not comparable to the target substance, copper oxide. Therefore it is proposed that the classification proposal in the RAR for copper oxide by the inhalation route be retained for this harmonised classification. Classification is not warranted by the inhalation route for copper oxide.

See non-confidential attachment.

ECHA note: The information below was provided in CLH dossier comments CuO ECI Jan 2014.doc [attachment no.2]

ECI COMMENTS TO

CLH REPORT: PROPOSAL FOR HARMONIZED CLASSIFICATION AND LABELLING OF COPPER OXIDE (CUO)

These comments also reflect the considerations of the following task forces and consortium;

European Antifouling Copper Task Force

Wood Preservative Copper Task Force

The European Union Copper Task Force (Plant Protection Products Regulation [PPPR])

Copper Compound Consortium

ABSTRACT

We acknowledge and appreciate the alignment with the copper risk assessment dossier as well as the incorporation of some post risk assessment data.

For most endpoints, the data used and interpretation of the data reflect the hazard profiles agreed in the copper risk assessment report (RAR) and used for the CuO REACH dossier.

For some endpoints, we noted some differences in data-interpretation between the copper oxide CLH report and REACH dossier. We have therefore focussed the review on these endpoints and propose to revise the classification to:

No classification warranted for acute inhalation[1]

---

[1] CLH report proposal: Acute Tox 2 – H330

Environmental hazard Acute category 1. M factor = 1[2].

Environmental hazard Chronic category 2[3].

1) INTRODUCTION

We appreciate the opportunity to review the CLH report but do regret the significant overlap between the public consultation period and the year-end holidays.

We acknowledge and appreciate the alignment between the CLH report and the copper RAR as well as the incorporation of some post risk assessment data. For most endpoints, the data used and interpretation of the data reflect the hazard profiles agreed in the copper risk assessment and used for the copper oxide REACH dossier.

Please find below a more detailed review for hazard endpoints, demonstrating differences in classification between the CuO CLH report and REACH dossier.

2) HUMAN HEALTH HAZARDS

Acute Inhalation Classification Proposal

In 2008 the RAR concluded that there was no need to classify copper oxide by the inhalation route (Human Health, Appendix 7). An alternative proposal is now presented in the CLH document. This is based on read-across from copper dihydroxide data and relies on the hypothesis that since these two compounds have similar water solubility values, the inhalation effects will also be comparable. Therefore, it has been proposed to classify copper oxide as H330, fatal if inhaled.

However, when the available acute toxicity and irritation classifications are compared between copper oxide and copper dihydroxide, it can be clearly seen that copper dihydroxide is a much more toxicologically significant compound than copper oxide. This is probably due to the alkaline nature of copper dihydroxide and the particle shape of this particular copper compound. The following table shows the proposed CLH classifications of copper oxide and copper dihydroxide.

Classification	Copper oxide	Copper dihydroxide
Oral	No classification	Acute Tox 4 (H302)
Inhalation	Fatal if inhaled (H330)*	Fatal if inhaled (H330)
Eye irritation	No classification	Risk of serious eye damage (H330)

*Based on read across

Due to the differences observed in acute toxicity studies, it does not appear to be justified to read-across from copper dihydroxide to copper oxide for the purposes of acute inhalation classification.

The effects observed in the inhalation study with copper hydroxide are probably influenced by pH and the effect of the needle particle shape on lung tissue and this effect would not be expected to occur with spherical particle like copper oxide.

Whereas the bioavailability of copper dihydroxide has been shown to be similar in relation to other copper compounds used in plant protection products, including dicopper oxide (Cu_2O) (Himmelstein, 2003), copper oxide has been shown to have a low bioavailability potential in comparison to other copper compounds in animal studies. These data are taken from the copper oxide REACH dossier and show that copper oxide is the

---

[2] CLH report proposal: Acute 1, M factor 10

[3] CLH report proposal: Chronic 1, M Factor 1

least bioavailable compound from those tested.

For the oral exposure route, in a series of bioavailability studies, conducted by several authors the bioavailability of copper sulfate was compared to other less soluble copper compounds including copper oxide, dicopper oxide and copper carbonate. .

In all cases, copper sulfate was shown to be more or equally bioavailable in relation to the other four copper salts (Table 1). Although the species tested are not usual species used in regulatory guidelines, the results are consistent when evaluating a number of studies and appear to be reproducible. In addition, the studies have measured copper levels in the most important organ and body fluid in determining copper adsorption from the gastro-intestinal tract, namely the liver and bile.

Table 1: Relative bioavailability of supplemental copper sources

Source of copper	Species			References (and applicable species)
	Poultry	Swine	Cattle	
Copper sulfate	100	100	100	Aoyagi and Baker, 1993 (poultry) Baker *et al.*, 1991 (poultry) Buescher *et al.*, 1961 (swine) Cromwell *et al.*, 1989 (swine) Kegley and Spears, 1994 (cattle)
Copper oxide	0 (3)	30 (4)	15 (2)	
Cuprous oxide	95.2(2)	-	-	Aoyagi and Baker, 1993 (poultry) Baker *et al.*, 1991 (poultry)
Basic copper carbonate	115 (1)	60 (1)	-	Allen *et al.*, 1961 (swine) Aoyagi and Baker, 1993 (poultry)
Copper carbonate	-	95 (1)	-	Buescher *et al.*, 1961 (swine)

Average numbers are rounded to the nearest ‘5’ and expressed relative to response obtained with copper sulfate. Number of studies or samples involved indicated within parenthesis.

The low bioavailability of copper in copper oxide, relative to that of copper in the sulfate salt, was also demonstrated in the rat following administration at adequate dietary levels (Rojas *et al.*, 1996).

The low bioavailability can also be observed in lung fluid bioelution data (see Table 2).

Data on the solubility of cupric oxide (CuO), cuprous oxide (Cu_2O) and cuprous thiocyanate (CuSCN) in lung fluids are taken from a bioelution study that is summarised as supporting information in the copper oxide REACH dossier (Rodriguez, 2009). Of two available studies, this one is considered most appropriate as the solubility level tested (100 mg/l) was equivalent to the doses used in the available animal studies.

Table 2: Comparison of Copper Compound Solubility in Water and Artificial Lung Fluid (ALF) with Acute Inhalation Classification Status.

Compound	Solubility in Water (mg/L)	Solubility in AAF** (Mean as Cu, mg/L)	Solubility in AIF** (Mean as Cu, mg/L)	Acute Inhalation Classification based on animal data
CuO	0.394 (pH 6.0)	3.44 – 7.32 (pH7.4)	3.09 – 7.86 (pH 7.4)	--
Cu_2O	0.639 (pH 6.5 – 6.6)	15.13 – 22.97 (pH 7.4)	17.93 – 21.50 (pH 7.4)	H302: Harmful*
CuSCN	1.91 – 2.03 (pH 7.0)	8.80 (pH 7.4)	6.20 (pH 7.4)	Not Classified

*Proposed classification based on available data.
**AIF = Artificial Interstitial Fluid; AAF = Artificial Alveolar Fluid.

For further information on the acute inhalation studies on Cu2O and CuSCN, please refer to the CLH documents on these compounds.

As shown in Table 2 the most soluble of the compounds considered in both water and ALF is cuprous oxide. This compound is classified as harmful by inhalation on the basis of a classic acute inhalation test in rats.

The other compound for which animal data are available is cuprous thiocyanate. While this is marginally more soluble in water than cuprous oxide, its solubility in ALF (and indicative of lower bioavailability) is significantly lower. This is reflected in the fact that cuprous thiocyanate is not classified on the basis of its acute inhalation toxicity in an equivalent acute inhalation study in the rat.

Copper oxide is less soluble in water than cuprous thiocyanate and cuprous oxide and is also significantly less soluble in ALF, and this is indicative of low bioavailability (also substantiated by the results of acute oral and dermal toxicity studies with cupric oxide).

When **all** of the available data on copper oxide are evaluated in a weight of evidence approach;

- Differences in pH,
- Differences in particle shape
- Differences in known toxicological profiles
- Differences in bioavailability when comparing animal data and in vitro bioelution data,

It can be concluded that the reference substance, copper dihydroxide, is not comparable to the target substance, copper oxide. Therefore it is proposed that the classification proposal in the RAR for copper oxide by the inhalation route be retained for this harmonised classification. Classification is not warranted by the inhalation route for copper oxide.

Dossier Submitter's Response

Human health hazard:

Based on the information provided during consultation by member states and other organisation, agree to delete the proposal classification of Acute tox 2 –H330.
Indeed, no other data supports its toxicity via inhalation in humans. Moreover, the detailed report in 'Derogation and classification proposals for acute inhalation toxicity of copper powder, copper oxide, copper sulphate pentahydrate' (2006) concluded that it did not require animal testing and should not be classified as toxic via inhalation.
There is also no evidence that it is implicated in metal fume fever in industry.

Environmental hazard:

In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document).

RAC's response

RAC agrees with the arguments put forward that read-across from copper dihydroxide is not appropriate. RAC also agrees that the solubility and particle size characteristics and the very low acute toxicity via other routes make it unlikely that copper(II) oxide is acutely toxic via inhalation. Available human data also do not warrant classification. Hence, RAC is in support of not classifying copper(II) oxide for acute inhalation toxicity.

RAC agrees with the DS response about the rapid removal concept, which affects the chronic classification. Our reasons are given in the opinion. The chronic classification and related M-factor will be adjusted according to that decision on rapid removal.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	Germany		MemberState	8

Comment received

The DE CA has general problems with some methodologies referring to the environmental classification used in the CLH-proposal:

i) Methodology for chronic classification
Regarding the chronic environmental classification and labeling, the proposal is based on the concept of "rapid removal" for assessment of environmental transformation. However, the interpretation of this concept is not yet finally agreed upon (cf. comment by the ECHA on page 503 of the Guidance Document for the application of CLP criteria).
In the view of the German Federal Environment Agency the concept of "rapid degradation" as foreseen by the CLP Regulation for organic substances cannot be compared to the risk based concept of "rapid removal/transformation" of inorganic substances (metals are not degraded but simply relocated from the water column to e.g. the sediment). Hence, the concept of "rapid removal" seems not adequate for the hazard based classification according to CLP. For this reason we cannot support the chronic classification proposed by FR.
As long as the concept of "rapid removal" for inorganic compounds is not finally agreed upon, the aquatic chronic classification should be based on the criteria for not rapidly degradable substances as it was done for all substances including metals before.

ii) Use of geometric mean for classification and labeling
According to the CLP Regulation (section 4.1.2.3) "the lowest of the available toxicity values shall normally be used to define the appropriate hazard category(ies)." In the Guidance Document on the application of the CLP criteria the following is stated: "Where more than one acceptable test is available for the same taxonomic group, the most sensitive (the one with the lowest L(E)C50 or NOEC/EC10) is generally used for classification. […] When larger data sets (four or more values) are available for the same species, the geometric mean of toxicity values may be used as the representative toxicity value for that species."
Accordingly, the geometric mean may be used for the derivation of the lowest acute and chronic endpoint for data rich substances, if four or more endpoints are available for one species. Please note that this is not always the case for the data used for classification in the CLH reports. We therefore suggest using the lowest effects value as it was proposed and agreed for example within the Competent Authority Assessment Reports (e.g. DAR for pesticides, CAR for biocides).

iii) Data basis for classification
Most of the data available on copper compounds has been submitted under the EU Voluntary risk assessment (VRA) under the Existing Substances Regulation. The adequacy of the data presented in the VRA is questionable with regard to classification and labeling as it has not been discussed by any technical group competent for classification as stated by FR in the CLH Report. Therefore we suggest taking into account the data which has recently been fully evaluated by competent authorities and which has been taken for a classification and labeling proposal (e.g. DAR for pesticides, CAR for biocides, see specific comments on environmental classification).

For these three indicated points, we propose to revise the CLH-Dossier accordingly.

Further points:

p. 162: Please clarify whether the given toxicity data refer to the copper ion only or a copper compound. p. 166: Why was in the calculation of the ERV Value the number of metal ions as 1 considered? Biocide Regulation: The lowest NOEC reported under the BPD for copper (e.g. in the Assessment Report for the biocidal active substance copper carbonate / Product type 8, RMS France, September 2011) is 2.2 µg Cu/L (growth of Oncorhynchus mykiss). This value is given in the CLH Report in the table on page 192, section 5.4.1.2 for the test organism O. mykiss in the column "all pHs". However, this endpoint has not been considered for the environmental classification in the CLH report (cf. Conclusion of environmental classification according to Regulation EC 1272/2008 on page 197). Please take this endpoint for the aquatic chronic classification of copper (II) oxide into account.
Dossier Submitter's Response
i) In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document). ii) We agree, however in this case there is no impact on classification iii) The biocide CAR is based on data submitted in the RAR. All data available in the pesticide DAR are also included in this dossier.
RAC's response
i) We agree with the comments made about the rapid removal concept, and note that the DS does too. This affects the chronic classification. ii) We agree with the comments about the use of the geometric mean, provided that the data are all reliable. Contrary to the response of the DS, the way that this is applied to some of the data could have implications for the environmental classification of some of the copper compounds (because of the way that molecular weight and number of copper atoms affects ERVs for individual substances based on the same ecotoxicity data point). iii) We are disappointed that the CLH dossier did not in fact include all relevant data available in the REACH CSRs (and voluntary risk assessment report, vRAR), such as for invertebrates. These data have been assessed to be reliable for use in REACH registrations, so we believe they should be used for classification purposes too, even if they have not been independently validated by a regulatory authority (we note that there *was* some oversight of the data assessment process provided by the Italian Competent Authority and the Technical Committee for New and Existing Substances (TC NES) under the former Existing Substances Regulation, and more recently agreement of the data set at the OECD CoCAM; the overall level of scrutiny provided is unclear – in particular the TC NES did not "agree" any of the data). The opinion therefore considers the impact of the additional data on the classification. The DS has not responded to the additional points that were made, which raise valid concerns about the transparency of the dossier. The opinion discusses the molecular weight of the hydrated and anhydrous forms where appropriate, the number of copper ions per substance and the use of the copper (II) hydroxide data for *Oncorhynchus mykiss*.

Date	Country	Organisation	Type of Organisation	Comment number
30.01.2014	Denmark		MemberState	9

Comment received

We do not agree that CuO can be regarded as rapidly "degrading", and therefore the M-factor to applied in the chronic classification should be 10 and not 1 as suggested in the dossier

ECHA note: The information below was provided in Rapid-degradation-CuO.doc [attachment no.5]

Danish comments on the environmental classification of CuO

We do not agree that CuO can be regarded as rapidly "degrading", and therefore the M-factor to applied in the chronic classification should be 10 and not 1 as suggested in the dossier.

In the section on classification for environmental hazards the concept of "rapid removal" has been applied as an analogy to rapid degradation.

However, the "rapid removal" concept is not generally accepted as an applicable tool in classification of metals in neither the CLP nor in the GHS.

Thus in the CLP guidance the paragraphs on "rapid removal" that were introduced in a draft were removed because of "lack of scientific consensus" (Guidance on the Application of the CLP Criteria, Version 4.0, November 2013, Appendix IV, IV.3).

Likewise, EUROMETEAUX and ICMM proposed to introduce the concept of "rapid removal" in the GHS guidance document, Annex A9.7, but the GHS correspondence group in December 2013 decided to leave it out for the same reasons as above in the CLP guidance.

The "rapid removal" concept is risk based, and not adequate for hazard classification purposes.

The outlined procedures and models in the "rapid removal" concept assume completely still-standing water, a situation you will hardly find anywhere in natural waters; certainly that would be rather special localities, and the concept is absolutely inapplicable to running waters. Thus, the suggested procedure not only represents risk assessment, it is not even generic risk assessment, but very, very local risk assessment.

Binding to particles in the water column with a following sedimentation and binding in the sediment has not been accepted for organic substances. The reason for this is that such processes will depend highly on local conditions. Also, the rate of such processes will vary with the depth of the water column, and this was the main argument for not taking volatility into account in the hazard assessment. For the same reasons these processes cannot be applied in the hazard assessment and classification of metals.

The Ticket-Unit-World model has been developed for lakes, so far without currents and turbulence. And the model will not be applicable to running waters. The model also employs binding to organic particles and precipitation of these to the sediment, which, as said above, cannot be accepted in the framework of hazard assessment and classification.

The binding in the sediment (e.g. to sulphides) is not really an irreversible process. It requires undisturbed sediment that doesn't get oxygenized, while in natural waters you will normally see a number of processes that can stir the sediment at different times, such as e.g. storms and burrowing animals. And again, it won't apply to running waters.

Thus the "rapid removal" concept is purely a risk assessment tool and not applicable to hazard identification and classification, and has not been accepted for hazard identification under the CLP and GHS.

Further, it is in the dossier suggested that 70% removal of the soluble form of a metal would be analogous to 70% degradation (mineralization) of an organic substance.

However, recall that the 70 % (or 60% depending on test-method) mineralization of organic substances really represents close to 100% degradation, as a substantial part of the last 30 % is built into microbial biomass. A 70% removal of a metal is therefore not at all equivalent with the 70 % mineralization of organics.

Also, looking at the transformation/dissolution protocol results given in the voluntary risk assessment (VRAR) Appendix K1, it is evident that there is a marked *increase* in soluble Cu from day 7 to day 28 (about a factor of 4). If there was a rapid transformation of soluble forms to insoluble forms this would be seen as a marked *decrease* of soluble forms in the T/D protocol tests. The table below is from VRAR:

Table 8: Summary of the transformation/dissolution data obtained for CuO, at different loadings and different pHs.

CuO loading rate (mg/l)	**Time (days)**	**Measured Cu concentration (µg/l)**		
		pH6	pH7	pH8
1	7	49	5	0
10	7	221	22	3
100	7	980	64	10
1	28	210	9	1

The implication of this is that the substance cannot be regarded as rapidly "degrading", and therefore the M-factor for Chronic 1 is 10.

Danish Environmental Protection Agency

Strandgade 29, DK-1401 Copenhagen C

Dossier Submitter's Response

In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document).

RAC's response

We agree with the comments made about the rapid removal concept, and note that the DS does too. This affects the chronic classification.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	Finland		MemberState	10

Comment received

Comments by the Finnish Competent Authority:

The CLH proposal includes an assumption that copper undergoes rapid removal from the water column, which is proposed to correspond to rapid environmental transformation as defined in the classification criteria. The Finnish CA considers that the provided justification for rapid environmental transformation based on the rapid removal of copper (i.e. more than 70% removal of copper from the water column within 28 days, as indicated by the TICKET-UWM model simulations), is not acceptable.

In the CLH report, it is mentioned that "the processes considered by the model include complexation by aqueous inorganic and organic ligands such as dissolved organic carbon (DOC), adsorption to particulate phases such as particulate organic carbon (POC) and iron/manganese oxides, binding to biological receptors (biotic ligands), dissolution kinetics of metals powders, and cycling of organic matter and sulfide production in lakes"

It is noted that the above-mentioned processes are dependent on site-specific factors and may vary spatially and temporally. Therefore, these factors cannot be used for hazard assessment which should be based on intrinsic properties of the substance and should not be dependent on local conditions.

It is also noted that in the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013)the parts concerning "rapid removal from water column" have been deleted for the time being as explained in the comment by ECHA (p.606 of the guidance).

Copper (II) oxide is considered as ready soluble metal compound in the CLH report. This argument is based on the water solubility values 0.394 mg/l and 0.01 mg/l at pH 6 and pH 9, respectively, being greater than acute ERV. The test item in the water solubility test should be indicated, as well as the basis of the solubility results (as Cu or CuO).

In the CLH report the lowest recorded geometric mean LC50 value was mentioned to be 0.0081 mg Cu/L for fish Pimephales promelas for pH 5.5-6.5. However, this value has not been used as in the table p. 165 the lowest reference value LC50 (mg/l) for pH 5.5-6.5 was claimed to be 0.0292 mg/l. It is unclear where this value comes from. The classification for acute hazard should be based on the lowest reference value of 0.0081 mg/l (acute ERV-CuO 0.01 mg/l) which, however, would not change the classification in this case.

Considering the proposal for chronic hazard, as there is no reliable evidence of rapid environmental transformation and taking into account the lowest chronic ERV- CuO value of 0.009 mg/l (<0.01), the classification for chronic hazard should be Category chronic 1, H410, with an M-factor of 10.

Dossier Submitter's Response

In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document).

RAC's response

RAC agrees with the comments made about the rapid removal concept, and note that the DS does too. This affects the chronic classification.

RAC notes that the DS has not responded to any of the other comments that were made. These include a question about the test item in the water solubility test and the expression of the results. We have considered solubility for all substances in the opinions (except for copper flakes, for which T/D data were used) – in our view, all of the substances are readily soluble metal compounds in accordance with the CLP Guidance.

The comments also point out inconsistencies in acute data presentation for fish, and we have clarified the choice of data in the opinion.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	Belgium		MemberState	11

Comment received

General remark for all copper dossiers. Why was the acute ERV for copper not based on the acute aquatic toxicity results on Pimephalus promelas which are considered of high quality?

We support the proposed classification of Cu (II)Oxide as aquatic acute 1, H400 and chronic cat 1, H410. However we only partially agree with the setting of the M-factors.

The measured water solubility of Copper(II)-oxide (pH6 = 0.394 mg/l, pH9 < 0.01 mg/l) is greater than the acute ERV of the dissolved metal ion and therefore the metal compound can be considered readily soluble. In water copper is rapidly bound to material resulting in very low levels of free Cu2+ ion in Solution. More than 70% of copper is removed from the water column within 28 days. Copper remobilization from the sediment is considered limited (the pseudo-steady state total and dissolved copper conc. were lower than the conc. corresponding to 70% removal, which is supported by sediment sensitivity analyses). Copper binds to the sediment organic carbon and the anaerobic sulphides with formation of Copper sulfide. The latter has a very low stability constant and thus the remobilization of the anaerobic sediment layer is considered limited. There is still lack of scientific consensus on the interpretation of rapid removal for classification purposes. The lowest Acute ERV (adjusted for molecular weight of the metal compound) < 1 mg/l and therefore copper(II) oxide should be classified as Aquatic acute 1, H400. However we do not agree with the proposed acute M-factor. The lowest acute ERV for copper at pH 5.5-6.5 was recorded for Pimephales promelas (geom. Mean LC50=0.0081 mg/l) instead of for Oncorhynchus mykiss (LC50=0.0290mg/l). If the number of datapoints <4, the lowest value should be taken. The lowest datapoint (n=2) for Pimephalus promelas = 0.0044mg/l which results, after correction for the molecular weight, in an acute ERV for the metal compound = 0.006 mg/l, resulting in a M-factor of 100 (0.001mg/l<acute ERV≤0.01mg/l for Copper(II)oxide. Based on the results of the aquatic chronic toxicity test on the most sensitive species (invertebrate Ceriodaphnia dubia, at pH >6.5-7.5), the lowest Chronic ERV for the metal compound is 0.009 mg/l. If the chronic ERVcompound ≤ 0.01 mg/l and there is evidence of rapid environmental transformation, than the compound should be classified as chronic category 1. A chronic M-factor of 1 should be applied (0.001mg/l<Chronic ERV≤0.01mg/l).
Dossier Submitter's Response
In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document). For the acute aquatic toxicity for fish, we agree, however in this case there is no impact on classification.
RAC's response
We note that the comment appears to support the approach to rapid removal proposed originally by the DS, but that this is no longer the position of the DS (or several other Member State stakeholders). As explained in the opinion, we do not believe that sufficient evidence has been provided to support the rapid removal concept for copper. The DS does not respond to the comment that the lowest datapoint (n=2) for *Pimephales promelas* (0.0044 mg/l) has an impact on the proposed M-factor for some substances. This is addressed in the opinion.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United Kingdom	Regulatory Compliance Limited	BehalfOfAnOrganisation	12

Comment received

Based on the comparison between the pH specific 7 days and 28 days transformation/ dissolution data and the pH specific acute and chronic ERVs (see Table 5), the following is concluded:

At pHs 6, 7 and 8, at a loading of 1 mg/L, the dissolved copper concentration after 7 days transformation/dissolution were measured. The dissolved copper concentration after 7 days transformation/dissolution at lower loadings (0.1 and 0.01 mg/l) were calculated from linear extrapolation of the 1 mg/L transformation/dissolution data (Table 5, see also Figure 1). Comparison between the acute ERVs and the 7 day dissolved copper concentrations (Table 5) shows copper concentrations exceed the ERV at the 1 mg/L (tested) but not at 0.1 mg/L (extrapolated). These data therefore allow for an aquatic Acute 1 - H400, M factor = 1

Taking account of the evidence for rapid removal of copper from the water column, the most stringent classification is taken from dissolution data at pH 6. At pH 6, the dissolved copper concentration triggers the lowest ERV (0.020 mg/L) at loadings between 0.01 and 0.1 mg/L. These data and assumptions lead to the environmental hazard Chronic 2 - H411.

See non-confidential attachment.

ECHA note: The information below was provided in CLH dossier comments CuO ECI Jan 2014.doc [attachment 2]

3) ENVIRONMENTAL HAZARDS

In the REACH dossier, we derived the following classification for environmental hazard:

Acute category 1. M factor = 1.
Chronic category 2.

The difference in classification is related to the assessment of the solubility of copper oxide (see section 3.1 below).

We also noted some differences in data-interpretation and data-aggregation between the CLH report and REACH report, without influence to the classification outcome (see section 3.2 below).

3.1 TRANSFORMATION/DISSOLUTION DATA

The CLH report used the solubility data from the RAR to conclude that CuO is fully soluble[4]. However, OECD protocols on water solubility are not applicable to metals and sparingly soluble metal compounds, which are characterized by transformation mediated solubilisation.

Rodriguez et al., 2000[5] performed transformation dissolution tests on CuO (also included in REACH 2013 update dossier). The resulting dissolved copper concentrations after 24 hours transformation dissolution demonstrated low solubility (<1%) with no exceedence of the ERV at 1 mg/L across the pH range (pH 6 to 8).

---

[4] Please note that the solubility reported in the RAR at pH 9 was not 0.01 mg/L but $\leq$0.01 mg/L

[5] Report available from the copper RAR (2008) (Annex K3)

These results suggest that CuO could be considered poorly soluble and data from the full transformation/dissolution test (Table 3) have been used to derive the environmental hazard classes for CuO. We therefore propose to consider transformation/dissolution in the classification of CuO.

Table 3: Transformation/dissolution of copper oxide at 1 mg/L loading, expressed as mg dissolved Cu/L

Transformation/dissolution				
Loading [mg CuO/l]	**Time [days]**	**mg dissolved Cu/L**		
		At pH 6	**At pH 7**	**At pH 8**
1	7	0.049	0.005	0.000
1	28	0.210	0.009	0.001

3.2 ECOTOXICITY DATA

The RAR ERVs, retained in the CLH report, are slightly higher than the ones defined in the REACH dossier because in the RAR geometric mean values were derived, even when only 2 and 3 data-points per species were available. However, in the REACH report, the geometric mean was only applied if 4 or more data-points were available, which slightly lowered some species-specific reference values (see Van Sprang and Delbeke, 2010 - Attachment 1). Table 4 summarises the ERVs retained from the DAR, RAR and REACH, expressed as dissolved copper-ions.

Table 4: Summary of the acute and chronic ERVs for copper, expressed as mg dissolved Cu/L

Source	pH range	Acute ERV Cu	Chronic ERV Cu
RAR	5.5-6.5	0.029	0.020
	>6.5-7.5	0.047	0.007
	>7.5-8.5	0.030	0.016
REACH	5.5-6.5	0.025	0.020
	>6.5-7.5	0.035	0.007
	>7.5-8.5	0.030	0.011
	across all pHs	0.034	0.015

Note: In the RAR and the REACH dossier, the ecotoxicity data from *P. promelas* at pH 6 (Erickson *et al.*, 1996) were rejected and it may be clarifying to also mention this in the CLH report.

> The test was performed with larvae (< 24 h old) in a flow-through with a very short retention time (± 45 min.), using a diluted reconstituted medium (prepared from Lake Superior water through reverse osmosis) with a low hardness (22 mg/l CaCO3) and DOC concentration (reverse osmosis). This test performed represent worst case conditions explaining therefore this low LC50 value. Moreover the observed pH dependency observed for *P. promelas* at (sensitivity at pH 6 versus pH 7) is unexpected and may be related to insufficient adaptation to low pH conditions (from Van Sprang and Delbeke, 2010 -Attachment 1).

This difference does not influence the classification outcome.

3.3 PROPOSED ENVIRONMENTAL CLASSIFICATION

Based on the comparison between the pH specific 7 days and 28 days transformation/ dissolution data and the pH specific acute and chronic ERVs (see Table 5), the following is concluded:

At pHs 6, 7 and 8, at a loading of 1 mg/L, the dissolved copper concentration after 7 days transformation/dissolution were measured. The dissolved copper concentration after 7 days transformation/dissolution at lower loadings (0.1 and 0.01 mg/l) were calculated from linear extrapolation of the 1 mg/L transformation/dissolution data (Table 5, see also Figure 1). Comparison between the acute ERVs and the 7 day dissolved copper concentrations (Table 5) shows copper concentrations exceed the ERV at the 1 mg/L (tested) but not at 0.1 mg/L (extrapolated). These data therefore allow for an aquatic **Acute 1 - H400, M factor = 1**[6].

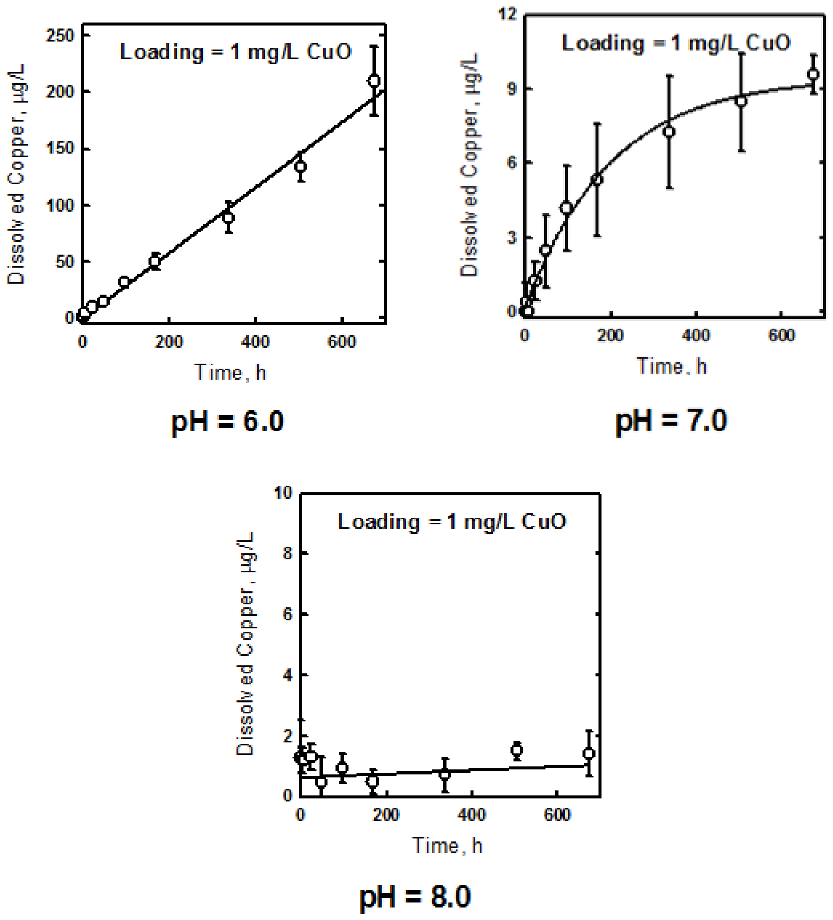
Table 5: Transformation/dissolution of CuO (measured at 1 mg/L and extrapolated to lower loadings) and ecotoxicity reference values, expressed as mg dissolved Cu/L

Transformation/dissolution				
Loading [mg CuO/l]	**Time [days]**	**mg dissolved Cu/l**		
		At pH 6	**At pH 7**	**At pH 8**
1 **0.1 (extrapolated)**	7	0.049 0.005	0.005 <0.001	0.000 <0.001
1 **0.1 (extrapolated)** **0.01 (extrapolated)**	28	0.210 0.021 0.002	0.009 <0.001 <0.001	0.001 <0.001 <0.001
Additional data: Ecotoxicity Reference Values - mg dissolved Cu/ l				
Acute ERV	LC_{50}	0.029 (0.025)	0.047 (0.035)	0.0298
Chronic ERV	NOEC	0.020	0.0074	0.016 (0.0114)

Environmental Reference Values for acute and chronic ecotoxicity, from the CLH report and between brackets from the REACH CSR.

---

[6] CLH report: Acute 1, M factor = 10



pH = 6.0

pH = 7.0

pH = 8.0

Figure 1: Copper release time course at pH 6.0, 7.0 and 8.0 at 1 mg/L loading. The 95% of confidence curve fit functions are shown.

For the assessment of chronic classification, the 28 day transformation/dissolution dissolved copper concentrations at pHs 6, 7 and 8, and a loading of 1 mg/L were measured. Dissolved copper concentrations after 28 days transformation/dissolution have been predicted for lower loadings (0.1 and 0.01 mg/L) by linear extrapolation from the data at 1 mg/L (Table 5). Comparison between the chronic ERVs and these dissolved copper concentrations (Table 5) shows that at pH 6 the dissolved copper concentrations were higher than the ERV at 0.1 mg/L, but not at 0.01 mg/L. At pH 7 the ERV is triggered at loadings between 1 mg/L and 0.1 mg/L. At pH 8, the dissolved copper concentration at 1 mg/L does not exceed the ERV.

Taking account of the evidence for rapid removal of copper from the water column, the most stringent classification is taken from dissolution data at pH 6. At pH 6, the dissolved copper concentration triggers the lowest ERV (0.020 mg/L) at loadings between 0.01 and 0.1 mg/L. These data and assumptions lead to the environmental hazard **Chronic 2 - H411.**

For comparison purposes, the classification versus solubility for copper compounds and copper flake is presented in Attachment 2 for completeness.

4) RELEVANT ATTACHMENTS

Attachment 1: Van Sprang and Delbeke, 2010

Attachment 2: Classification versus solubility of copper compounds and copper flake

CONTACTS

For more information, please contact:

Katrien Delbeke, *Director Health Environment and Sustainable Development*. European Copper Institute,
Tervurenlaan 168 b-10. B-1150 Brussels: Tel: +32 2 777 7083, katrien.delbeke@copperalliance.eu

Carol Mackie *Secretariat of the Copper Compound Consortium,* Regulatory Compliance Ltd, 6 Dryden Road, Bilston Glen, Loanhead, Midlothian, EH20
9LZ. Tell: +44(0)131 448 1086, cmackie@regcs.co.uk

ECHA note: The information below was provided in Classification versus pH and solubility.doc [attachment no.4]

ECI ATTACHMENT (2)

FOR INFORMATION - CLASSIFICATION VERSUS SOLUBILITY FOR COPPER COMPOUNDS AND COPPER FLAKE

This paper also reflects the considerations of the following task forces and consortium;

European Antifouling Copper Task Force

Wood Preservative Copper Task Force

The European Union Copper Task Force (Plant Protection Products Regulation [PPPR])

Copper Compound Consortium

1) INTRODUCTION

Following the review of the ANSES CLH documents for copper compounds and copper flakes, ECI in collaboration with the various copper task forces[7] would like to raise the following discussion as applicable to all the available compounds under consideration.

The ecotoxicity reference values (ERVs) for copper/copper compounds are based on the reliable/relevant ecotoxicity tests carried out with soluble copper compounds (e.g. CuSO4, CuCl) and retained in the copper risk assessment. The test results (e.g. LC50) from various compounds are combined and expressed as soluble copper ions (RAR and Van Sprang and Delbeke, 2010). For classification purposes, the ERV values are obtained after data-aggregation and translation to the respective copper compounds using a molecular weight translation (soluble compounds) or using the results of the transformation/dissolutions (sparingly soluble copper compounds, copper powders and copper massives). Therefore, consistency in classification across copper/copper compounds can be assessed based in information of molecular weight and solubility (see Table 1). From Table 1, the highest classification of CuSO4 is thus expected. In addition, the available data in the CLH reports and transformation dissolution (TD) data also show that the solubility of all the other compounds including copper flakes currently under consideration is dependent on pH.

Table 1: Solubility of copper compound/flakes across the pH range tested

a) Standard OECD solubility testing

Compound	pH range	Source

---

[7] European Antifouling Copper Task Force; Wood Preservative Copper Task Force; The European Union Copper Task Force (Plant Protection Products Regulation [PPPR]); Copper Compound Consortium

	5.5-6.5	**>6.5-7.5**	**>7.5-8.5**	**>8.5-10**	
	Solubility (mg/L)				
CuSO4.5H2O	220000				1
BCC	-	4.68	-	0.01	1
Bordeaux Mixture	-	2.2	-	1.1	1
Cu4(OH)6(SO4)	3.42	-	-	0.255	1
CuSCN	-	2.3	-	0.12	1
CuOCl	1.19	-	-	0.525	1
CuOH	-	0.9318	-	0.0066	1
Cu2O	-	0.639	-	0.539	1
Copper flakes*	-	0.27**	-	0.13	2
CuO	0.394	-	-	0.01	1

b) Transformation/dissolution testing

Compound	**pH range**				**Source**
	5.5-6.5	**>6.5-7.5**	**>7.5-8.5**	**>8.5-10**	
	Solubility (mg/L)				
Cu2O	0.236	0.098	<1	-	3
Copper flakes	0.721	0.363	-	-	4
CuO	0.049	0.005	0.00	-	5

Key

* Data at pH 4 was reported as 192 mg/L but not presented in table as this was more likely to reflect the oxido-reduction reaction of the copper metal into ionic copper [Cu(0) → Cu(I) → Cu (II)] which is promoted at low pH.

**Carried out at 20°C at 30°C 0.32 mg/L was reported

1 - Endpoints taken from standard OECD solubility studies see Section 5.6 of CLH report from ANSES

2 - Endpoints taken from standard OECD solubility studies see Section 1.3; Table 9 of CLH report from ANSES

3 - Results from T/D study reported for ISO 6341. Data presented to the 2001 'Meeting on environmental effects' part of the Commission Working Group on the Classification and Labelling of Dangerous Substances ref: ECBI/61/95 Add. 135.

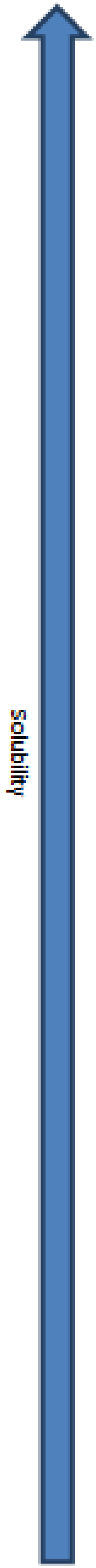
4 - Schaefers and Klawonn (2013) data provided by ECI within commenting document to CLH

5 - Rodriguez et al., 2000 - data presented in REACH 2013 updates and available in Report available from the copper RAR (2008) (Annex K3)

The overall impact of solubility on the classification proposals by the CLH report across all the compounds and copper flakes can be seen in see Table 2 in addition the classifications as proposed by ECI and task force commenting documents.

Table 2: ECI Proposed Classification of copper compounds and copper flake across pH

Compound	Classification	Proposed CLH	Proposed by ECI at pH range			Proposed ECI
			5.5-6.5	>6.5-7.5	>7.5-8.5	
CuSO4	Acute	1	1	1	1	1
	M-Factor	10	10	10*	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
BCC	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
Bordeaux Mixture	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
Cu4(OH)6(SO4)	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
CuSCN	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
CuOCl	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	2	2	2	2	2
	M-Factor	-	-	-	-	-
CuOH	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	1	2	2	2	2
	M-Factor	1	-	-	-	-
Cu2O	Acute	1	1	1	1	1
	M-Factor	100**	10	10	10	10
	Chronic	1	2	2***	2	2
	M-Factor	1	-	-	-	-
Copper flake	Acute	1	1	1	1	1
	M-Factor	10	10	10	10	10
	Chronic	1	2	2	n/c	2
	M-Factor	1	-	-	-	-
CuO	Acute	1	1	1	1	1
	M-Factor	10	1	1	1	1
	Chronic****	1	2	3	n/c	2
	M-Factor	1	-	-	-	-



n/c – Not Classified

**M=1 for RAR data with ERV of 0.119 mg/l*

*** considered to be an error introduced to CLH document by ANSES (see individual commenting document)*

**** judgment made since compound is of relative low solubility and ERV of 0.008 mg/l is borderline, Chronic 1 is considered an over prediction when comparing toxicity with soluble data of CuSO4*

***** Calculated from 28 d TD study by dividing 1 mg/l result by factor of 10*

2) OVERALL CONCLUSION

The ERV values for copper and copper compounds for both acute and chronic environmental endpoints have historically been derived using high quality ecotoxicity studies using soluble copper compounds. This ensures that consistent ERV values are derived across compounds. This consistent ERV allows to compare classification based on potential bioavailability, according to the results of solubility studies (derived using OECD guidelines or by transformation/dissolution). Using this proposal, the most soluble copper compounds would carry the most stringent environmental classification (see Table 2).

CONTACTS

For more information, please contact:

Katrien Delbeke, *Director Health Environment and Sustainable Development.* European Copper Institute,
Tervurenlaan 168 b-10. B-1150 Brussels: Tel: +32 2 777 7083, katrien.delbeke@copperalliance.eu

Carol Mackie *Secretariat of the Copper Compound Consortium,* Regulatory Compliance Ltd, 6 Dryden Road, Bilston Glen, Loanhead, Midlothian, EH20
9LZ. Tell: +44(0)131 448 1086, cmackie@regcs.co.uk

Dossier Submitter's Response

In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document).

RAC's response

We agree with the DS response about the rapid removal concept, which affects the chronic classification. Our reasons are given in the opinion.

We note that the DS has not responded to any of the other comments that were made. These point out differences in data aggregation between the REACH registration dossiers and the CLH report which result in different ERV values for some substances. We have considered this in the opinion and shown how the ERVs are calculated for each substance.

The comments also highlight some concerns about the ecotoxicity data for *P. promelas* at pH 6 (Erickson et al., 1996), which are used in the CLH report but rejected in the REACH registration dossiers. This study is important as it appears to be the most sensitive for fish, and we have discussed some of the issues in the opinion.

The comments also refer to transformation/dissolution (T/D) data and relative solubility of the different substances, and state that the most soluble copper compounds would carry the most stringent environmental classification. We note that only some substances have T/D data. We have considered solubility for each substance in the opinions (except for copper flakes, for which T/D were used) – in our view, all of the substances can be considered to be readily soluble metal compounds in accordance with the CLP Guidance. The stringency of the classification depends not only on solubility but also molecular weight and the number of copper atoms per substance. This is clarified in each opinion.

Date	Country	Organisation	Type of Organisation	Comment number
03.02.2014	United		MemberState	13

	Kingdom			

Comment received

It is important to note that our comments reflect the general classification approach used for the range of copper compounds and are not specific to individual substances.

Many of the copper compound CLH Reports refer extensively to biocide CARs or pesticide DARs. Whilst we appreciate the time since the reports were initially prepared, we note that a more recent EFSA opinion and agreed endpoints for pesticidal uses of copper (dated 2013) than the one referred to (2008) is available. The authors may wish to consider the final agreed key endpoints and data gaps identified by EFSA (along with more recent biocide reviews) to see if there are any significant changes or new data.

For all the copper compounds, it would help to be clear throughout the reports whether they are referring to the whole technical substance in question, the pure substance, total copper, or dissociated ionic copper (Cu2+). This is important when it comes to how the exposure and (eco)toxicity units are presented. Wherever units are quoted (e.g. µg/L), it should say in what form that copper is expressed.

It is useful to have noted that nano-forms of Cu exist - and we agree with the suggestion that these are considered separately pending further information on representivity/read-across of the existing bulk Cu data. This would be a useful principle to note for all future substances where nano-forms also exist and we feel this distinction should also appear in the final

Environmental fate assessment

Much of the env.fate section attempts to equate removal of dissolved ionic copper from the water phase with the rapid degradation criterion for organic substances of >70% degradation in 28 days. It is noted in the reports that transformation of one metal ‘species’ to another does not equate with degradation of an organic substance and that (bio)availability of the different forms of copper is a key consideration. The current ECHA CLP Guidance for metals (Annex IV) focuses mainly on exposure to metals and metal compounds dissolved in the water phase and on transformation processes that occur only within the water column. The focus in the guidance is on determining ‘rapid environmental transformation’. However, it does suggest that it may be possible to incorporate other processes such a water-column residence times, deposition and subsequent re-mobilisation. Whilst the copper CLH reports clearly attempt to do this, there is currently no standard means of incorporating removal, e.g. to dissolved organic carbon (DOC) or sediment, within the hazard classification system for organic or inorganic substances.

The approach used in the reports to indicate rapid environmental transformation or removal relies on a number of assumptions which are not well supported; for example:

- It assumes that there is sediment present to act as a ‘sink’ for copper, which may not always be the case.
- It is not always clear what form the initial loading comprised in each case - was it already as dissolved Cu2+ and if so, can the model (and fate studies) account for different loading rates and the different forms of copper discussed here (which presumably initially dissociate at different rates)?
- The main scenario discussed is a generalized 3 m deep lake situation. Lakes are usually large, static, permanent and have sediment of some description, however this may not reflect many other EU surface water bodies such as ponds, rivers and streams - where increased water movement, turbidity, less sediment, different depths, etc.. could affect the amount of copper remaining in solution or suspension. We therefore wonder whether a ‘realistic worst case’ situation has indeed been modelled?

- With various adjustments, e.g. to settling velocity, suspended solids, the TICKET-UWM model appears able to reflect the fate of copper in some (not all) of the available field/semi-field tests. However, it is not then used to extrapolate to other water body types with very different characteristics. We think this should be the main point of the modelling, to add value to the existing field data set, rather than to simply interpret it.
- Where there was continuous 'post-loading' in the MELIMEX experiment, this was more difficult to model and indicated that the rapid removal benchmark was not met. In the 'real-world' there may be continuous or repeated exposures, particularly of larger water bodies, from multiple sources. The chronic criteria (+ M-factor) are meant to address hazards over a longer time period than just a few days - so, for hazard classification purposes we would expect rapid transformation/removal to be able to cover the majority of situations, not just one-off exposures.
- The reports considers that most copper reaches the sediment, where much of this is then locked up in different forms (especially with sulphides) and is no longer available. This relies upon the assumption that most sediment, if present, is anaerobic and this process is fairly instantaneous. In reality, the top layers of sediment might well be aerobic - and the transit and mixing time with more anaerobic layers will vary according to the water body and sediment type, as well as temporally and spatially. Is this variability covered? Are the levels of sulphide assumed in the model (based on the Flanders data set) representative of other EU water bodies? Also, what happens if the sediment is already contaminated with metals, is there always enough 'spare' AVS left or will there be cases where it is already saturated so not available for new metal?

Because of these difficulties in describing and modelling all (or even one) relevant/realistic 'worst case' scenario for removal to sediment or to DOC/POC - such mitigating factors are rarely used to refine the hazard classification for organic substances. Most tests for organic substances in fact try to minimise such removal mechanisms to make them as bioavailable as possible, therefore taking account of this for metals would be inconsistent with usual practice. Ready biodegradability tests are difficult to pass, so metal transformation/removal should also face a similarly stringent test. Because of this, we cannot currently support the claim of rapid removal of copper based on the evidence in the dossiers.

On bioaccumulation; we agree this is probably not an issue, provided internal homeostatic excretion, transformation and detoxification mechanisms can always regulate levels within organisms under realistic worst case exposure conditions. Could the bioaccumulation potential of copper be related to the standard CLP triggers in a similar way as attempted for rapid degradation?

Ecotoxicity assessment

It isn't always clear why some ecotoxicological endpoints (e.g. from the DAR) are quoted for some forms of copper but not others. They're not just the worst case values and its not always clear between the various reports why they've been selected and how they're treated. Whilst there may be limitations to what was measured and reported in the studies and DAR, some endpoints appear as both total and dissolved Cu, as nominal or measured. Could these all be adjusted and expressed in the same consistent way? The form in which data from the EU Voluntary Risk Assesment Report (VRAR) are expressed is also unclear in the tables (dissolved copper?).

The separation of the VRAR endpoints into the different pH ranges is potentially useful, although there is no explanation why the particular bands have been chosen and only the lowest values are selected anyway, which makes it unclear why the separation was performed in the first place. There is also no discussion of the impact of other water quality parameters (e.g. hardness) on toxicity. Ultimately, at least for some of the substances, the

DAR endpoints are preferred anyway - so it is not always clear what role the VRAR data have. As mentioned, these data have never been considered by a 'technical group competent for classification' and there is uncertainty over transformation/dissolution of some of the substances. It might therefore be useful to present more information on data from the VRAR in an Appendix - if their basis and validity were described in more detail, then greater reliance and use might be made of them. All of the DAR and VRAR endpoints might then be considered together instead of separately?

The use of geometric means may be accepted if they cover the same effect end points for the same species, tested under similar enough conditions (the dossiers do not provide any rationale for the derivation of geometric means for individual species). The CLP guidance also indicates that at least four endpoints are preferred for each geomean. This may be important for key values such as the short-term Pimephales promelas data at pH 5.5-6.5, where only two studies are available. In this case, might it be better to select the lowest value of 0.0044 mg/L for this pH range? Ideally 'sensitive' species in acute tests should also be reflected in the chronic data set. As there is no long-term test for P. promelas at this pH range, might this require use of the surrogate approach and affect the acute and chronic reference values that have been selected? For long-term toxicity to fish, it also appears that an Oncorhynchus mykiss ELS NOEC of 0.0017 mg dissolved Cu/L (from DAR data) is missing from the study on 'Copper Hydroxide WP' - this would be equivalent to (and lower than) the dissolved Cu values apparently from the VRAR.

Given the amount of ecotoxicological data on copper, could more use be made of species sensitivity distributions (SSD) and HC5 values (if presented separately for each trophic group and for short and long-term). It appears that there are more ecotox data on copper than those given here, particularly for invertebrates where only Daphnia/Ceriodaphnia are presented in the reports. Data on various other invertebrates are reported in the VRAR but its not clear why these are omitted.

Additional SSDs are presented in the VRAR, are any of these appropriate? Discussion with colleagues working on the Water Framework Directive highlight that they have derived Environmental Quality Standards (EQS) for copper using the whole available data set, including data in the VRAR. These EQS were, in part, determined using SSDs and Biotic Ligand Model (BLM) calculations and a fairly high degree of confidence was expressed in their derivation. Since there are analogies with at least the chronic classification endpoint for copper, we wonder whether use could also be made of this EQS work? The use of SSDs and HC5s for copper would set new precedents for hazard classification however, so it might be questioned whether we should always default to the lowest value when we have such a data-rich substances.

One HC5 is mentioned in the CLH Reports for sediment dwellers. Given the suggested removal to and persistence in sediment, there is relatively little discussion of the exposure and hazard to sediment dwellers - even though it is said that uncertainty here is high. The SSD behind this HC5 is not presented and there is also little information on the chironomid study from the tribasic copper sulphate DAR (included under algal endpoints at 5.5). Presumably this is based on a water spiking study whereas the VRAR HC5 (in mg/kg) is from sediment spiked studies? With further information from the studies, might it be possible to recalculate the endpoints according to sediment pore water concentrations? How the aquatic hazard classification should be determined in the presence of sediment is still unclear however.

Further reference to the studies reported in the copper DARs for algae may allow presentation of their NOEC values for inclusion in the long-term hazard assessment.

The final 2013 EFSA Conclusion on pesticidal use of copper compounds reports a microcosm 'NOEC' of 0.0048 mg dissolved Cu/L (rather than 0.00312 mg/L at 5.4.4 and 5.5), although it is unclear how this would be used for hazard classification. In the table at Section 5.5 a 21-day endpoint for O. mykiss is reported, but it is not clear how relevant this is for comparison with the classification criteria. Ideally it would help to have briefly explained the Ecotoxicity Reference Value (ERV) concept, as it is not initially clear why endpoints expressed as either the substance in question, or total Cu, or ionic Cu2+ (whichever is considered the most appropriate form) cannot be used at face value. We haven't checked all of the ERV calculations, however, whilst the chronic ERVs from the VRAR can be back-calculated to identifiable endpoints, we could not find the endpoint used to derive the acute VRAR ERV at pH 5.5-6.5 of 0.045 mg/L. Overall, the selection of appropriate short and long-term endpoints for each trophic group and the workings for these ERV calculations, could be presented more clearly for each substance. Overall, and depending on the response to our comments, we do not currently agree that the substances can be considered rapidly removed, therefore we feel that all of the substances should be classified H400/410 with relevant M factors.
Dossier Submitter's Response
In the current published version of the CLP guidance (Guidance on the Application of the CLP Criteria Version 4.0 – November 2013) the parts concerning "rapid removal from water column" have indeed been deleted. Moreover, as no consensus was found during the ECHA workshop on the concept of rapid removal on February 8th, 2012, and taking into account comments from several MS (Finland, Germany, Denmark, Belgium, UK) this concept might be not considered in the current assessment. The long–term classification and M factors would therefore need to be updated accordingly (see final proposal for Chronic classification and M factor at the end of this document). For bioaccumulation, the question would need further clarification before answering. All endpoints are expressed in all available forms in the tables for better transparency. For the VRA, as mentioned in the introduction of section 5.4, all endpoints are expressed in dissolved copper. Concerning VRAR endpoints, a link to the appendix related to classification could be added in the document. For the question on whether or not data from the DAR and VRAR should be considered together, we considered that they shouldn't as data from the VRAR are not specific for Dicopper oxide; copper (I) oxide, when data from the DAR are. Considering the use of geo mean values, we agree, however in this case there is no impact on classification. For long term data on fish issued form the DAR, data on specific salts were related to each compound. Concerning SSD, it is our knowledge that HC5 are not used for classification purposes. Concerning the remark on microcosm study, it is our understanding that these values are neither used for classification purposes. In the table at Section 5.5 a 21-day endpoint for O. mykiss is reported for information. For ERV calculations, all endpoints used were expressed in dissolved copper before

transformation.

RAC's response

We note that the DS did not respond to the suggestion to check the most recent EFSA opinion for pesticidal uses of copper (dated 2013), which includes microcosm data (a NOEC of 0.0048 mg dissolved Cu/L). Given the amount of data already available, we do not think that significant changes are likely.

In terms of how the test results were reported (i.e. technical substance, pure substance, total copper or dissociated ionic copper), we note the comments of the DS so have assumed that the results are expressed in terms of dissolved copper ions unless otherwise indicated.

We agree with the comments made about the rapid removal concept, and note that the DS does too. This affects the chronic classification. The comment about bioaccumulation potential was not addressed by the DS, but it does not affect the classification given the decision on rapid removal.

The comments suggest that more information should be provided about the data from the vRAR. The DS said that an appendix could be added, but that the data should not be combined with those for the substance because they are not substance-specific (unlike the DAR). We do not think this is correct – classification has to take account of all reliable relevant data on copper ecotoxicity. This has been done in the opinion.

The DS agrees with the comment that the use of geometric means may not be appropriate for the short-term *P. promelas* data at pH 5.5-6.5 (implying that the surrogate approach should be considered), but states that there is no impact on the classification. We think there is an impact, and this is considered in the opinion. The DS prefers data from the DAR for each substance, but as noted above, all relevant data should be considered, including the missing *O. mykiss* ELS NOEC. This is also considered in the opinion.

The DS does not consider that species sensitivity distributions (SSD) or microcosm data are relevant for classification. We think that these could be used with an adequate justification, especially for data rich substances such as copper, provided that they do not mask differences in sensitivity under different abiotic conditions. The DS does not respond to the comment that copper data have been considered for EQS setting by some Member States, but as no references were provided, this cannot be followed up by RAC.

We do not think that toxicity to sediment dwellers is relevant for the proposal.

The DS does not respond to the comment that it is unclear which end points were used to derive the ERVs. RAC has therefore clarified this in the opinion and shown how the ERVs are calculated for each substance.

Dossier Submitter's New Chronic Clasification proposal without rapid removal concept
chronic 1 M = 10

ATTACHMENTS RECEIVED:

1. **ECHA consultation on proposed harmonised classifications for some copper compounds (19/12/13-03/02/14) CLEAPSS points re proposal for Acute Toxicity (inhalation) 2 for copper(II) oxide** (file name: ECHA consultation on

proposed harmonised classifications for some copper compounds.docx) submitted by CLEAPSS on 3 February 2014 [The content was copied to comment no. 6]

2. **ECI comments to CLH report: Proposal for harmonized classification and labelling of copper oxide (CuO)** (file name: CLH dossier comments CuO ECI Jan 2014.doc) submitted by Regulatory Compliance Limited on 3 February 2014 [The content was copied to comments no.7 and 12]
3. **Acute & chronic ecotoxicity of soluble copper species in view of hazard classification of copper and copper compounds** (file name: Van Sprang and Delbeke_2010.pdf) submitted by Regulatory Compliance Limited on 3 February 2014 [please refer to comment no. 7]
4. **For information - classification versus solubility for copper compounds and copper flake** (file name: Classification versus pH and solubility.doc) submitted by Regulatory Compliance Limited on 3 February 2014 [The content was copied to comment no. 12]
5. **Danish comments on the environmental classification of CuO** (file name: Rapid-degradation-CuO.doc) submitted by Denmark on 30 January 2014 [The content was copied to comment no. 9]