**Committee for Risk Assessment**

**RAC**

Annex 2

# Response to comments document (RCOM)

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

**Lead**
**EC number: 231-100-4**
**CAS number: 7439-92-1**

CLH-O-0000002512-83-02/A2

**Adopted**

**5 December 2013**

## COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

**Substance name: Lead**
**CAS number: 7439-92-1**
**EC number: 231-100-4**
**Dossier submitter: Sweden**

# RCOM summary - For a quick overview of the most commented issues in the public consultation on lead

*The RCOM-document for lead is extensive and many of the comments are similar in nature. Therefore, the dossier submitter has assembled this summary to highlight the most common comments, while providing a quick overview of our responses.*

1. Regarding how to calculate the SCL (Specific Concentration Limit):

**Dossier Submitter's Response:** We agree that our approach to calculate the $ED_{10}$ can be discussed, and there may be more complex models that can be used for calculating a more finely tuned $ED_{10}$. Unfortunately, there is no specific guidance on how to set a SCL based on human data. However, whatever model is chosen for the calculations there will be inaccuracies and the resulting SCL could be discussed. Our "$ED_{10}$"-calculation should be seen as an indication, where the take-home-message is that lead is highly potent; in the range of many orders of magnitude more potent than what is required for assigning a SCL lower than the generic concentration limit of 0.3%.

2. Regarding the challenging of the bioavailability of metallic lead:

**Dossier Submitter's Response**: Lead metal can indeed be bioavailable. Please see page 11 of the CLH-report; "There are numerous cases of lead poisoning described in the literature caused by oral ingestion of a piece of lead (e.g. lead containing jewellery, buttons, etc.), even death has been reported. These case reports prove that pieces of lead ingested orally are indeed bioavailable."

And page 18; "There have been a number of clearly identified cases of lead poisoning resulting from the misuse of lead-containing jewels, most often by children who have swallowed or repeatedly mouthed them *(CDC 2006; CDC 2004; Levin et al. 2008; Jones et al. 1999; Canada Gazette 2005; InVS 2008; KEMI 2007).* The observed symptoms of these cases go from headaches and diarrheas to death. One report of a fatal case of lead poisoning describes the death of a 4 year old boy in the USA after he ingested a bracelet charm containing 99 % lead *(CDC 2006).* The initial symptoms of poisoning manifested as vomiting, abdominal pain and fatigue, and the child had a final PbB level of 180 μg/dL at the time of death."

Regarding "hand-to-mouth" transfer of lead via oxidized lead surfaces: it may be true that lead-metal-to-hand exposure is more likely to take place via oxidized lead on the metal surface than by the actual metal "rubbing-off" onto the hand. Either way, the hand is exposed to lead in some form and if this lead gets into the body via hand-to mouth behavior, lead ions will result in the body and exert their toxicity. The resulting lead ions in the body will in both cases have metallic lead as the source, even if the paths to get there are different.

3. Regarding when lead-induced IQ-impairments take place, and whether post-natally induced developmental neurotoxicity is covered by developmental toxicity in the sense of the CLP-criteria:

**Dossier Submitter's Response:** Both pre- and post natal exposure to lead can lead to developmental effects in the form of impaired IQ. The nervous system is still under development for several years after birth (see **Davison and Dobbing (1968)*); therefore also post natal toxic insults to the nervous system can be considered to be developmental in nature. The mechanism by which lead causes impaired IQ is not specific for prenatal development; the same effects on IQ also occur after post natal exposure but only if exposure takes place during the (early) years of child hood when the nervous system is still under development. IQ-effects are *not* seen in adults exposed to lead as their nervous systems are already fully developed and no longer susceptible to developmental effects.

The latest version of the ECHA guidance for CLP (under 3.7.1.5.4) states that *"Developmental toxicity includes, in its widest sense, any effect which interferes with normal development of the conceptus,* ***either before or after birth,*** *and resulting from exposure of either parent prior to conception, or exposure of the developing offspring during prenatal development,* ***or postnatally****,* ***to the time of sexual maturation****"*.

And in REACH - information requirements (p.316, chapter R.7a: Endpoint specific guidance. Version 2.0 November 2012) the following is written regarding the two-generation reproduction study (EU B.35, OECD TG 416): *"…using an extended F1 generation* ***dosing period (to PND day 70)*** *endpoints addressing* ***developmental neurotoxicity****"*. This means that the dosing period continues until post natal day 70 in the extended F1 generation study that assesses developmental neurotoxicity.

Comments suggested considering the study by Braun et al. (2012). However, Braun et al was published in October 2012 while the final version of the CLH-report for Lead was submitted in September 2012; basing the CLH-report on the Braun-study was therefore impossible. It is also worth noting that Braun et al. (2012) is based partly on the same cohort (from Mexico City) as in the pooled analysis by Lanphear et al. (2005). The conclusion made by Braun et al. (2005) is that high blood lead concentrations at 2 years of age were most predictive of decreased cognitive abilities among the children in the Mexico City cohort; this conclusion does not contradict the conclusions made my Lanphear et al. (2005).

*Reference: Davison, A.N., and Dobbing, J. (1968). The developing brain. *Applied Neurochemistry,* 178-221, 253-316.

4. Comments challenged the so called *"read-across"* between lead and lead compounds:

**Dossier Submitter's Response:** Regardless of how exposure occurs (via lead compounds or via lead metal); it is the lead ion that is responsible for lead toxicity in the body. In all the studies presented, the toxic effects of lead are therefore caused by the same transformation product, i.e. the lead ion, regardless of which lead compound was responsible for the initial exposure.

Therefore this can not be considered as read across in the classical sense, as it is always the ***same*** (not just similar) lead ion exerting its negative effects on the body.

The following excerpts are from guidance:

- In the CLP guidance, version 3.0, section 1.4.3 (p.48) the following is written regarding common significant metabolites: *"For certain substances without test data the formation of common significant metabolites or information with those of tested substances or information from precursors may be valuable information (IR/CSA, Chapter R.6.2.5.2 and OECD 2004)."*

- The REACH-guidance on information requirements and chemical safety assessment, section R.6.2.5.2 (p.106) states the following regarding metabolic pathways: *"The underlying hypothesis for a metabolic series is a sequential metabolism of a parent chemical to downstream blood metabolites that are chemicals of interest. Hazard identification studies with the parent compound could then be used to identify the hazards associated with systemic blood levels of the downstream primary and secondary metabolites and once quantified can be used in place of studies using direct exposure to primary and secondary metabolites themselves."*

Taking into account the excerpts above, our way of reasoning regarding "read across", common metabolites and transformation products is supported by the CLP-legislation.

## COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

*ECHA has compiled the comments received via the internet that refer to several hazard classes and entered them under each of the relevant categories/headings as comprehensively as possible. Please note that some of the comments might occur under several headings, when splitting the information provided is not reasonable.*

**Substance name: Lead**
**CAS number: 7439-92-1**
**EC number: 231-100-4**
**Dossier submitter: Sweden**

## GENERAL COMMENTS

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/11/2012 | Germany | Xstrata Zink GmbH | Company-Downstream user | 1 |

**Comment received**

Lead has to be in ionic form to be uptaken into the human body. This is not the case for Lead metal, and there is no scientific background to expand the extisting classification for Lead compounds to Lead metal. The proposal is not founded by a study on Lead metal and should be refused.

**Dossier Submitter's Response**

Lead metal can indeed be bioavailable. Please see page 11 of the CLH-report; "There are numerous cases of lead poisoning described in the literature caused by oral ingestion of a piece of lead (e.g. lead containing jewellery, buttons, etc.), even death has been reported. These case reports prove that pieces of lead ingested orally are indeed bioavailable."

And page 18; "There have been a number of clearly identified cases of lead poisoning resulting from the misuse of lead-containing jewels, most often by children who have swallowed or repeatedly mouthed them *(CDC 2006; CDC 2004; Levin et al. 2008; Jones et al. 1999; Canada Gazette 2005; InVS 2008; KEMI 2007).* The observed symptoms of these cases go from headaches and diarrheas to death. One report of a fatal case of lead poisoning describes the death of a 4 year old boy in the USA after he ingested a bracelet charm containing 99 % lead *(CDC 2006).* The initial symptoms of poisoning manifested as vomiting, abdominal pain and fatigue, and the child had a final PbB level of 180 µg/dL at the time of death."

**RAC's response**

RAC supports the statement of the DS that swallowing pieces of lead containing metals leads to increased blood lead concentrations and symptoms of acute intoxication. RAC also notes that lead in jewellery is restricted and a restriction of lead in articles, which can be placed in the mouth by children is under discussion. Thus exposure at least of children from lead containing articles will be minimized.
Lead can be processed into different physical forms in industry and at home e.g. by casting bullets and fishing weights. It can be ground or polished potentially causing small, easily inhalable particles.
RAC also notes that lead as a soft metal can easily rub off on the skin becoming systemically available as metal or the oxide by hand to mouth contact, especially to adults.
Studies in rats have shown that lead from lead particles is bioavailable (Barltrop and Meek, 1979a, b).

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 20/11/2012 | United Kingdom | Individual | Individual | 2 |

**Comment received**

The United Kingdom, like some other European countries, has already restricted the use of lead shot over wetlands as part of our obligations under the African-Eurasian Waterbird Agreement (AEWA). There is absolutely no evidence that the use of lead shot outside wetlands has any environmental impact and there is likewise no evidence of any impact on human health.

The United Kingdom has a very long tradition of shotgun shooting and has led the world in the development of the sporting shotgun. It is estimated that nearly 1 million people take part in shooting sports in the United Kingdom, from informal shoots to Olympic competition. Game shooting is worth £1.6 billion to the British economy and supports nearly 70,000 full time jobs, many in remote rural areas. Shooting also contributes nearly 2.7 million man days on conservation of the British countryside every year.

A ban on lead in ammunition could have a serious negative effect on the shooting industry because most of the guns made by the historic British gun makers, and many from abroad, are unsuitable for use with economically comparative alternatives to lead. Alternatives to lead with comparative ballistic capability can cost up to 10 times more.

**Dossier Submitter's Response**

Classification under the CLP-legislation should be based solely on the intrinsic properties of the substance. It neither can nor should take into account the socio-economic impacts it might cause due to downstream legislation.

A classification according to CLP will not directly affect lead metal in bullets and shots. According to REACH annex XVII, a substance classified as Repro 1A shall not be placed on the market or used as a substance in mixtures; bullets and shots are articles and will therefore not be affected by classification.

**RAC's response**

See response to comment 1.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 03/12/2012 | United Kingdom | Individual | Individual | 3 |

**Comment received**

Calder Group is a member of the International Lead Association and the Pb REACH Consortium. ILA has provided a consolidated response on behalf of members of the Pb REACH consortium. Calder Group fully supports and subscribes to the comments made by ILA.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 04/12/2012 | Norway | | MemberState | 4 |

**Comment received**

CLH report for lead - Comments from Norway

Norway would like to thank Sweden for the proposal for harmonised classification and labeling of lead, CAS no 7439-92-1.

We support the proposal to classify lead for reproductive toxicity with Repr. 1A - H360. We agree with the dossier submitter that classification should be based on intrinsic properties only and not on risk assessment. Consequently metallic lead should be classified in the same way, regardless of particle size.

**Dossier Submitter's Response**

We appreciate your support.

**RAC's response**

Noted

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 04/12/2012 | United Kingdom | Eco-Bat Technologies Ltd | Company- | 5 |

| | | | | |
|---|---|---|---|---|
| | | | Manufacturer | |

**Comment received**

Eco-Bat Technologies Ltd is a member of the International Lead Association and the Pb REACH Consortium. ILA has provided a consolidated response on behalf of members of the Pb REACH consortium. As a consequence, Eco-Bat Technologies Ltd fully supports and subscribes to the comments made by ILA."

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 04/12/2012 | Germany | EppsteinFOILS GmbH & Co.KG | Company-Downstream user | 6 |

**Comment received**

Page 11 Chapter A 3: CLH report dated Sept 20th 2012 is proposing classification of lead metal as toxic for reproduction Category 1 / reproductive toxicity A1 H360DF. Our company producing lead foil for special applications disagrees on that entirely: As proven in other metals, whilst lead powder might be subject to classification the facts for lead metal are substantially different and the solid metal should not be classified on same or even similar terms as lead compounds. Further, at other substances as well chemical or physical treatment like mechanical abrasion does not have an impact on classification, so why on lead?

**Dossier Submitter's Response:** According to the CLP regulation, substances shall be classified based on their intrinsic properties (hazard). Risk should not be considered.

Page 10 Chapter A 2.1: CLH report is referring to the fact that all lead compounds except for those listed singularily are classified. However, this classification of all lead compounds is a simplification which possibly is politically motivated. Reactivity and bioavailability of "all lead compounds" is certainly different from compound to compound.

**Dossier Submitter's Response:** Yes bioavailability may differ between different lead compounds; this does not change the fact that lead metal indeed can be bioavailable. Numerous cases of lead poisoning caused by oral ingestion of a piece of lead (e.g. lead containing jewellery, buttons, etc.), have been described in the literature, even death has been reported. These case reports prove that pieces of lead ingested orally are indeed bioavailable.

Page 10 Chapter A 2.2 ff Lead metal vs. lead compounds and lead ions
Public discussion as well as jurisdiction repeatedly is mixing up metallic lead and lead compounds.
Page 17 Chapter B 2.2: The applications of lead quoted in CLH report are mainly applications of lead compounds. The necessary differentiation towards lead metal is not stated clearly enough. Current applications of lead metal are mostly applications taking advantage of the unique properties of lead.
Contemporary sources of information very often refer to a -as a precaution simplified- classification of all lead compounds as an evidence of enhanced risks. This is possibly a circular argument. Because of public awareness of lead risks the VRAR is suggesting to classify lead powder as a precaution. Central argument is the higher surface-mass-ratio which is making chemical reaction to lead compounds more likely- just like at other metal powders. To use this precaution as an argument to classify lead metal in any shape and condition is a misuse. For other chemical substances possible reactions to toxic compounds is not an issue to discuss classification of the chemical element.
Data for lead toxicity cited are typically gained for lead compounds and soluble lead ions and – following the habits of public discussion- in the CLH report are used for metallic lead as well.

**Dossier Submitter's Response:** See previous answers; in short: substances shall be classified based on their intrinsic properties (hazard), and metallic lead has indeed proved to be bioavailable.

Page 20 Chapter B 4.1.3: The CLP report is claiming that "…as a worst case assumption, one can assume that the bioavailability of metallic lead is equivalent to soluble lead compounds such as e.g. lead acetate." This is a statement which is not proved under scientifically reasonable conditions.

Risks in use of lead and possibilities for improvement through CLP
As far as lead is concerned CLP-regulation will most likely only affect professional use. Occupational lead risks are well known and in professional use well handled. There are already existing regulations for handling of non-metallic and metallic lead and related processes. There is no need for additional pressure on lead use regarding occupational health.

**Dossier Submitter's Response:** The fact that risks arising from professional use (perhaps) already are well handled is not an argument for refraining to classify lead under CLP.

Page 17 Chapter B 2.2: Use of lead in private sector is primarily limited to special applications where the acting persons generally are well aware of possible dangers (fishing, shooting, ballast). Problems arise when recommendations of use are not followed. In these cases more strict declaration does not help.

**Dossier Submitter's Response:** The fact that some or most people may be aware of the possible dangers of lead is not an argument for refraining to classify lead under CLP.

Page 11 Chapter A 3 and Page 17 Chapter B 2.2: Cited examples for intoxications especially of children seem to be related to articles which are not covered by CLP-Regulation (EC) Nr. 1272/2008. As articles from domestic production as well as imported articles will not be covered by this classification this approach does not give a higher standard of safety.

**Dossier Submitter's Response:** This argument is not relevant for not classifying under the CLP-legislation.

Page 17 Chapter B 2.2: There are many products with strong economic impact consisting of lead and which are produced within the EC. Batteries for cars and storage are until now without economic and safe alternative. Shielding applications, as well as intensifying equipment for radiography are most reliable if made of lead and still without technically and economically reasonable alternatives. Classification will affect existing safe domestic production and not affect imported products. Classification will affect European industry without granting a higher standard of safety.
Lead risk awareness could not be enhanced
There are risks in handling lead. There are risks to transform metallic lead to biologically available lead ions as well. On the other hand lead and lead risks are in peoples mind. Classification will not be able to enlarge this awareness. In respect of getting a place on the top of the agenda lead is to be regarded as a topic of yesterday.
Why classification of lead?
Substances with possible dangers after chemical or physical alteration must not necessarily be classified.

**Dossier Submitter's Response:** The CLP-legislation clearly states that substances that have CMR-properties ***shall*** be classified under CLP, it is not optional.

There are other substances of daily use, which in the typical application are hazardous and lethal in actual cases for a considerable number of people today and do not represent a potential threat only. One of the reasons why we believe that a distinction should be made between lead compounds and lead metal.
Promoting classification of lead is a simple idea to demonstrate activity for organizations having no better idea how to try to make our lives safer. Public applause is guaranteed and whilst questions if this is really making an improvement for the environment remains unheard, as they are only expected by those who are affected economically.
We appeal to the politicians in charge to act responsibly with an open mind to facts.

**Dossier Submitter's Response**

Comments have been inserted directly into the above text under each relevant section.

**RAC's response**

The RAC supports the responses of the DS to the comments.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 05/12/2012 | United Kingdom | International Lead Association | Industry or trade | 7 |

| | | | | |
|---|---|---|---|---|
| | | | association | |

**Comment received**

General Comments

About the ILA. The International Lead Association is a membership body that supports companies involved in the mining, smelting, refining and recycling of lead. The ILA represents the producers of about 3 million tons of lead and almost two thirds of lead production in the western world.

As secretariat to the Lead (Pb) REACH Consortium, ILA Europe (a regional branch of the International Lead Association) is acting on behalf of the Lead Registrants for several lead substances including lead metal (CAS 7439-92-1).

ILA provides secretariat services to the European Lead Sheet Association (ELSIA).

The following companies are members of the Pb REACH Consortium, ILA or ELSIA (please refer to Appendix A).

These comments represent the view of member companies.

Executive Summary

We do not believe that the dossier presented by Sweden provides an adequate justification for the classification of massive lead metal and or that the specific concentration limit proposed is scientifically justified. There is a lack of scientific robustness in many of arguments presented and insufficient relevant technical data, supported by references etc., to validate the conclusions reached. We would request that the authors consider the following specific points:

1. Scope: The document draws heavily on evidence offered by Lanphear et al (2005) on effects of blood lead on childhood IQ. Whilst this may be of relevance to discussing risk of children from lead exposure we do not believe it should be cited as the lead effect in CLP classification or in the development of a SCL for reproductive toxicity endpoints. According to the latest ECHA guidance on CLP "it is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, developmental toxicity essentially means adverse effects induced during pregnancy or as a result of parental exposure". New information by Braun et al. 2012 provides the best available data for assessing the developmental windows of susceptibility for the effects of lead on IQ and supports the conclusion that these effects occur postnatally. We therefore question the significance of using postnatal effects on childhood IQ for assessing developmental toxicity classification in relation to CLP and propose that an alternative endpoint such as effects on foetal growth or obstetric outcome be evaluated.

**Dossier Submitter's Response:** Both pre- and post natal exposure to lead can lead to developmental effects in the form of impaired IQ. The nervous system is still under development for several years after birth (see **Davison and Dobbing (1968)*); therefore also post natal toxic insults to the nervous system can be considered to be developmental in nature. The mechanism by which lead causes impaired IQ is not specific for prenatal development; the same effects on IQ also occur after post natal exposure but only if exposure takes place during the (early) years of child hood when the nervous system is still under development. IQ-effects are *not* seen in adults exposed to lead as their nervous systems are already fully developed and no longer susceptible to developmental effects.

The latest version of the ECHA guidance for CLP (under 3.7.1.5.4) states that *"Developmental toxicity includes, in its widest sense, any effect which interferes with normal development of the conceptus, **either before or after birth,** and resulting from exposure of either parent prior to conception, or exposure of the developing offspring during prenatal development, **or postnatally**, **to the time of sexual maturation**".*

And in REACH - information requirements (p.316, chapter R.7a: Endpoint specific guidance. Version 2.0 November 2012) the following is written regarding the two-generation reproduction study (EU B.35, OECD TG 416): *"…using an extended F1 generation **dosing period (to PND day 70)** endpoints addressing **developmental neurotoxicity**".* This means that the dosing period continues until post natal day 70 in the extended F1 generation study that assesses developmental neurotoxicity.

Braun et al. 2012 was published in October 2012 while the final version of the CLH-report for Lead was submitted in September 2012; basing the CLH-report on the Braun-study was therefore impossible. It is also worth noting that Braun et al. (2012) is based partly on the same cohort (from

Mexico City) as in the pooled analysis by Lanphear et al. (2005). The conclusion made by Braun et al. (2005) is that high blood lead concentrations at 2 years of age were most predictive of decreased cognitive abilities among the children in the Mexico City cohort; this conclusion does not contradict the conclusions made my Lanphear et al. (2005).

*Reference: Davison, A.N., and Dobbing, J. (1968). The developing brain. *Applied Neurochemistry,* 178-221, 253-316.

2. Read Across: There is little experimental or human data available on the health effects of lead metal. Evidence included in the Annex XV dossier is for model bioavailable/soluble lead compounds and hence any conclusions on effect of metallic lead are derived by read across. This is not made clear in the dossier and the relevance of using read across for CLP and SCL derivation requires a robust scientific justification. Without such justification the data should not be used.
For many of the conclusions made in the dossier this read across requires three steps. To derive the conclusion as to whether lead metal meets the criteria for classification as Repr. 1A the authors have cited human epidemiology following post natal exposure to children to lead compounds (step 1), assumed that lead metal would have the same effect and dose response (step 2) and then extrapolated this to pre-natal exposures (step 3). We do not think this is scientifically sound, especially when used to derive a SCL which requires detailed quantitative data on dose response.

**Dossier Submitter's Response:** Regardless of how exposure occurs (via lead compounds or via lead metal); it is the lead ion that is responsible for lead toxicity in the body. In all the studies presented, the toxic effects of lead are therefore caused by the same transformation product, i.e. the lead ion, regardless of which lead compound was responsible for the initial exposure.

Therefore this can not be considered as read across in the classical sense, as it is always the ***same*** (not just similar) lead ion exerting its negative effects on the body.

The following excerpts are from guidance:

1. In the CLP guidance, version 3.0, section 1.4.3 (p.48) the following is written regarding common significant metabolites: *"For certain substances without test data the formation of common significant metabolites or information with those of tested substances or information from precursors may be valuable information (IR/CSA, Chapter R.6.2.5.2 and OECD 2004)."*

2. The REACH-guidance on information requirements and chemical safety assessment, section R.6.2.5.2 (p.106) states the following regarding metabolic pathways: "*The underlying hypothesis for a metabolic series is a sequential metabolism of a parent chemical to downstream blood metabolites that are chemicals of interest. Hazard identification studies with the parent compound could then be used to identify the hazards associated with systemic blood levels of the downstream primary and secondary metabolites and once quantified can be used in place of studies using direct exposure to primary and secondary metabolites themselves."*

Taking into account the excerpts above, our way of reasoning regarding "read across", common metabolites and transformation products is supported by the CLP-legislation.

3. Bioavailability: Insufficient consideration is made for the effects of bioavailability of metallic lead when compared to soluble lead compounds. Physico-chemical properties such as surface area play a large role in bioaccessibility (a concept included in the CLP guidance on the classification of metals for effects on aquatic organisms). This needs to be considered in relation to the human health endpoints and merits treating lead in powder and massive form differently for human health classification purposes.
General Comments
• P7 table 3 and p9 table 4 Whilst we appreciate that the scope of the harmonised classification proposal is limited to reproductive toxicity it would appear to be misleading that tables 3 and 4 cite reasons for no classification for endpoints other than toxicity to reproduction as "conclusive but not sufficient for classification" as this is not the case for all endpoints (for example with lead in powder

form the REACH dossier includes a classification as STOT Rep. Exp. 1 (Hazard statement: H372: Causes damage to organs through prolonged or repeated exposure). Therefore the statement in tables 3 and 4 on reason for no classification is misleading. Since the dossier is restricted to consideration of the reproductive toxicity endpoints we would suggest amending entries in the column headed "reason for no classification" to indicate that the endpoints were not considered or include a dash (-) as is the case for other columns in the table

**Dossier Submitter's Response:** We agree that writing something like "not evaluated in this dossier" in the "reason for no classification"-field would provide the clearest information and be less confusing. However; in the IUCLID-dossier for lead these same tables are presented but with a drop-down menu under "reason for no classification". Currently the dossier submitter can only choose one of the following: "data lacking", "inconclusive" or "conclusive but not sufficient for classification". Out of these three options we chose "conclusive but not sufficient for classification" and subsequently put the same phrase in the CLH-report to ensure consistency between the IUCLID-dossier for lead and the CLH-report for lead in word/pdf-format.

• P9 Table 4. We question whether it is correct to include a specific concentration limit of 0.03% in relation to the Dangerous Substances Directive? What is the legal basis for this since the applied methodology utilised in this CLH for defining specific concentration limits for reproductive toxicity was not included in the DSD?

**Dossier Submitter's Response:** Yes, the 0.03% specific concentration limit is copied directly from the "proposed classification according to the CLP-regulation" and not derived separately for DSD. We believe this will not be a problem since the old system; classification according to DSD, will very soon no longer be used at all when CLP takes over completely.

• P9 Labelling. It appears illogical that the proposed R-phrases for lead metal of R60, R61 are more severe than those used for other lead compounds in Annex VI to CLP (R61, R62) when the lead metal classification has been derived by read across from experimental and epidemiology studies undertaken on the aforementioned soluble lead compounds.

**Dossier Submitter's Response:** The proposed R-phrases R60-R61 are consistent with the proposed classification under CLP which is Repr. 1A; H360**DF**. Regarding "read across", see dossier submitter's response under point 2 (page 5-6). Regarding epidemiological studies the source of the exposure is usually not known.

• P10 section 2.1. We do not see the need for the statement "lead is a well-known human toxicant and lead poisoning has been documented way back in history …etc and suggest that this is removed. Lead was certainly used by ancient cultures and there are historical documents describing adverse health events attributed to lead but we fail to see how this is relevant to a 21st Century review of scientific evidence supporting classification and labelling (and specifically to harmonised classification as Repr.1A).

**Dossier Submitter's Response:** Some general history regarding lead is presented in this section and we don't see why this statement should be removed as it is true. The section contains general, historical information about lead and it is there to provide a little background information for the reader.

• P10 section 2.2. Hazard identification of metals, metal compounds and complex metal containing substances (alloys and concentrates) are related to the toxicity of the metal ion and importantly the release or relative bioavailability of the metal ion. We would suggest that the authors pay attention to some of the conclusions made in the short summary for scientific justification for the CLH proposal. Whilst it is the case that many authorities consider lead to be toxic to reproduction, this conclusion is based upon read-across from experimental studies and epidemiological investigations on more bioavailable forms of lead such as soluble lead salts and tetraethyl lead in gasoline. To our knowledge there are no experimental studies undertaken on lead metal. We would argue that it is not necessarily the case that extrapolation of test data from bioavailable forms of lead to elemental lead (especially in a massive form) will necessarily result in a scientifically robust conclusion with respect to classification. Consideration of bioavailability data should be reflected in the relative potency of effects on reproductive function. It is for this reason that we proposed a different classification of lead in massive form in the REACH registration dossier compared to the Annex VI entry for lead compounds. We believe there is quantitative data available to illustrate that extrapolating or read across from reproductive toxicity data on bioavailable lead salts to elemental

lead (especially in the massive form) is over conservative and that no classification or a different category or hazard may be appropriate. The authors need to make it clear that any conclusion reached in section 2.2 is based upon read across.

**Dossier Submitter's Response:** Again, regarding "read across", see dossier submitter's response under point 2 (page 5-6).
And yes, the bioavailability of lead metal massive in large pieces compared to smaller pieces of lead metal (under 1 mm in diameter) may differ, as already discussed in the CLH-report (surface to volume ratio etc.). But larger pieces of lead (over 1 mm in diameter) have indeed been proven to be bioavailable, look at the large number of case reports that describe lead toxicity after the ingestion of a "larger" lead containing article (such as jewellery, buttons etc). And according to CLP, substances shall be classified according to their intrinsic properties.

P10 section 2.2. We believe that further discussion is necessary to support the statements made on the effect of lead. While it is true that studies of men exposed occupationally to high concentrations of lead have documented effects upon semen quality, testicular atrophy has not been observed. Histopathological effects upon the testes have been suggested in animal studies, but uncertainty exists as to whether mechanisms of impact on male reproductive function in animals are the same as is observed in humans. Read across from animal studies is inappropriate under such circumstances.
We are further concerned about conclusions made on neurobehaviorial effects mediated by prenatal lead exposure. Whilst there is evidence in the scientific literature that supports an effect on childhood IQ following postnatal exposure to lead in bioavailable forms, the evidence for effects following pre-natal exposure is weaker and in many cases confounded by continued postnatal exposures.
The best available data available is a recent study by Braun et al 2012. These authors tried to assess windows of susceptibility to lead induced cognitive effects in children. Four Mexico City cohorts were combined which has yielded for analysis 1035 mother-child pairs with gestational and postnatal blood lead available at 1, 2, 3, and 4 years of age and assessment of cognition at 4 years. After adjusting for confounders, postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels. This most recent finding mirrors the conclusions of Pocock et al (1994) whose systematic review found little relationship between prenatal blood levels and subsequent IQ test scores in prospective studies of child development.
The current CLH guidelines further indicate that classification for reproductive toxicity should be restricted to consideration of effects on fertility and developmental toxicity (which is generally considered to mean adverse effects induced during pregnancy or as a result of parental exposure). We thus question the relevance of including discussion of IQ effects resulting from post-natal exposure during childhood in the justification. The statement that "there is no safe exposure level for lead induced developmental neurotoxicity" refers to conclusions drawn from studies of postnatal lead exposure. Again we argue that, in the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure", a statements that there is no safe prenatal exposure levels is not supported by the quantitative scientific evidence.

**Dossier Submitter's Response:** See dossier submitter's comment under point 1 (page 5).

• P11 Section 2.4. The Industrial DSD self-classification for lead metal powder (particle size ,1mm) cited in the CLH report is not that included in the REACH registration dossier which was R60 May impair fertility, R61 May cause harm to the unborn child. We appreciate that this is not consistent with the CLP self-classification reported by Industry for the same substance of Repr. 1.A (H360Df) and can only presume that the Swedish CA amended the Industry DSD self-classification so that it is aligned with that reported for CLP? We question whether this was the correct action and it may have been more appropriate to flag up the discrepancy noted.

**Dossier Submitter's Response:** Your observations are correct, it is our mistake and this should be corrected. It should say "R60, R61" (and not "R61, R62") on page 11 under *2.4.2; Current self-classification and labelling based on DSD criteria*. However, as you mentioned, this DSD self-classification is not consistent with the CLP self-classification.

• P11 Section 3. Industry proposed a different classification for lead in massive form because the reproductive toxicity classification for elemental lead is based upon "read across" from more bio-available forms and that in massive form there is limited opportunity under normal handling and use

for exposure to lead -metal itself. Processing of the massive metal results in exposure to lead compounds [predominantly oxides] and not lead metal powder of fume.

**Dossier Submitter's Response:** These questions have already been discussed and answered previously; see p.5-6 (read across).

• We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must be given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative oral bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). This two-order of magnitude difference in bioavailability is quantitatively significant and the CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that whereas metallic powder at extremely small particle sizes, exhibits oral bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979), massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited oral bioavailability. This observation of limited bioaccessibility of lead in massive form is supported by data obtained during transformation and dissolution tests (T/dp) [OECD 2001] undertaken to establish aquatic toxicity classification of lead in massive and powder form. Lead in powder form (<75µm) showed high rates of dissolution (>3000 µg/l following 24hr incubation at pH 6) compared to massive lead (300 µg/l) following 24hr incubation under the same conditions. This differential in relative bioaccessibility results in powdered lead receiving an environmental classification as Aquatic Acute and Chronic 1 whereas the massive form is not classified. This concept should equally be applied to evaluation of the relative human health hazard assessment.

**Dossier Submitter's Response:** This question has been answered previously but in short; a large number of case reports show that larger pieces of lead are indeed bioavailable after oral consumption. The transformation and dissolution tests performed to assess aquatic toxicity can not be used to assess human bioavailability after oral consumption; relative bioavailability in these aquatic tests can not be directly translated into relative bioavailability in the human body. After a quick look at other classified metals in annex VI of CLP it can be noted that no other metals have different classifications for different particle sizes when it comes to the human health hazard end points. Only for the environmental end points discrepancies can be found between the classifications for different particle sizes (example from table 3.1 in annex VI: Nickel: no environmental classification; Nickel powder: aquatic chronic 3).

• Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification.
Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size and surface area available for metal dissolution modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property relevant for purposes of classification.

**Dossier Submitter's Response:** Size matters, but is not an intrinsic property. Lead surfaces may give dermal contamination which can lead to ingestion via the hands. Handling of metallic lead may also cause exposure.

• P11 Section 3. The vast majority of massive lead produced is not easily ingested due to its large size. When ingestion of small objects does occur, most transit the gastrointestinal tract without yielding significant exposure. Quantitative data specific to lead objects is not available but studies of other small metallic objects confirm this generalization (Litovitz et al., 2010). Only rarely do such objects lodge in the gastrointestinal tract for a period of time that permits dissolution (and thus exposure) of biological significance. We further note that adults are far less likely than children to engage in the ingestion of non-food items. Adult human exposure to lead via ingestion of metallic objects is thus contingent upon two low probability events (ingestion and retention in the GI tract) that seem to exceed the criteria of "reasonably foreseeable" events. We further note that risks to children (and adults) presented by this rare occurrence are being addressed by various restrictions that are in progress related to the REACH regulation (e.g. jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity.

**Dossier Submitter's Response:** This question has been adressed previously. In short, classification should be based on intrinsic properties and not on risk of exposure. The fact that lead is being addressed by various restrictions in e.g. REACH should and can not exclude a classification according to CLP.

• P11 Section 3. The justification for a harmonised classification for all physical forms cannot be made on the basis of mandating production of a safety data sheet as a method for addressing risk from exposures in the home environment as safety data sheets are only required for use by professional users. Moreover whilst we support the observation that melting lead in the home to produce "bullets and fishing weights" is not appropriate we do not believe this is a good argument for justifying the harmonised classification proposed. This behaviour would not be mitigated by this risk management option and would be better addressed through education or possibly a REACH restriction.

**Dossier Submitter's Response:** This argument is not relevant for not classifying under the CLP-legislation.

• P11 Section 3 The comment that lead is a soft metal that can easily "rub off" on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being "rubbed off" on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and determined it to be quite low (1 – 3
ingestion further determined that only modest impacts upon blood lead would result under typical exposure scenarios. It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable

**Dossier Submitter's Response:** It may be true that lead-metal-to-hand exposure is more likely to take place via oxidized lead on the metal surface than by the actual metal "rubbing-off" onto the hand. Either way, the hand is exposed to lead in some form and if this lead gets into the body via hand-to mouth behavior, lead ions will result in the body and exert their toxicity. The resulting lead ions in the body will in both cases have metallic lead as the source, even if the paths to get there are different.

• P17 Section 2.1 In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores. We suggest the authors review the lead REACH registration dossier for more information on manufacturing and use of lead.

**Dossier Submitter's Response:** Noted, but this has no relevance for classification.

• P17 Section 2.2. We do not believe this section accurately reflects current use of lead in the EU and requires a re-write. It implies that there is significant use in consumer products/articles which is not the case.
o Over 70% of lead used in the EU is for lead-acid batteries for both automotive and back-up power use.
o Lead sheet is also used as a weather-proofing material in the construction industry across Northern Europe.
o Lead is widely used for radiation shielding, for example in healthcare, airport security, defence, nuclear decommissioning, non-destructive testing, underwater cable sheathing etc.
o Lead has essential industrial applications in the chemicals, steel and other industries. It is also widely used in ballast, counterbalance and some ballistic applications
Consumer items such as fishing sinkers, "tin soldiers", jewellery and brass buttons/zips are extremely minor applications, representing much less than 1% of annual use. Many of these minor applications are already subject to existing or planned EU or national restrictions and a harmonised classification of lead as Repr. 1A would not have any impact as a risk management measure.
It is misleading to state that lead is used in paint. Lead metal has never been used in paint and the use of lead compounds in household paint has been banned under the Marketing & Use Directive since 1989 (although lead compounds may rarely be used for some specialised applications)

It is misleading to state that lead is frequently used in solders and electronics. Most solders used in the electronics industry must be lead-free. Finally lead metal is not used in crystal glass manufacture. In this case lead monoxide is the entity used.

**Dossier Submitter's Response:** The section on identified uses is meant to give examples on how lead is used and in which products it can be found. The intention is not to give quantitative information on annual use, but rather to give an overview of where the "ordinary person" could be exposed.

• P18 Section 4. We question the relevance of providing information on blood lead levels in children as this is not the result of exposure to lead metal. If the authors believe it relevant to include data on blood lead in children they may also wish to report that blood lead levels in the general population in the EU has significantly fallen since the introduction of a ban of tetraethyl lead in petrol. This is illustrated by the situation in Sweden where an average decline in children's blood lead is reported to be approximately 5% per year between 1995 and 2007 (Strőmberg et al 2008).

**Dossier Submitter's Response:** The only blood lead level mentioned in section 4 is the one of the four year old boy that died from lead poisoning (blood lead 180 µg/dL), after ingesting a bracelet charm containing *metallic* lead.

• P18 Section 4.1.2 Oral absorption rate. This section could benefit from inclusion of information on relative absorption of soluble lead compounds (from which the data on reproductive toxicity is derived) compared to metallic or elemental lead. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds (Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.

**Dossier Submitter's Response:** The bio-availability of metallic lead has been discussed previously (see previous comments on e.g. p1 and p3). The data on children's uptake of lead is indeed relevant; the developmental effects of lead are caused by both pre- and post natal exposure.

• P19 Inhalation rate We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.

**Dossier Submitter's Response:** Particle size has already been discussed, see previous comments on e.g. p3 and p7.

• P 19 Dermal Absorption Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surface is far lower than suggested here. We also note that the occupational exposure scenarios described entail the deposition of inorganic lead compounds as dust fallout from occupational aerosols. There is little or no metallic lead in these dusts as they are predominantly lead oxides.

**Dossier Submitter's Response:** Lead is the source of the exposure. If the exposure takes place via lead oxide which results in lead ions in the body it is still the lead that shall be classified.

• P19 Metabolism While urinary excretion is an important route of elimination of lead from the body, biliary excretion is comparable in magnitude and should be noted. We recommend that the authors include information presented in the Lead REACH Registration dossier and the VRAL (ILA-Europe 2008)

**Dossier Submitter's Response:** Excretion via the urine and bile is discussed under "Elimination" on page 20 in the CLH-report.

• P20 Section 4.1.3 As described previously it is not appropriate to take a worst case assumption that the bioavailability of metallic lead is equivalent to that of soluble lead compounds. Whilst dependent upon factors such as particle size etc there is evidence to show that metallic lead is much less bioavailable that soluble lead compounds (approx. 1%). We also wish to emphasize yet again that exposure of adults is of primary concern for reproductive toxicity – not the exposure of young children.

**Dossier Submitter's Response**: As you mention, oral bioavailability is dependent on many factors such as particle size, amount of time spent in the GI tract, pH of the GI tract etc. As a worst case scenario, the bioavailability of metallic lead can be assumed to be equal to that of soluble lead compounds. And as stated previously; young children's exposure to lead is indeed relevant; the developmental effects of lead are caused by both pre- and post natal exposure.

**Dossier Submitter's Response**

Comments have been inserted directly into the above text under each relevant section.

**RAC's response**

RAC generally supports the response of the DS to the comments.
The RAC specifically supports the DS in that the CLP-criteria for developmental toxicity can also apply to post-natally induced neurotoxicity. Although section 3.7.1.4 of Annex I to CLP places emphasis on pre-natal effects, the criteria do not specifically exclude adverse effects from post-natal exposure. However, lead clearly demonstrates adverse effects on neurodevelopment after pre-natal exposure.
Regarding the DS proposal for C&L lead of all its physical form see RAC responses to comment 1.
RAC discussed the rationale how to derive a SCL value following the CLP Guidance (3.7.2.5.) as for lead the setting of the SCL is based on expert judgement of human data. In its analysis RAC used key examples to calculate ED10 equivalents that represent worst case or best case calculations of external doses. Taking remaining uncertainties into account RAC decided to propose a SCL of 0.03% for developmental toxicity; from a purely formal point of view the calculations could also result in a lower SCL. potent.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 05/12/2012 | Finland | | MemberState | 8 |

**Comment received**

We concur with the dossier submitter that there is a need for a harmonised classification for lead in its metallic form. The CLH report is in our opinion very clear and well presented.

**Dossier Submitter's Response**

Thank you, your support is appreciated.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | | MemberState | 9 |

**Comment received**

The German CA supports the proposed classification Repr. 1A – H360 according to CLP-regulation (CLP) and Repr. Cat. 1; R60-61 according to directive 67/548/EEC (DSD), respectively. There is clear evidence of reproductive toxicity as an intrinsic and hazardous property of lead in a large body of human studies. The same classification for all physical forms, regardless of particle size, is supported. Potential exposures for different routes and bioavailability from different forms of lead have been demonstrated by several case reports.
Additionally, the current industrial self-classification as STOT RE 1, H372: 'Causes damage to the central nervous system and systems for reproduction through prolonged or repeated exposure' should at least be mentioned in the CLH report. Especially, as the developmental toxicity of lead is based on neurodevelopmental effects in the offspring the neurotoxicity should have been addressed in the CLH report as well.

References:
p.43, WHO (2003): The background document has been revised.
The current version is of 2011.

**Dossier Submitter's Response**

Thank you for your support. Yes, the industrial self-classification for STOT-RE should have been mentioned in the CLH-report. Thank you for pointing out the update in the background document from WHO.

| RAC's response | | | | |
|---|---|---|---|---|
| Noted, see response to comment 7. | | | | |
| **Date** | **Country** | **Organisation** | **Type of Organisation** | **Comment number** |
| 06/12/2012 | United Kingdom | Britannia Refined Metals Ltd. | Company-Manufacturer | 10 |
| **Comment received** | | | | |
| Britannia Refined Metals Ltd. supports the submission made by the International Lead Association. | | | | |
| **Dossier Submitter's Response:** | | | | |
| Noted. | | | | |
| **RAC's response** | | | | |
| Noted. | | | | |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | United Kingdom | Lead Shield Engineering Ltd | Company-Manufacturer | 11 |
| **Comment received** | | | | |
| As director of a very specialised engineering firm, we already pay fees for manufacturing lead and our factory is regularly checked for health and safety relating to the use of lead. Any further costs or restrictions to this process could well determine that the future of this firm is financially not viable! There are very few firms like us in the UK and Europe. | | | | |
| **Dossier Submitter's Response:** | | | | |
| Your concern is understandable, but this is no reason for not classifying under CLP. | | | | |
| **RAC's response** | | | | |
| Noted. | | | | |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | BSB Recycling GmbH | Company-Manufacturer | 12 |
| **Comment received** | | | | |

P7, table 3, Classification table: While it is clearly stated, that the scope of the harmonised classification proposal is limited to reproductive toxicity, this table implies that also other endpoints have been considered. The statement "conclusive, but not sufficient for classification" is misleading, since lead metal has no PC-hazards and some endpoints are considered as relevant for the powder form of lead. We would suggest amending entries in the column headed "reason for no classification" to indicate that the endpoints were not considered or include a dash (-) as was the case for other columns in the table.

P9, labelling: We do not understand why the proposed R-phrases for lead metal of R60, R61 are more severe than other lead compounds on Annex VI to CLP (R61, R62).

P11 Section A 3, Justification that action is needed at community level: Industry proposed a different classification for lead in massive form due the arguments that in massive form there is limited opportunity under normal handling and use for exposure to lead. In many cases processing of the massive results in exposure to lead compounds - predominantly oxides - and not lead metal. Related risk management measures are already part of the supply chain communication. We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). A two-order of magnitude difference in bioavailability is quantitatively significant and CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited bioavailability. We acknowledge that bioavailability varies as a function of particle size and increases as particle size decreases. At extremely small particle sizes, metallic lead particles exhibit bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979). For example, a 200 µm particle has a relative bioavailability of 14% and progressively

increases to 100% as particle size decreases to 6 µm. Although the form of a substance might not be a consideration under normal circumstances, the fact that particle size has a significant impact upon bioavailability indicates that particle size affects the intrinsic properties (bioavailability) of metallic lead. Industry thus proposed classification of lead metal powder but not massive forms of lead. This distinction was reinforced by exposure route considerations. Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification. Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property for purposes of classification.
The risks related to use and exposure of lead and lead compounds have been discussed for years. Aiming at limiting the risks for human beings and the environment, regulations have been implemented in different areas and lead has been substituted in several products. Manufacture, use and recycling have been improved for other products. As a result of these activities a decrease of lead concentration in the environment and a decrease of lead blood levels, which is the main indicator for human exposure, have been reported.
80% of the lead produced in Europe (primary and secondary metal) is used for the production of lead acid batteries. The Berzelius Metall GmbH (http://www.berzelius.de/berzelius_en/batterieentsorgung/?navid=6) is a major collector and recycler of these accumulators in Germany. In Germany nearly 100% of lead batteries are collected and material utilization rate is > 90%, which exceeds the requirements of the Battery Directive (2006/66/EC). The manufacture and recycling process is subject to IPPC (Dir 2008/1/EC) and IED (Dir 2010/75/EU) and implementation of BREF notes is mandatory. Related to cars, life cycle emission has been reduced by 99.6% mainly due to increased battery recycling efforts (Ökoinstitut 2010 ).
Reprotoxic effects of lead-ion detected in the human body have been widely discussed and accepted and trigger a high standard of risk management in lead industry. This is also reported in the CSR in the registration framework and the voluntary risk assessment report VRAR). These documents are already providing valuable information on how risks from lead can be effectively managed, for example in the case of worker health, and industry is committed to implementing these measures. The report is also helping to identify areas where further research is needed and again industry is committed to delivering this.
On the other hand exposure to lead is still an issue. But exposure of the general population cannot be explained by the use of products containing lead metal. More bioavailable lead compounds are still in use and diffuse sources (agriculture, past pollution, contaminated food) play an imported role in human exposure. To reduce risks related to the latter completely different measures have to be implemented.
Swallowable pieces, especially those containing lead, should be kept out of reach for children. Consumer products with potential direct contact like toys (even for adults), decoration, furniture should not contain lead. We further note that risks to children (and adults) are being addressed by various restrictions that are in progress related to the REACH regulation (eg jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity. In most cases the related products have been imported from outside EU and there is not legal requirement to label consumer articles with related information.
We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.
We can assume that the source for lead exposure of the general population is rather diffuse than the result of contact with lead metal or lead containing articles. It is thus questionable, whether exposure of the general population will be influenced by classification of lead metal
According to a report by Fraunhofer ISI on behalf of the German UBA (UBA 2003) there is a basic need for action to reduce the environmental burden due to non-point emissions of lead. As main sources for lead burden traffic (cars) and agriculture have been identified. Reduction potentials are described for lead free brake linings and wheel weights (replacement already ongoing) and measures reducing erosion of soil of agricultural areas (lead input trough mineral fertilizer and other fertilizers). These sources are in no way affected by classification or authorization since the concentrations in the fertilizers are far below concentration threshold for classification.
In the past 20 years the blood levels in the general population have been significantly fallen since the introduction of a ban of tetraethyl lead in petrol (Kemi 2007, p. 8, UBA 2007b). The average decline

in children's blood lead has been approximately 5% per year between 1995 and 2007. The general population is exposed to lead principally via food. For adults more than 80% of the daily uptake of lead happens via food. The sources are dust deposition on plants and on feeding for animals. Children may take up lead via ingestion of soil and dust particles.
The comment that lead is a soft metal that can easily "rub off" on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being "rubbed off" on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and determined it to be quite low (1 – 3 µg/cm2 of exposed skin). It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable.

P17 Section B 2.1 Manufacture: In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores.

P17, section B 2.2, Identified uses: Please consider that aviation fuel, paints and crystal glass do not contain lead in the metallic form but lead compounds which are not subject to this classification proposal. The main application of metallic lead is in lead acid batteries (80-90%). In many applications and articles the essential lead is embedded in the object with no relevant contact for the user (machinery, weights, radiation protection, batteries).
Articles containing unwanted and also unessential lead parts with directly accessible surfaces are found more often in imported products (buttons, zippers, jewelries).

P18, section 4.1.2, Oral absorption rate. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds (Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.
P19 Inhalation rate: We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.
P 19 Dermal Absorption: Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surfaced is far lower than suggested here.
---
*ECHA's comment: The literature list below was provided as an attachment.*

Literature Cited (Lead CLH Public Consultation Comments Berzelius)

Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env. Health 34: 280-285.

Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.

Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN, Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899

Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.

Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory

approach to assess the potency of substances toxic to the reproduction Regul Toxicol Pharmacol: 63(1):97-105

OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media

Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.

Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71.

U.S. Environmental Protection Agency (2007). Estimation of the relative bioavialablity of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77.

UBA 2003: Einträge von Kupfer, Zink und Blei in Gewässer und Böden - Analyse der Emissionspfade und möglicher Emissionsminderungsmaßnahmen, Forschungsbericht 202 242 20/02, UBA-FB 000824, Fraunhofer ISI 2003

Kemi 2007: lead in articles: http://www.kemi.se/Documents/Publikationer/Trycksaker/Rapporter/Report5_07_Lead_in_articles.pdf

UBA 2007: Blei im Blut: http://www.umweltbundesamt-daten-zur-umwelt.de/umweltdaten/public/theme.do?nodeIdent=2887

Ökoinstitut 2010: End-of-Life vehicle directive 2000/53/EC Annex II: Study on analysis of costs and environmental benefits of heavy metal ban, and proposal for better regulation, November 2010
Lead CSR: chemical safety report of lead metal, LR: Berzelius Stolberg GmbH, lead REACH consortium, 2010, full document can be provided on request.

ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)

**Dossier Submitter's Response**

The comments are much the same as those presented by the International Lead Association, please see Dossier submitter's responses under comment number 7 (ILA), starting on page 4.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | JL Goslar GmbH | Company-Downstream user | 13 |

**Comment received**

JL Goslar GmbH is in line with the consolidated response of the ILA/ Pb Reach Consortium. We are not able to give basic scientific comments to all items discussed in the dossier of the Swedish Chemicals Agency. That's why we support the response of the ILA. We are working in Goslar with lead for more than 100 years. Based on this long term experiences we can not follow the explanation of the above called dossier.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Denmark | | MemberState | 14 |

**Comment received**

The Danish CA supports the proposal for a harmonised classification of lead with Repr. 1A (H360 DF). We agree that this classification shall apply regardless of the physical form of the metal (i.e. both massive and powder form). See specific comments on the SCL.

**Dossier Submitter's Response**

Thank you for your support.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Berzelius Stolberg (BBH) | Company - Manufacturer | 15 |

**Comment received**

P7 table 3 and p9 table 4 Whilst we appreciate that the scope of the harmonised classification proposal is limited to reproductive toxicity it would appear to be misleading that tables 3 and 4 cite reasons for no classification for endpoints other than toxicity to reproduction as "conclusive but not sufficient for classification" as this is not the case for all endpoints (for example with lead in powder form the REACH dossier includes a classification as STOT Rep. Exp. 1 (Hazard statement: H372: Causes damage to organs through prolonged or repeated exposure). Therefore the statement in tables 3 and 4 on reason for no classification is misleading. Since the dossier is restricted to consideration of the reproductive toxicity endpoints we would
suggest amending entries in the column headed "reason for no classification" to indicate that the endpoints were not considered or include a dash (-) as was the case for other columns in the table

P9 Table 4. We question whether it is correct to include a specific concentration limit of 0.03% in relation to the Dangerous Substances Directive? What is the legal basis for this since the applied methodology utilised in this CLH for defining specific concentration limits for reproductive toxicity was not included in the DSD?

P9 Labelling. It appears illogical that the proposed R-phrases for lead metal of R60, R61 are more severe than those used for other lead compounds in Annex VI to CLP (R61, R62) when the lead metal classification has been derived by read across from experimental and epidemiology studies undertaken on the aforementioned soluble lead compounds.
P10 section 2.1. We do not see the need for the statement "lead is a well-known human toxicant and lead poisoning has been documented way back in history …etc and suggest that this is removed. Lead was certainly used by ancient cultures and there are historical documents describing adverse health events attributed to lead but we fail to see how this is relevant to a 21st Century review of scientific evidence supporting classification and labelling (and specifically to harmonised classification as Repr.1A).

P10 section 2.2. Hazard identification of metals, metal compounds and complex metal containing substances (alloys and concentrates) are related to the toxicity of the metal ion and importantly the release or relative bioavailability of the metal ion. We would suggest that the authors pay attention to some of the conclusions made in the short summary for scientific justification for the CLH proposal. Whilst it is the case that many authorities consider lead to be toxic to reproduction, this conclusion is based upon read-across from experimental studies and epidemiological investigations on more bioavailable forms of lead such as soluble lead salts and tetraethyl lead in gasoline. To our knowledge there are no experimental studies undertaken on lead metal. We would argue that it is not necessarily the case that extrapolation of test data from bioavailable forms of lead to elemental lead (especially in a massive form) will necessarily result in a scientifically robust conclusion with respect to classification. Consideration of bioavailability data should be reflected in the relative potency of effects on reproductive function. It is for this reason that we proposed a different classification of lead in massive form in the REACH registration dossier compared to the Annex VI entry for lead compounds. We believe there is quantitative data available to illustrate that extrapolating or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is over conservative and that no classification or a different category or hazard may be appropriate. The authors need to make it clear that any conclusion

reached in section 2.2 is based upon read across.

P10 section 2.2. We believe that further discussion is necessary to support the statements made on the effect of lead. While it is true that studies of men exposed occupationally to high concentrations of lead have documented effects upon semen quality, testicular atrophy has not been observed. Histopathological effects upon the testes have been suggested in animal studies, but uncertainty exists as to whether mechanisms of impact on male reproductive function in animals are the same as is observed in humans. Read across from animal studies is inappropriate under such circumstances.
We are further concerned about conclusions made on neurobehaviorial effects mediated by prenatal lead exposure. Whilst there is evidence in the scientific literature that supports an effect on childhood IQ following postnatal exposure to lead in bioavailable forms, the evidence for effects following pre-natal exposure is weaker and in many cases confounded by continued postnatal exposures.
The best available data available is a recent study by Braun et al 2012. These authors tried to assess windows of susceptibility to lead induced cognitive effects in children. Four Mexico City cohorts were combined which has yielded for analysis 1035 mother-child pairs with gestational and postnatal blood lead available at 1, 2, 3, and 4 years of age and assessment of cognition at 4 years. After adjusting for confounders, postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels. This most recent finding mirrors the conclusions of Pocock et al (1994) whose systematic review found little relationship between prenatal blood levels and subsequent IQ test scores in prospective studies of child development.
The current CLH guidelines further indicate that classification for reproductive toxicity should be restricted to consideration of effects on fertility and developmental toxicity (which is generally considered to mean adverse effects induced during pregnancy or as a result of parental exposure). We thus question the relevance of including discussion of IQ effects resulting from post-natal exposure during childhood in the justification. The statement that “there is no safe exposure level for lead induced developmental neurotoxicity” refers to conclusions drawn from studies of postnatal lead exposure. Again we argue that, in the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean “adverse effects induced during pregnancy or as a result of parental exposure”, a statements that there is no safe prenatal exposure levels is not supported by the quantitative scientific evidence.

P11 Section 2.4. The Industrial DSD self-classification for lead metal powder (particle size ,1mm) cited in the CLH report is not that included in the REACH registration dossier which was R60 May impair fertility, R61 May cause harm to the unborn child. We appreciate that this is not consistent with the CLP self-classification reported by Industry for the same substance of Repr. 1.A (H360Df) and can only presume that the Swedish CA amended the Industry DSD self-classification so that it is aligned with that reported for CLP?

P11 Section 3. Industry proposed a different classification for lead in massive form because the reproductive toxicity classification for elemental lead is based upon “read across” from more bio-available forms and that in massive form there is limited opportunity under normal handling and use for exposure to lead -metal itself. Processing of the massive metal results in exposure to lead compounds [predominantly oxides] and not lead metal powder of fume.
We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must be given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative oral bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). This two-order of magnitude difference in bioavailability is quantitatively significant and the CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that whereas metallic powder at extremely small particle sizes, exhibits oral bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979), massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited oral bioavailability. This observation of limited bioaccessibility of lead in massive form is supported by data obtained during transformation and dissolution tests (T/dp) [OECD 2001] undertaken to establish aquatic toxicity classification of lead in massive and powder form. Lead in powder form (<75µm) showed high rates of dissolution (>3000 µg/l following 24hr incubation at pH 6) compared to massive lead (300 µg/l) following 24hr incubation under the same conditions. This differential in relative bioaccessibility results in powdered lead receiving an

environmental classification as Aquatic Acute and Chronic 1 whereas the massive form is not classified. This concept should equally be applied to evaluation of the relative human health hazard assessment.
Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification.
Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size and surface area available for metal dissolution modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property relevant for purposes of classification.

P11 Section 3. The vast majority of massive lead produced is not easily ingested due to its large size. When ingestion of small objects does occur, most transit the gastrointestinal tract without yielding significant exposure. Quantitative data specific to lead objects is not available but studies of other small metallic objects confirm this generalization (Litovitz et al., 2010). Only rarely do such objects lodge in the gastrointestinal tract for a period of time that permits dissolution (and thus exposure) of biological significance. We further note that adults are far less likely than children to engage in the ingestion of non-food items. Adult human exposure to lead via ingestion of metallic objects is thus contingent upon two low probability events (ingestion and retention in the GI tract) that seem to exceed the criteria of “reasonably foreseeable” events. We further note that risks to children (and adults) presented by this rare occurrence are being addressed by various restrictions that are in progress related to the REACH regulation (e.g. jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity.

P11 Section 3. The justification for a harmonised classification for all physical forms cannot be made on the basis of mandating production of a safety data sheet as a method for addressing risk from exposures in the home environment as safety data sheets are only required for use by professional users. Moreover whilst we support the observation that melting lead in the home to produce “bullets and fishing weights” is not appropriate we do not believe this is a good argument for justifying a harmonised classification. This behaviour would not be mitigated by adoption of a harmonised classification of Repr. 1A and would be better addressed through education or possibly a REACH restriction.

P11 Section 3 The comment that lead is a soft metal that can easily “rub off” on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being “rubbed off” on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and
determined it to be quite low (1 – 3 Modelling of hand to mouth transfer
and subsequent ingestion further determined that only modest impacts upon blood lead would result under typical exposure scenarios. It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable

P17 Section 2.1 In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores. We suggest the authors review the lead REACH registration dossier for more information on manufacturing and use of lead.

P17 Section 2.2. We do not believe this section accurately reflects current use of lead in the EU and implies that there is significant use in consumer products/articles which is not the case.
- Over 70% of lead used in the EU is for lead-acid batteries for both automotive and back-up power use.
- Lead sheet is also used as a weather-proofing material in the construction industry across Northern Europe.
- Lead is widely used for radiation shielding, for example in healthcare, airport security, defence, nuclear decommissioning, non-destructive testing, underwater cable sheathing etc.
- Lead has essential industrial applications in the chemicals, steel and other industries. It is also widely used in ballast, counterbalance and some ballistic applications

Consumer items such as fishing sinkers, “tin soldiers”, jewellery and brass buttons/zips are extremely minor applications, representing much less than 1% of annual use. Many of these minor applications are already subject to existing or planned EU or national restrictions and a harmonised classification of lead as Repr. 1A would not have any impact as a risk management measure.
It is misleading to state that lead is used in paint. Lead metal has never been used in paint and the use of lead compounds in household paint is now banned in the EU (although lead compounds may rarely be used for some specialised applications)
It is misleading to state that lead is frequently used in solders and electronics. Most solders used in the electronics industry must be lead-free. Finally lead metal is not used in crystal glass manufacture. In this case lead monoxide is the entity used.

P18 Section 4 . If the authors believe it relevant to include data on blood lead in children they may also wish to report that blood lead levels in the general population in the EU has significantly fallen since the introduction of a ban of tetraethyl lead in petrol. The average decline in children’s blood lead has been approximately 5% per year between 1995 and 2007.

P18 Section 4.1.2 Oral absorption rate. This section could benefit from inclusion of information on relative absorption of soluble lead compounds (from which the data on reproductive toxicity is derived) compared to metallic or elemental lead. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds ( Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.

P19 Inhalation rate We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.

P 19 Dermal Absorption Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surface is far lower than suggested here. We also note that the occupational exposure scenarios described entail the deposition of inorganic lead compounds as dust fallout from occupational aerosols. There is little or no metallic lead in these dusts as they are predominantly lead oxides.

P19 Metabolism While urinary excretion is an important route of elimination of lead from the body, biliary excretion is comparable in magnitude and should be noted. We recommend that the authors include information presented in the Lead REACH Registration dossier and the VRAL (ILA-Europe 2008)

P20 Section 4.1.3 As described previously it is not appropriate to take a worst case assumption that the bioavailability of metallic lead is equivalent to that of soluble lead compounds. Whilst dependent upon factors such as particle size etc there is evidence to show that metallic lead is much less bioavailable that soluble lead compounds (approx. 1%). We also wish to emphasize yet again that exposure of adults is of primary concern for reproductive toxicity – not the exposure of young children.
---

*ECHA’s comment: The text below was submitted as an attachment.*

Lead CLH Public Consultation

Executive Summary
We do not believe that the dossier presented by Sweden provides an adequate justification for the classification of massive lead metal and or that the specific concentration limit proposed is scientifically justified. There is a lack of scientific robustness in many of arguments presented and insufficient relevant technical data, supported by references etc., to validate the conclusions reached. We would request that the authors consider the following specific points:
1. Scope: The document draws heavily on evidence offered by Lanphear et al (2005) on effects of

blood lead on childhood IQ. Whilst this may be of relevance to discussing risk of children from lead exposure we do not believe it should be cited as the lead effect in CLP classification or in the development of a SCL for reproductive toxicity endpoints. According to the latest ECHA guidance on CLP "it is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, *developmental toxicity essentially means adverse effects induced during pregnancy or as a result of parental exposure*". New information by Braun et al. 2012 provides the best available data for assessing the developmental windows of susceptibility for the effects of lead on IQ and supports the conclusion that these effects occur postnatally. We therefore question the significance of using postnatal effects on childhood IQ for assessing developmental toxicity classification in relation to CLP and propose that an alternative endpoint such as effects on foetal growth or obstetric outcome be evaluated.

2. Read Across: There is little experimental or human data available on the health effects of lead metal. Evidence included in the Annex XV dossier is for model bioavailable/soluble lead compounds and hence any conclusions on effect of metallic lead are derived by read across. This is not made clear in the dossier and the relevance of using read across for CLP and SCL derivation requires a robust scientific justification. Without such justification the data should not be used.
For many of the conclusions made in the dossier this read across requires three steps. To derive the conclusion as to whether lead metal meets the criteria for classification as Repr. 1A the authors have cited human epidemiology following post natal exposure to children to lead compounds (step 1), assumed that lead metal would have the same effect and dose response (step 2) and then extrapolated this to pre-natal exposures (step 3). We do not think this is scientifically sound, especially when used to derive a SCL which requires detailed quantitative data on dose response.

3. Bioavailability: Insufficient consideration is made for the effects of bioavailability of metallic lead when compared to soluble lead compounds. Physico-chemical properties such as surface area play a large role in bioaccessibility (a concept included in the CLP guidance on the classification of metals for effects on aquatic organisms). This needs to be considered in relation to the human health endpoints and merits treating lead in powder and massive form differently for human health classification purposes.
---
*ECHA's comment: The literature list below was submitted as an attachment.*

Literature Cited (Lead CLH Public Consultation Comments Berzelius Stolberg)
Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env. Health 34: 280-285.

Bonde, J.P., Joffe, M., Apostoli, P., Dale, A., Kiss, P., Spano, M., Caruso, F., Giwercman, A., Bisanti, L., Porru, S., Vanhoorne, M., Comhaire, F., Zschiesche, W. (2002). Sperm Count And Chromatin Structure In Men Exposed To Inorganic Lead: Lowest Adverse Effect Levels. Occup Environ Med 59: 234-242.

Bornschein, R.L., Grote, J., Mitchell, T., Succop, P.A., Dietrich, K.N., Krafft, K.M., Hammond, P.B. (1989). Effects Of Prenatal Lead Exposure On Infant Size At Birth. In Lead Exposure and Child Development: An International Assessment. Smith, M.A., Grant, L.D. and Sors, A. I (eds), Kluwer Academic Publishers.

Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.

Furst, A., Schlauder, M., Sasmore, D. (1976 ) Tumorigenic Activity of Lead Chromate. Cancer Res 36:1779-1783

ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)

Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN,

Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899

Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.

Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory approach to assess the potency of substances toxic to the reproduction
Regul Toxicol Pharmacol: 63(1):97-105

OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media

Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.

Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71.

U.S. Environmental Protection Agency (2007). Estimation of the relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77.

**Dossier Submitter's Response**

These comments are the same as those presented by the International Lead Association; please see Dossier submitter's responses under comment number 7 (ILA) starting on page 4.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | JL Goslar GmbH | Company-Downstream user | 16 |

**Comment received**

Executive Summary

We do not believe that the dossier presented by Sweden provides an adequate justification for the classification of massive lead metal and or that the specific concentration limit proposed is scientifically justified. There is a lack of scientific robustness in many of arguments presented and insufficient relevant technical data, supported by references etc., to validate the conclusions reached. We would request that the authors consider the following specific points:

1. Scope: The document draws heavily on evidence offered by Lanphear et al (2005) on effects of blood lead on childhood IQ. Whilst this may be of relevance to discussing risk of children from lead exposure we do not believe it should be cited as the lead effect in CLP classification or in the development of a SCL for reproductive toxicity endpoints. According to the latest ECHA guidance on CLP "it is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, developmental toxicity essentially means adverse effects induced during pregnancy or as a result of parental exposure". New information by Braun et al. 2012 provides the best available data for assessing the developmental windows of susceptibility forthe effects of lead on IQ and supports the conclusion that these effects occur postnatally. We therefore question the significance of using postnatal effects on childhood IQ for assessing developmental toxicity classification in relation to CLP and propose that an alternative endpoint such as effects on foetal growth or obstetric outcome be evaluated.

2. Read Across: There is little experimental or human data available on the health effects of lead metal. Evidence included in the Annex XV dossier is for model bioavailable/soluble lead compounds and hence any conclusions on effect of metallic lead are derived by read across. This is not made

clear in the dossier and the relevance of using read across for CLP and SCL derivation requires a robust scientific justification. Without such justification the data should not be used. For many of the conclusions made in the dossier this read across requires three steps. To derive the conclusion as to whether lead metal meets the criteria for classification as Repr. 1A the authors have cited human epidemiology following post natal exposure to children to lead compounds (step 1), assumed that lead metal would have the same effect and dose response (step 2) and then extrapolated this to pre-natal exposures (step 3). We do not think this is scientifically sound, especially when used to derive a SCL which requires detailed quantitative data on dose response.

3. Bioavailability: Insufficient consideration is made for the effects of bioavailability of metallic lead when compared to soluble lead compounds. Physico-chemical properties such as surface area play a large role in bioaccessibility (a concept included in the CLP guidance on the classification of metals for effects on aquatic organisms). This needs to be considered in relation to the human health endpoints and merits treating lead in powder and massive form differently for human health classification purposes.

General Comments

- P7 table 3 and p9 table 4 Whilst we appreciate that the scope of the harmonised classification proposal is limited to reproductive toxicity it would appear to be misleading that tables 3 and 4 cite reasons for no classification for endpoints other than toxicity to reproduction as “conclusive but not sufficient for classification” as this is not the case for all endpoints (for example with lead in powder form the REACH dossier includes a classification as STOT Rep. Exp. 1 (Hazard statement: H372: Causes damage to organs through prolonged or repeated exposure). Therefore the statement in tables 3 and 4 on reason for no classification is misleading. Since the dossier is restricted to consideration of the reproductive toxicity endpoints we would suggest amending entries in the column headed “reason for no classification” to indicate that the endpoints were not considered or include a dash (-) as was the case for other columns in the table

- P9 Table 4. We question whether it is correct to include a specific concentration limit of 0.03% in relation to the Dangerous Substances Directive? What is the legal basis for this since the applied methodology utilised in this CLH for defining specific concentration limits for reproductive toxicity was not included in the DSD?

- P9 Labelling. It appears illogical that the proposed R-phrases for lead metal of R60, R61 are more severe than those used for other lead compounds in Annex VI to CLP (R61, R62) when the lead metal classification has been derived by read across from experimental and epidemiology studies undertaken on the aforementioned soluble lead compounds.

- P10 section 2.1. We do not see the need for the statement “lead is a well-known human toxicant and lead poisoning has been documented way back in history …etc and suggest that this is removed. Lead was certainly used by ancient cultures and there are historical documents describing adverse health events attributed to lead but we fail to see how this is relevant to a 21st Century review of scientific evidence supporting classification and labelling (and specifically to harmonised classification as Repr.1A).

- P10 section 2.2. Hazard identification of metals, metal compounds and complex metal containing substances (alloys and concentrates) are related to the toxicity of the metal ion and importantly the release or relative bioavailability of the metal ion. We would suggest that the authors pay attention to some of the conclusions made in the short summary for scientific justification for the CLH proposal. Whilst it is the case that many authorities consider lead to be toxic to reproduction, this conclusion is based upon read-across from experimental studies and epidemiological investigations on more bioavailable forms of lead such as soluble lead salts and tetraethyl lead in gasoline. To our knowledge there are no experimental studies undertaken on lead metal. We would argue that it is not necessarily the case that extrapolation of test data from bioavailable forms of lead to elemental lead (especially in a massive form) will necessarily result in a scientifically robust conclusion with respect to classification. Consideration of bioavailability data should be reflected in the relative potency of effects on reproductive function. It is for this reason that we proposed a different classification of lead in massive form in the REACH registration dossier compared to the Annex VI entry for lead compounds. We believe there is quantitative data available to illustrate that

extrapolating or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is over conservative and that no classification or a different category or hazard may be appropriate. The authors need to make it clear that any conclusion reached in section 2.2 is based upon read across.

-P10 section 2.2. We believe that further discussion is necessary to support the statements made on the effect of lead. While it is true that studies of men exposed occupationally to high concentrations of lead have documented effects upon semen quality, testicular atrophy has not been observed. Histopathological effects upon the testes have been suggested in animal studies, but uncertainty exists as to whether mechanisms of impact on male reproductive function in animals are the same as is observed in humans. Read across from animal studies is inappropriate under such circumstances. We are further concerned about conclusions made on neurobehaviorial effects mediated by prenatal lead exposure. Whilst there is evidence in the scientific literature that supports an effect on childhood IQ following postnatal exposure to lead in bioavailable forms, the evidence for effects following pre-natal exposure is weaker and in many cases confounded by continued postnatal exposures. The best available data available is a recent study by Braun et al 2012. These authors tried to assess windows of susceptibility to lead induced cognitive effects in children. Four Mexico City cohorts were combined which has yielded for analysis 1035 mother-child pairs with gestational and postnatal blood lead available at 1, 2, 3, and 4 years of age and assessment of cognition at 4 years. After adjusting for confounders, postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels. This most recent finding mirrors the conclusions of Pocock et al (1994) whose systematic review found little relationship between prenatal blood levels and subsequent IQ test scores in prospective studies of child development.
The current CLH guidelines further indicate that classification for reproductive toxicity should be restricted to consideration of effects on fertility and developmental toxicity (which is generally considered to mean adverse effects induced during pregnancy or as a result of parental exposure). We thus question the relevance of including discussion of IQ effects resulting from post-natal exposure during childhood in the justification. The statement that “there is no safe exposure level for lead induced developmental neurotoxicity” refers to conclusions drawn from studies of postnatal lead exposure. Again we argue that, in the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean “adverse effects induced during pregnancy or as a result of parental exposure”, a statements that there is no safe prenatal exposure levels is not supported by the quantitative scientific evidence.

- P11 Section 2.4. The Industrial DSD self-classification for lead metal powder (particle size ,1mm) cited in the CLH report is not that included in the REACH registration dossier which was R60 May impair fertility, R61 May cause harm to the unborn child. We appreciate that this is not consistent with the CLP self-classification reported by Industry for the same substance of Repr. 1.A (H360Df) and can only presume that the Swedish CA amended the Industry DSD self-classification so that it is aligned with that reported for CLP?

- P11 Section 3. Industry proposed a different classification for lead in massive form because the reproductive toxicity classification for elemental lead is based upon “read across” from more bio-available forms and that in massive form there is limited opportunity under normal handling and use for exposure to lead -metal itself. Processing of the massive metal results in exposure to lead compounds [predominantly oxides] and not lead metal powder of fume.

- We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must be given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative oral bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). This two-order of magnitude difference in bioavailability is quantitatively significant and the CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that whereas metallic powder at extremely small particle sizes, exhibits oral bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979), massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited oral bioavailability. This observation of limited bioaccessibility of lead in massive form is supported by data obtained during transformation and dissolution tests (T/dp)

[OECD 2001] undertaken to establish aquatic toxicity classification of lead in massive and powder form. Lead in powder form (<75µm) showed high rates of dissolution (>3000 µg/l following 24hr incubation at pH 6) compared to massive lead (300 µg/l) following 24hr incubation under the same conditions. This differential in relative bioaccessibility results in powdered lead receiving an environmental classification as Aquatic Acute and Chronic 1 whereas the massive form is not classified. This concept should equally be applied to evaluation of the relative human health hazard assessment.

- Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification.
Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size and surface area available for metal dissolution modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property relevant for purposes of classification.

- P11 Section 3. The vast majority of massive lead produced is not easily ingested due to its large size. When ingestion of small objects does occur, most transit the gastrointestinal tract without yielding significant exposure. Quantitative data specific to lead objects is not available but studies of other small metallic objects confirm this generalization (Litovitz et al., 2010). Only rarely do such objects lodge in the gastrointestinal tract for a period of time that permits dissolution (and thus exposure) of biological significance. We further note that adults are far less likely than children to engage in the ingestion of non-food items. Adult human exposure to lead via ingestion of metallic objects is thus contingent upon two low probability events (ingestion and retention in the GI tract) that seem to exceed the criteria of “reasonably foreseeable” events. We further note that risks to children (and adults) presented by this rare occurrence are being addressed by various restrictions that are in progress related to the REACH regulation (e.g. jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity.

- P11 Section 3. The justification for a harmonised classification for all physical forms cannot be made on the basis of mandating production of a safety data sheet as a method for addressing risk from exposures in the home environment as safety data sheets are only required for use by professional users. Moreover whilst we support the observation that melting lead in the home to produce “bullets and fishing weights” is not appropriate we do not believe this is a good argument for justifying a harmonised classification. This behaviour would not be mitigated by adoption of a harmonised classification of Repr. 1A and would be better addressed through education or possibly a REACH restriction.

- P11 Section 3 The comment that lead is a soft metal that can easily “rub off” on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being “rubbed off” on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and determined it to be quite low (1 – 3 µg/cm2 of exposed skin). Modelling of hand to mouth transfer and subsequent ingestion further determined that only modest impacts upon blood lead would result under typical exposure scenarios. It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable.

- P17 Section 2.1 In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores. We suggest the authors review the lead REACH registration dossier for more information on manufacturing and use of lead.

- P17 Section 2.2. We do not believe this section accurately reflects current use of lead in the EU and implies that there is significant use in consumer products/articles which is not the case.
o Over 70% of lead used in the EU is for lead-acid batteries for both automotive and back-up power use.
o Lead sheet is also used as a weather-proofing material in the construction industry across Northern

Europe.
o Lead is widely used for radiation shielding, for example in healthcare, airport security, defence, nuclear decommissioning, non-destructive testing, underwater cable sheathing etc.
o Lead has essential industrial applications in the chemicals, steel and other industries. It is also widely used in ballast, counterbalance and some ballistic applications
Consumer items such as fishing sinkers, “tin soldiers”, jewellery and brass buttons/zips are extremely minor applications, representing much less than 1% of annual use. Many of these minor applications are already subject to existing or planned EU or national restrictions and a harmonised classification of lead as Repr. 1A would not have any impact as a risk management measure.
It is misleading to state that lead is used in paint. Lead metal has never been used in paint and the use of lead compounds in household paint is now banned in the EU (although lead compounds may rarely be used for some specialised applications)
It is misleading to state that lead is frequently used in solders and electronics. Most solders used in the electronics industry must be lead-free. Finally lead metal is not used in crystal glass manufacture. In this case lead monoxide is the entity used.

- P18 Section 4 . If the authors believe it relevant to include data on blood lead in children they may also wish to report that blood lead levels in the general population in the EU has significantly fallen since the introduction of a ban of tetraethyl lead in petrol. The average decline in children’s blood lead has been approximately 5% per year between 1995 and 2007.

- P18 Section 4.1.2 Oral absorption rate. This section could benefit from inclusion of information on relative absorption of soluble lead compounds (from which the data on reproductive toxicity is derived) compared to metallic or elemental lead. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds ( Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.

- P19 Inhalation rate We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.

- P 19 Dermal Absorption Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surface is far lower than suggested here. We also note that the occupational exposure scenarios described entail the deposition of inorganic lead compounds as dust fallout from occupational aerosols. There is little or no metallic lead in these dusts as they are predominantly lead oxides.

- P19 Metabolism While urinary excretion is an important route of elimination of lead from the body, biliary excretion is comparable in magnitude and should be noted. We recommend that the authors include information presented in the Lead REACH Registration dossier and the VRAL (ILA-Europe 2008).

- P20 Section 4.1.3 As described previously it is not appropriate to take a worst case assumption that the bioavailability of metallic lead is equivalent to that of soluble lead compounds. Whilst dependent upon factors such as particle size etc there is evidence to show that metallic lead is much less bioavailable that soluble lead compounds (approx. 1%). We also wish to emphasize yet again that exposure of adults is of primary concern for reproductive toxicity – not the exposure of young children.

**Dossier Submitter’s Response**

The comments are the same as those presented by the International Lead Association, please see Dossier submitter’s responses under comment number 7 (ILA) starting on page 4.

**RAC’s response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment |
|---|---|---|---|---|

| | | | | number |
|---|---|---|---|---|
| 06/12/2012 | Belgium | European Copper Institute | Industry or trade association | 17 |

**Comment received**

The copper industry has, during the last 10-15 years, invested substantially to reduce the lead content in its materials (alloys, slags). The initiatives have been mandatory and/or voluntarily (drinking water applications, jewellery, consumer products, OELs…).
The copper industry performed an assessment on the potential impact of lowering the classification cut-off value of lead and lead compounds, from 0.3 to 0.03%, due to its potential characterisation as a "high potency substance for reproductive effects".

Important socio-economic and environmental impacts are expected from the proposed classification scenario, specifically on the copper alloy markets, copper slag uses and copper concentrates markets. Instead of a blanket hazard cut-off value, it is proposed to continue to assess on a case by case basis, that the production/use scenarios are safe. This will avoid unnecessary impacts on the production, market and international trade of copper, copper alloys, final copper slags and copper concentrates.

**Dossier Submitter's Response**

The CLP-legislation does not offer the option of assessing the specific concentration limit on a case by case basis, and socio-economic impacts neither can nor should be taken into account when classifying under CLP.
However, we understand your concern and would like to pass on the discussion regarding setting a SCL to RAC.

**RAC's response**

It is to be noted that socio-economic impacts are not a matter that should be considered when classifying a substance or setting a SCL. RAC notes that the accuracy of the DS rational to derive a SCL value of 0.03% which is 10fold lower that the generic concentration limit of 0.3% have been questioned. In its analysis of the potency of lead RAC has addressed several parameters that may affect the level of the external dose and came to the conclusion that metallic lead is a highly potent compound.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Metallwerk Dinslaken GmbH & Co.KG | Company-Manufacturer | 18 |

**Comment received**

About the ILA The International Lead Association is a membership body that supports companies involved in the mining, smelting, refining and recycling of lead. The ILA represents the producers of about 3 million tons of lead and almost two thirds of lead production in the western world. As secretariat to the Lead (Pb) REACH Consortium, ILA Europe (a regional branch of the International Lead Association) is acting on behalf of the Lead Registrants for several lead substances including lead metal (CAS 7439-92-1).
The following companies are members of the Pb REACH Consortium or ILA (please refer to Appendix A).
These comments represent the view of consortium and ILA member companies.
Executive Summary
We do not believe that the dossier presented by Sweden provides an adequate justification for the classification of massive lead metal and or that the specific concentration limit proposed is scientifically justified. There is a lack of scientific robustness in many of arguments presented and insufficient relevant technical data, supported by references etc., to validate the conclusions reached. We would request that the authors consider the following specific points:
1. Scope: The document draws heavily on evidence offered by Lanphear et al (2005) on effects of blood lead on childhood IQ. Whilst this may be of relevance to discussing risk of children from lead exposure we do not believe it should be cited as the lead effect in CLP classification or in the development of a SCL for reproductive toxicity endpoints. According to the latest ECHA guidance on CLP "it is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, developmental toxicity essentially

means adverse effects induced during pregnancy or as a result of parental exposure". New information by Braun et al. 2012 provides the best available data for assessing the developmental windows of susceptibility for the effects of lead on IQ and supports the conclusion that these effects occur postnatally. We therefore question the significance of using postnatal effects on childhood IQ for assessing developmental toxicity classification in relation to CLP and propose that an alternative endpoint such as effects on foetal growth or obstetric outcome be evaluated.
2. Read Across: There is little experimental or human data available on the health effects of lead metal. Evidence included in the Annex XV dossier is for model bioavailable/soluble lead compounds and hence any conclusions on effect of metallic lead are derived by read across. This is not made clear in the dossier and the relevance of using read across for CLP and SCL derivation requires a robust scientific justification. Without such justification the data should not be used.
For many of the conclusions made in the dossier this read across requires three steps. To derive the conclusion as to whether lead metal meets the criteria for classification as Repr. 1A the authors have cited human epidemiology following post natal exposure to children to lead compounds (step 1), assumed that lead metal would have the same effect and dose response (step 2) and then extrapolated this to pre-natal exposures (step 3). We do not think this is scientifically sound, especially when used to derive a SCL which requires detailed quantitative data on dose response.
3. Bioavailability: Insufficient consideration is made for the effects of bioavailability of metallic lead when compared to soluble lead compounds. Physico-chemical properties such as surface area play a large role in bioaccessibility (a concept included in the CLP guidance on the classification of metals for effects on aquatic organisms). This needs to be considered in relation to the human health endpoints and merits treating lead in powder and massive form differently for human health classification purposes.
General Comments
☐ P7 table 3 and p9 table 4 Whilst we appreciate that the scope of the harmonised classification proposal is limited to reproductive toxicity it would appear to be misleading that tables 3 and 4 cite reasons for no classification for endpoints other than toxicity to reproduction as "conclusive but not sufficient for classification" as this is not the case for all endpoints (for example with lead in powder form the REACH dossier includes a classification as STOT Rep. Exp. 1 (Hazard statement: H372: Causes damage to organs through prolonged or repeated exposure). Therefore the statement in tables 3 and 4 on reason for no classification is misleading. Since the dossier is restricted to consideration of the reproductive toxicity endpoints we would suggest amending entries in the column headed "reason for no classification" to indicate that the endpoints were not considered or include a dash (-) as was the case for other columns in the table
☐ P9 Table 4. We question whether it is correct to include a specific concentration limit of 0.03% in relation to the Dangerous Substances Directive? What is the legal basis for this since the applied methodology utilised in this CLH for defining specific concentration limits for reproductive toxicity was not included in the DSD?
☐ P9 Labelling. It appears illogical that the proposed R-phrases for lead metal of R60, R61 are more severe than those used for other lead compounds in Annex VI to CLP (R61, R62) when the lead metal classification has been derived by read across from experimental and epidemiology studies undertaken on the aforementioned soluble lead compounds.
☐ P10 section 2.1. We do not see the need for the statement "lead is a well-known human toxicant and lead poisoning has been documented way back in history …etc and suggest that this is removed. Lead was certainly used by ancient cultures and there are historical documents describing adverse health events attributed to lead but we fail to see how this is relevant to a 21st Century review of scientific evidence supporting classification and labelling (and specifically to harmonised classification as Repr.1A).
☐ P10 section 2.2. Hazard identification of metals, metal compounds and complex metal containing substances (alloys and concentrates) are related to the toxicity of the metal ion and importantly the release or relative bioavailability of the metal ion. We would suggest that the authors pay attention to some of the conclusions made in the short summary for scientific justification for the CLH proposal. Whilst it is the case that many authorities consider lead to be toxic to reproduction, this conclusion is based upon read-across from experimental studies and epidemiological investigations on more bioavailable forms of lead such as soluble lead salts and tetraethyl lead in gasoline. To our knowledge there are no experimental studies undertaken on lead metal. We would argue that it is not necessarily the case that extrapolation of test data from bioavailable forms of lead to elemental lead (especially in a massive form) will necessarily result in a scientifically robust conclusion with respect to classification. Consideration of bioavailability data should be reflected in the relative potency of effects on reproductive function. It is for this reason that we proposed a different

classification of lead in massive form in the REACH registration dossier compared to the Annex VI entry for lead compounds. We believe there is quantitative data available to illustrate that extrapolating or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is over conservative and that no classification or a different category or hazard may be appropriate. The authors need to make it clear that any conclusion reached in section 2.2 is based upon read across.
P10 section 2.2. We believe that further discussion is necessary to support the statements made on the effect of lead. While it is true that studies of men exposed occupationally to high concentrations of lead have documented effects upon semen quality, testicular atrophy has not been observed. Histopathological effects upon the testes have been suggested in animal studies, but uncertainty exists as to whether mechanisms of impact on male reproductive function in animals are the same as is observed in humans. Read across from animal studies is inappropriate under such circumstances.
We are further concerned about conclusions made on neurobehaviorial effects mediated by prenatal lead exposure. Whilst there is evidence in the scientific literature that supports an effect on childhood IQ following postnatal exposure to lead in bioavailable forms, the evidence for effects following pre-natal exposure is weaker and in many cases confounded by continued postnatal exposures.
The best available data available is a recent study by Braun et al 2012. These authors tried to assess windows of susceptibility to lead induced cognitive effects in children. Four Mexico City cohorts were combined which has yielded for analysis 1035 mother-child pairs with gestational and postnatal blood lead available at 1, 2, 3, and 4 years of age and assessment of cognition at 4 years. After adjusting for confounders, postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels. This most recent finding mirrors the conclusions of Pocock et al (1994) whose systematic review found little relationship between prenatal blood levels and subsequent IQ test scores in prospective studies of child development.
The current CLH guidelines further indicate that classification for reproductive toxicity should be restricted to consideration of effects on fertility and developmental toxicity (which is generally considered to mean adverse effects induced during pregnancy or as a result of parental exposure). We thus question the relevance of including discussion of IQ effects resulting from post-natal exposure during childhood in the justification. The statement that “there is no safe exposure level for lead induced developmental neurotoxicity” refers to conclusions drawn from studies of postnatal lead exposure. Again we argue that, in the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean “adverse effects induced during pregnancy or as a result of parental exposure”, a statements that there is no safe prenatal exposure levels is not supported by the quantitative scientific evidence.

☐ P11 Section 2.4. The Industrial DSD self-classification for lead metal powder (particle size ,1mm) cited in the CLH report is not that included in the REACH registration dossier which was R60 May impair fertility, R61 May cause harm to the unborn child. We appreciate that this is not consistent with the CLP self-classification reported by Industry for the same substance of Repr. 1.A (H360Df) and can only presume that the Swedish CA amended the Industry DSD self-classification so that it is aligned with that reported for CLP?
☐ P11 Section 3. Industry proposed a different classification for lead in massive form because the reproductive toxicity classification for elemental lead is based upon “read across” from more bio-available forms and that in massive form there is limited opportunity under normal handling and use for exposure to lead -metal itself. Processing of the massive metal results in exposure to lead compounds [predominantly oxides] and not lead metal powder of fume.
☐ We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must be given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative oral bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). This two-order of magnitude difference in bioavailability is quantitatively significant and the CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that whereas metallic powder at extremely small particle sizes, exhibits oral bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979), massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited oral bioavailability. This observation of limited bioaccessibility of lead in massive form is supported by data obtained during transformation and dissolution tests (T/dp) [OECD 2001] undertaken to establish aquatic toxicity classification of lead in massive and powder

form. Lead in powder form (<75µm) showed high rates of dissolution (>3000 µg/l following 24hr incubation at pH 6) compared to massive lead (300 µg/l) following 24hr incubation under the same conditions. This differential in relative bioaccessibility results in powdered lead receiving an environmental classification as Aquatic Acute and Chronic 1 whereas the massive form is not classified. This concept should equally be applied to evaluation of the relative human health hazard assessment.

☐ Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification.

Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size and surface area available for metal dissolution modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property relevant for purposes of classification.

☐ P11 Section 3. The vast majority of massive lead produced is not easily ingested due to its large size. When ingestion of small objects does occur, most transit the gastrointestinal tract without yielding significant exposure. Quantitative data specific to lead objects is not available but studies of other small metallic objects confirm this generalization (Litovitz et al., 2010). Only rarely do such objects lodge in the gastrointestinal tract for a period of time that permits dissolution (and thus exposure) of biological significance. We further note that adults are far less likely than children to engage in the ingestion of non-food items. Adult human exposure to lead via ingestion of metallic objects is thus contingent upon two low probability events (ingestion and retention in the GI tract) that seem to exceed the criteria of “reasonably foreseeable” events. We further note that risks to children (and adults) presented by this rare occurrence are being addressed by various restrictions that are in progress related to the REACH regulation (e.g. jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity.

☐ P11 Section 3. The justification for a harmonised classification for all physical forms cannot be made on the basis of mandating production of a safety data sheet as a method for addressing risk from exposures in the home environment as safety data sheets are only required for use by professional users. Moreover whilst we support the observation that melting lead in the home to produce “bullets and fishing weights” is not appropriate we do not believe this is a good argument for justifying a harmonised classification. This behaviour would not be mitigated by adoption of a harmonised classification of Repr. 1A and would be better addressed through education or possibly a REACH restriction.

☐ P11 Section 3 The comment that lead is a soft metal that can easily “rub off” on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being “rubbed off” on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and determined it to be quite low (1 – 3

further determined that only modest impacts upon blood lead would result under typical exposure scenarios. It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable

☐ P17 Section 2.1 In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores. We suggest the authors review the lead REACH registration dossier for more information on manufacturing and use of lead.

☐ P17 Section 2.2. We do not believe this section accurately reflects current use of lead in the EU and implies that there is significant use in consumer products/articles which is not the case.

o Over 70% of lead used in the EU is for lead-acid batteries for both automotive and back-up power use.

o Lead sheet is also used as a weather-proofing material in the construction industry across Northern Europe.

o Lead is widely used for radiation shielding, for example in healthcare, airport security, defence, nuclear decommissioning, non-destructive testing, underwater cable sheathing etc.

o Lead has essential industrial applications in the chemicals, steel and other industries. It is also widely used in ballast, counterbalance and some ballistic applications

Consumer items such as fishing sinkers, “tin soldiers”, jewellery and brass buttons/zips are extremely minor applications, representing much less than 1% of annual use. Many of these minor

applications are already subject to existing or planned EU or national restrictions and a harmonised classification of lead as Repr. 1A would not have any impact as a risk management measure.
It is misleading to state that lead is used in paint. Lead metal has never been used in paint and the use of lead compounds in household paint is now banned in the EU (although lead compounds may rarely be used for some specialised applications)
It is misleading to state that lead is frequently used in solders and electronics. Most solders used in the electronics industry must be lead-free. Finally lead metal is not used in crystal glass manufacture. In this case lead monoxide is the entity used.

☐ P18 Section 4 . If the authors believe it relevant to include data on blood lead in children they may also wish to report that blood lead levels in the general population in the EU has significantly fallen since the introduction of a ban of tetraethyl lead in petrol. The average decline in children's blood lead has been approximately 5% per year between 1995 and 2007.
☐ P18 Section 4.1.2 Oral absorption rate. This section could benefit from inclusion of information on relative absorption of soluble lead compounds (from which the data on reproductive toxicity is derived) compared to metallic or elemental lead. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds ( Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.
☐ P19 Inhalation rate We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.
☐ P 19 Dermal Absorption Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surface is far lower than suggested here. We also note that the occupational exposure scenarios described entail the deposition of inorganic lead compounds as dust fallout from occupational aerosols. There is little or no metallic lead in these dusts as they are predominantly lead oxides.
☐ P19 Metabolism While urinary excretion is an important route of elimination of lead from the body, biliary excretion is comparable in magnitude and should be noted. We recommend that the authors include information presented in the Lead REACH Registration dossier and the VRAL (ILA-Europe 2008)
☐ P20 Section 4.1.3 As described previously it is not appropriate to take a worst case assumption that the bioavailability of metallic lead is equivalent to that of soluble lead compounds. Whilst dependent upon factors such as particle size etc there is evidence to show that metallic lead is much less bioavailable that soluble lead compounds (approx. 1%). We also wish to emphasize yet again that exposure of adults is of primary concern for reproductive toxicity – not the exposure of young children.

**Dossier Submitter's Response**

The comments are the same as those presented by the International Lead Association, please see Dossier submitter's responses under comment number 7 (ILA), starting on page 4.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Belgium | EUROBAT | Industry or trade association | 19 |

**Comment received**

EUROBAT supports and endorses all comments submitted to this consultation by the International Lead Association (ILA).

P17 Section 2.1: EUROBAT confirms that the majority of the lead placed on the market in automotive and industrial batteries is manufactured from recycled scrap rather than from primary ores. The vast majority (>>95%) of industrial and automotive lead-based batteries are collected and recycled by the battery industry and other smelters in a closed-loop system.

P17 Section 2.2: EUROBAT confirms that over 70% of the lead used in the EU is for automotive and industrial lead-based batteries. Risk of any lead exposure to the consumer and environment during use of a battery is negligible due to the fact that batteries are sealed and most of them are maintenance free. There is not significant use in consumer products/articles.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Exide Technologies GmbH | Company-Downstream user | 20 |

**Comment received**

Exide Technologies GmbH is a member of the Pb REACH Consortium. ILA has provided a consolidated response on behalf of members of the Pb REACH consortium. As a consequence, Exide Technologies GmbH fully supports and subscribes to the comments made by ILA ."

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | Saarstahl AG | Company-Manufacturer | 21 |

**Comment received**

We, the Saarstahl AG agree with the robust scientific position laid down by the International Lead Association (ILA) in their consultation response paper.

We produce free cutting steel. The concentrations of lead reaches up to 0,35% of the overall article. The produced steel is placed onto the market as articles. The main downstream user markets are the machinists sector, automotive and heavy vehicles industry.

Classification of lead metal is not verified by the data of the dossier. The situation for lead alloys is much more uncertain. There are strong differences between lead alloys, lead in massive form and lead in powder form, which should be taken into account and is highlighted in the ILA comments paper. The leaching characteristics of steel in massive form are not comparable to those of lead in pure form or lead in lead compounds. A read across from lead compounds to lead alloyed steel is not possible. Therefore we do not agree with the lowest Specific Concentration Limit of 0.03%.

In REACH there already restrictions for lead. The considered the cut-off value 0,03% is much lower than those restrictions. The different treatment of lead in different laws is not acceptable. The proposed CLP classification is also in contradiction with a number of other European legislation. The following are those which we foresee to be significantly impacted, Waste Framework Directive (WFD) (H10), End of Life Vehicle Directive (ELVD) (Lead derogation in Annex II), Restriction of Hazardous Substance Directive (RoHS) and the Waste Electrical Electronic Equipment Directive (WEEE). This impact should be taken into account before any formal decision by the Commission and the RAC is reached.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted. See RAC response to comment 17.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Netherlands | RIVM | National Authority | 22 |

**Comment received**

This CLH proposal focuses on the reproductive toxicity of lead and proposes classification for effects on fertility and development. However, no proposal is made regarding effects on or via lactation. In

our opinion classification for this additional effect should be considered based on the assessment of the Health Council of the Netherlands on this (http://www.gezondheidsraad.nl/sites/default/files/03@03osh.pdf).

**Dossier Submitter's Response**

Thank you for this information. We did not have it while compiling the CLH-report so therefore we will consider adding a proposal for lactation later.

**RAC's response**

Noted. RAC considers classification for effects on or via lactation warranted for lead.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | German Electrical and Electronic Manufacturers' Association - German Cable Makers Association | Industry or trade association | 23 |

**Comment received**

p.17 2.2 identified uses
It is state of the art to use lead as lead sheaths for, among others, submarine cables or instrumentation cables.
The lead sheath has the function of a diffusion barrier and has proven itself as excellent resistance to sea water and aggressive chemicals, especially in industrial applications.
There is actually no equivalent alternative to lead regarding the substance characteristics and in economic terms. The use of lead as a cable material is therefore indispensable.
Restrictions would affect for example the expansion of the use of wind power from offshore wind farms or would affect other industrial applications.
A stricter classification as a reproductive toxic substance would also entail extensive changes in the storage, production and handling for cable manufacturers.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | United Kingdom | Tata Steel Europe | Industry or trade association | 24 |

**Comment received**

The European Steel Association and its members agree with the robust scientific position laid down by the International Lead Association (ILA) in their consultation response paper.

The European Steel Industry produces free cutting steel. The concentrations of lead reaches up to 0,35% of the overall article. The produced steel is placed onto the market as articles. The main downstream user markets are the machinists sector, automotive and heavy vehicles industry.

Classification of lead metal is not verified by the data of the dossier. The situation for lead alloys is much more uncertain. There are strong differences between lead alloys, lead in massive form and lead in powder form, which should be taken into account and is highlighted in the ILA comments paper. The leaching characteristics of steel in massive form are not comparable to those of lead in pure form or lead in lead compounds. A read across from lead compounds to lead alloyed steel is not possible. Therefore we do not agree with the lowest Specific Concentration Limit of 0.03%.

In REACH there already restrictions for lead. The considered the cut-off value 0,03% is much lower than those restrictions. The different treatment of lead in different laws is not acceptable. The proposed CLP classification is also in contradiction with a number of other European legislation. The following are those which we foresee to be significantly impacted, Waste Framework Directive (WFD) (H10), End of Life Vehicle Directive (ELVD) (Lead derogation in Annex II), Restriction of Hazardous Substance Directive (RoHS) and the Waste Electrical Electronic Equipment Directive (WEEE). This impact should be taken into account before any formal decision by the Commission and the RAC is

reached.

**Dossier Submitter's Response**

These questions have been discussed previously, see e.g. comment number 7. Classification should be based on intrinsic properties and not on risk of exposure. The fact that lead is being addressed by various restrictions in e.g. REACH should and can not exclude a classification according to CLP.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comment 1, 2 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | Wirtschaftsvereinigung Stahl | Industry or trade association | 25 |

**Comment received**

Lead CLH consultation response Dec 2012
The German Steel Association and its members agree with the robust scientific position laid down by the International Lead Association (ILA) in their consultation response paper.
The German and European Steel Industry produces free cutting steel. The concentrations of lead reaches up to 0,35% of the overall article. The produced steel is placed onto the market as articles. The main downstream user markets are the machinists sector, automotive and heavy vehicles industry.
Classification of lead metal is not verified by the data of the dossier. The situation for lead alloys is much more uncertain. There are strong differences between lead alloys, lead in massive form and lead in powder form, which should be taken into account and is highlighted in the ILA comments paper. The leaching characteristics of steel in massive form are not comparable to those of lead in pure form or lead in lead compounds. A read across from lead compounds to lead alloyed steel is not possible. Therefore we do not agree with the lowest Specific Concentration Limit of 0.03%.
In REACH there already restrictions for lead. The considered the cut-off value 0,03% is much lower than those restrictions. The different treatment of lead in different laws is not acceptable. The proposed CLP classification is also in contradiction with a number of other European legislation. The following are those which we foresee to be significantly impacted, Waste Framework Directive (WFD) (H10), End of Life Vehicle Directive (ELVD) (Lead derogation in Annex II), Restriction of Hazardous Substance Directive (RoHS) and the Waste Electrical Electronic Equipment Directive (WEEE). This impact should be taken into account before any formal decision by the Commission and the RAC is reached.

**Dossier Submitter's Response**

Please see dossier submitter's response under comment number 24.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Sweden | ABB AB High Voltage Cables | Company-Downstream user | 26 |

**Comment received**

Response on Harmonized Classification document on lead

Massive lead is used as sheathing in sea cables. This response aims at briefly describing how massive lead is handled during the portion of its life cycle where it is used by ABB High Voltage Cables (ABB HVC) during production of sea cables, and the low hazard of massive lead during this part of the life cycle.

1. At present massive lead is (self) classified as having no human health hazard properties in the REACH registration dossier. The registration dossier submitted by the industry in 2010 argues that massive lead (particle size >1 mm Ø) should not be classified for human health. The harmonized classification dossier submitter (Swedish Chemicals Agency) argues that lead should be classified as a reproductive toxicant in category 1A regardless of particle size. One main argument for this position is that "reasonable expected use" includes the whole life cycle of lead.

2. This response aims to describe how lead is handled during the portion of its life cycle where it is used by ABB High Voltage Cables (ABB HVC), an important downstream user/producer of articles. The response shows that:

i) ABB's lead extrusion and forming for cable sheathing do not cause increased occupational exposure.

ii) Manufacturing, operation and recycling of sea cable does not cause increased human health hazards related to lead.

iii) Manufacturing, operation and recycling of sea cable does not cause increased environmental health risks related to lead.

3. Massive lead is used as impermeable protective sheathing for sea cables at ABB HVC where it is handled during cable manufacturing in the following processes /steps:

i) The lead is supplied as massive ingots to the factory

ii) Lead ingots are melted in lead pots. The melting process results in lead slag that is skimmed from the surface of the lead pots and disposed of separately.

iii) Lead is pumped to the lead extrusion/lead press

iv) Lead is processed to the cable via a continuous extrusion process

4. ABB HVC continuously measures blood levels of lead in the workforce. The average and standard deviation blood lead concentration in the workforce during the period 1997 to 2011 (n=201) showed no significant deviation from the background blood lead concentrations in Swedish adults (0.12 - 0.15 µmol/l as measured from 2000 to 2005)[1].

Consequently, lead levels are not elevated in the ABB HVC workforce showing that occupational exposure is minimal. This correlates with science [2] and with the arguments from the industry in the registration dossier and voluntary risk assessment report, i.e. that inherent properties of massive lead causes minimal systemic uptake.

5. Solid lead waste is generated in the manufacturing process at ABB HVC (< 20% of total usage). This lead is delivered to professional scrap/metal recycling enterprises where it is recycled to other types of solid lead products (melted and processed into new lead containing alloys). It is unlikely that non-occupational/home reprocessing of lead from ABB occurs.

6. It is important to note that, during storage, transportation, installation and use, of the cable, the lead sheath is not exposed to the external environment, since the lead sheath is covered with an outer protective polyethylene jacket and also further outer protective layers/shields. Thus, a pathway for environmental exposure to lead contained in sea cables does not exist. Furthermore, the superior corrosion performance of lead and lead alloys is attributed to the formation of a strong, adherent and impermeable self-protective lead oxide film layer in air, which is stable or insoluble in most natural air, water, marine water and soil environments [3]. Lead exposure and environmental transport of lead from solid lead surfaces is consequently low/very low and this should also be considered as a hazard-decreasing inherent property of massive lead.

References

[1] Skerfving, S. (2005) Inorganic lead - an update 1991-2004. Criteria Document for Swedish Occupational Standards. Arbetslivsinstitutet. Arbete och Hälsa. ISBN 91-7045-734-3.
[2] Barltrop, D. and Meek, F. (1979) Effect of Particle Size on Lead Absorption from the Gut. Archives of Environmental Health, 34. 280-285.
Hodgkins, D.G. et al. (1991) The effect of airborne lead particle size on worker blood-lead levels: an empirical study of battery workers. Journal of Occupational Medicine, 33. 1265-1273.
[3] Craig, D. (1995) Handbook of Corrosion Data, 2nd edition. ASM International. 998 pages.

**Dossier Submitter's Response**

Noted. Thank you for the information.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Belgium | | MemberState | 27 |

**Comment received**

CLH proposal SW CA
Proposed classification based on CLP criteria
Repr. 1A – H360DF
Proposed classification based on Directive 67/548/EEC criteria
Repr. Cat. 1; R60-611

Overall conclusion and Comments:
We would like to thank Sweden for the CLH report on lead.
We agree to classify lead toxic for reproduction as the other lead compounds are already classified Rep. Cat 1A H360 Df and the kinetics data show that the bioavailability of lead would be sufficient to cause the effects. We support the classification Rep.1A H360. We understand the concern of Sweden for the fertility but we think that the classification of all lead compounds should be revised accordingly because it seems to us logical to have the same classification for lead and lead compounds.
We have some remarks regarding the studies.
Concerning human studies, some evidence showing the adverse effects on lead on both fertility and development are not so clear. The Bonde *et* al. study (2002) has assessed the exposure of workers to lead in 10 companies and data indicated a reduction of mean sperm concentration (49%) at PbB level > 50µg/dL. It is not mentioned in the dossier the number of workers presenting PbB level > 50 µg/dL nor the number by company. Besides, the data don't indicate the adverse effects observed in each company. It is not so clear in the study if the reduction of the mean sperm concentration is correlated to PbB level or is due to a problem of the exposure to other substances in one of the 10 companies. In Telisman et al. study (2000), the data indicate "*a significant (p=0.05) correlation with PbB and decrease in sperm density, count, motility and viable sperm and abnormal sperm head morphology".* We would like to request the DS to provide more data on those effects (e.g.: percentage of workers showing this decrease) in order to assess the adversity of the effects.
Concerning the animals studies, the animals were administrated lead acetate, which is classified Rep. cat 1 A; H360Df. As it was previously discussed, it may be more consistent if an explanation is added regarding the animal studies in which lead was administered in the form of lead acetate. Indeed, it was agreed that the presence of lead ion in systemic circulation is responsible for the adverse effects on fertility.

**Dossier Submitter's Response**

Your support is appreciated. We agree that all the studies presented are not optimal in all aspects when viewed individually, but together they still provide a clear picture regarding the reprotoxic properties of lead.

**RAC's response**

The RAC supports the DS response.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Sweden | Höganäs Sweden AB | Company-Downstream user | 28 |

**Comment received**

Lead CLH consultation response Dec 2012
The European Steel Association and its members agree with the robust scientific position laid down by the International Lead Association (ILA) in their consultation response paper. The European Steel Industry produces free cutting steel. The concentrations of lead reaches up to 0,35% of the overall article. The produced steel is placed onto the market as articles. The main downstream user markets are the machinists sector, automotive and heavy vehicles industry. Classification of lead metal is not verified by the data of the dossier. The situation for lead alloys is much more uncertain. There are strong differences between lead alloys, lead in massive form and lead in powder form, which should be taken into account and is highlighted in the ILA comments paper. The leaching characteristics of steel in massive form are not comparable to

those of lead in pure form or lead in lead compounds. A read across from lead compounds to lead alloyed steel is not possible. Therefore we do not agree with the lowest Specific Concentration Limit of 0.03%.
In REACH there already restrictions for lead. The considered the cut-off value 0,03% is much lower than those restrictions. The different treatment of lead in different laws is not acceptable. The proposed CLP classification is also in contradiction with a number of other European legislation. The following are those which we foresee to be significantly impacted, Waste Framework Directive (WFD) (H10), End of Life Vehicle Directive (ELVD) (Lead derogation in Annex II), Restriction of Hazardous Substance Directive (RoHS) and the Waste Electrical Electronic Equipment Directive (WEEE). This impact should be taken into account before any formal decision by the Commission and the RAC is reached.

**Dossier Submitter's Response**

Noted. Please see Dossier submitter's responses under comment number 7 (ILA) starting on page 4.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | France | | MemberState | 29 |

**Comment received**

FR agrees with the classification proposal in Repro 1A H360 FD for all the particle size of metallic lead.

**Dossier Submitter's Response**

Your support is appreciated.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | Verband Deutscher Metallhändler e.V. | Industry or trade association | 30 |

**Comment received**

We are very surprised at the Swedish proposal, to classify lead as reprotoxic metal. According to our understanding, this should be done as part of the harmonization and for reasons of the precautionary principle. However, the consequences of such a classification were apparently not sufficiently thought through.

In the following we want to show why such a classification from the perspective of the recycling industry is strictly rejected.

Lead is appreciated and valued as an alloying element for decades as it improves the workability of metals significantly without affecting the mechanical qualities of the material. Due to the alloying of lead the machinability of certain metal alloys can partly be improved as well as the strength of the material can be increased. There is clear scientific evidence that lead can be used harmlessly in these alloys. More information on this can be found in the comment of the International Copper Association (ICA).

The classification of lead metal as reprotoxic would limit the European recycling circulations strongly. All scraps and waste / clinkers in the field of alloying in the steel, copper, lead and zinc area and other areas would become dangerous waste all at once. This would lead to plenty of problems and additional expenses for the recycling companies and therefore influence the trade / trading and recycling adversely according to European legal provisions, such as the Abfallverbringungsverordnung (VO 1013/2006).

In the EU lead is extracted primarily from recycled scrap instead of by primary production. Aggravation of recycling would lead to a decrease in secondary production of lead metal, so the primary production would be demanded more. As is well known, this is accompanied with a much higher CO2-emission, the environment would be harmed at this point more than before. This would be rather adversely in view of the higher resource efficiency that is desired. It must be assumed, that a reduction in recycling in the EU the material would be increasingly exported. In turn, this would

mean a loss of the metal out of the market which may not be in the sense of the European automotive industry and battery manufacturers.

It also has to be considered that the previous use of lead can be made by an appropriate surrogate and must be made economically. What kind of surrogate this will be and whether this also has an endangering potential is completely undetermined. The damage caused by the use of surrogates could be much larger than the desired protective effects through the classification of lead metal as reprotoxic.

As a result, we would strictly militate against such a classification of lead metal. As long as there are no clear sounds and resilient scientific results for a proved repro toxic effect of lead metal, there is no reason for such a heavy intervention in the economy. Furthermore, we agree with the opinion of the International Lead Association (ILA).

**Dossier Submitter's Response**

The CLH-proposal is indeed based on robust data that clearly demonstrates the developmental effects of lead. Furthermore, classification under the CLP-legislation should be based solely on the intrinsic properties of the substance. It neither can nor should take into account risk of exposure or potential socio-economic impacts.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | WirtschaftsVereinigung Metalle | Industry or trade association | 31 |

**Comment received**

Comments on the Dossier proposing harmonised Classification & Labelling (CLH) of Lead
Substance name: Lead
CAS Number: 7439-92-1
EC Number: 231-100-4

About WVM

WirtschaftsVereinigung Metalle (WVM), the German Non-Ferrous Metals Association, represents the German non ferrous (NF) metals industry towards politics and economy. We support our members in regulatory, occupational health & safety affairs in order to maintain and establish measures at a very high level. Today, WVM has about 650 member companies, including producers and processors of most base metals and compounds.
Some of our members also produce and handle lead metal. Nearly all of them are finally affected by a classification of lead as they are producing, handling or recycling lead containing alloys or scrap.
Herewith we and would like to take the opportunity to comment on the proposal as a national stakeholder representing our member companies.

General Comments
WVM fully supports and subscribes to the comments already made by ILA, the International Lead Association. ILA has provided a consolidated response on behalf of members of the Pb REACH consortium.
However, WVM would like to emphasize on some aspects which are from our point of view very important aspects to be taken into account carefully at the very beginning of the upcoming discussions on lead:

1. Motivation for the proposal of a harmonized classification of lead metal seems to be the idea that some specific consumer products (like fishing sinkers) or uses (like melting lead in the home to produce bullets and fishing weights) should be prohibited in order to avoid any intoxication. We think that this intension is clearly extractable from the proposal which immediately raises the question if harmonized classification will be the appropriate risk management option here. We think that this kind of concerns is more likely to be addressed via a REACH restriction proposal. In addition this would fit well to the parallel and ongoing Swedish approach for consumer product restrictions. Obviously an upfront targeted risk management analysis could help avoiding double work and might doubt the need for a

harmonized classification procedure.

**Dossier Submitter's Response:** The CLP-legislation clearly states that substances that have CMR-properties ***shall*** be classified under CLP, it is not optional. In addition, the fact that lead is being addressed by various restrictions in e.g. REACH should and can not exclude a classification according to CLP.

2. The use of the new concept of SCL for reprotoxic substances is neither appropriate nor procedural correct. The updated guidance was only published in the middle of the commenting phase for this classification proposal and could therefore not be addressed appropriately. Furthermore the consequences of the SCL concept for reprotoxic substances are not discussed with respect to massive materials like metals or alloys. Although bioavailability has to be taken into account for massive metals and alloys for environmental endpoints within the CLP this is not yet the case for human health endpoints. This will create huge impacts on all metal markets and one cannot overlook all the existing technical specifications that are based on the existing legislation. Changing this would significantly provoke damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials.

**Dossier Submitter's Response:** In the outcome of the accordance check, the dossier submitter was specifically asked by ECHA to derive a SCL according to the new guidelines and add it to the CLH-report under the appropriate section.
We agree that our approach to calculate the $ED_{10}$ can be discussed, and there may be more complex models that can be used for calculating a more finely tuned $ED_{10}$. Unfortunately, there is no specific guidance on how to set a SCL based on human data. However, whatever model is chosen for the calculations there will be inaccuracies and the resulting SCL could be discussed. Our "$ED_{10}$"-calculation should be seen as an indication, where the take-home-message is that lead is highly potent; in the range of many orders of magnitude more potent than what is required for assigning a SCL lower than the generic concentration limit of 0.3%.

In addition, classification under the CLP-legislation should be based solely on the intrinsic properties of the substance. It neither can nor should take into account risk of exposure or potential socio-economic impacts.

3. Coming to the scientific evaluation itself we think that the data presented clearly not warrant the proposed classification of lead metal. Read across arguments via various steps of assumed effects does not fulfill the CLP criteria for a Repr. 1A classification. Available data show that extrapolating or read across from reproductive toxicity on bioavailable lead salts to elemental lead (especially in the massive form) is not appropriate. Therefore we feel that the dossier presented by Sweden does not provide an adequate justification for the classification of massive lead metal.

**Dossier Submitter's Response:** Regarding "read across", see dossier submitter's response under comment 7, point 2 (page 5-6).

Berlin, 07th December 2012

**Dossier Submitter's Response**

Comments have been inserted directly into the above text under each relevant section.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | Wieland-Werke AG | Company-Downstream user | 32 |

**Comment received**

Most of the copper alloys contain lead, either as a functional element or as impurity due to recycling. The proposed classification and the proposed cut-off value will affect copper alloys significantly.

The copper industry has, during the last 10-15 years, invested substantially to reduce the lead content in its alloys. The initiatives have been mandatory and/or voluntarily (drinking water applications, jewellery, consumer products, OELs…). The copper industry performed an assessment on the potential impact of lowering the classification cut-off value of lead and lead compounds, from 0.3 to 0.03%, due to its potential characterisation as a "high potency substance for reproductive effects". Important socio-economic and environmental impacts are expected from the proposed classification scenario, specifically on the copper alloy markets, copper slag uses and copper concentrates markets.
Instead of a blanket hazard cut-off value, it is proposed to continue to assess on a case by case basis, that the production/use scenarios are safe. This will avoid unnecessary impacts on the production, market and international trade of copper, copper alloys, final copper slags and copper concentrates. For details, we refer to the comments of the European Copper Institute, which we fully support.

**Dossier Submitter's Response**

The CLP-legislation does not offer the option of assessing the specific concentration limit on a case by case basis, and socio-economic impacts neither can nor should be taken into account when classifying under CLP.
However, we understand your concern and would like to pass on the discussion regarding setting a SCL to RAC.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Romania | SC ROMBAT SA | Company-Manufacturer | 33 |

**Comment received**

SC ROMBAT SA is a member of the International Lead Association or the Pb REACH Consortium. ILA has provided a consolidated response on behalf of the Pb REACH Consortium. As a consequence, SC ROMBAT SA fully support and subscribes to the comments made by ILA.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Muldenhütten Recycling und Umwelttechnik GmbH | Company-Manufacturer | 34 |

**Comment received**

P7, table 3, Classification table: While it is clearly stated, that the scope of the harmonised classification proposal is limited to reproductive toxicity, this table implies that also other endpoints have been considered. The statement "conclusive, but not sufficient for classification" is misleading, since lead metal has no PC-hazards and some endpoints are considered as relevant for the powder form of lead. We would suggest amending entries in the column headed "reason for no classification" to indicate that the endpoints were not considered or include a dash (-) as was the case for other columns in the table.

P9, labelling: We do not understand why the proposed R-phrases for lead metal of R60, R61 are more severe than other lead compounds on Annex VI to CLP (R61, R62).

P11 Section A 3, Justification that action is needed at community level: Industry proposed a different classification for lead in massive form due the arguments that in massive form there is limited opportunity under normal handling and use for exposure to lead. In many cases processing of the massive results in exposure to lead compounds - predominantly oxides - and not lead metal. Related

risk management measures are already part of the supply chain communication. We believe ample quantitative data illustrates that extrapolation or read across from reproductive toxicity data on bioavailable lead salts to elemental lead (especially in the massive form) is overly conservative and that due consideration must be given to relative bioavailability and physical form. Based upon numerous in vitro and animal feeding studies, the relative bioavailability of metallic lead is estimated to be 1% or less than that of soluble lead forms (USEPA, 2007). A two-order of magnitude difference in bioavailability is quantitatively significant and CLP Guidance indicates that bioavailability merits consideration in consideration of appropriate classification. During self-classification, industry judged that massive forms of metallic lead were highly unlikely to yield human exposures associated with reproductive toxicity due to limited bioavailability. We acknowledge that bioavailability varies as a function of particle size and increases as particle size decreases. At extremely small particle sizes, metallic lead particles exhibit bioavailability that approaches soluble lead substances (Barltrop and Meek, 1979). For example, a 200 µm particle has a relative bioavailability of 14% and progressively increases to 100% as particle size decreases to 6 µm. Although the form of a substance might not be a consideration under normal circumstances, the fact that particle size has a significant impact upon bioavailability indicates that particle size affects the intrinsic properties (bioavailability) of metallic lead. Industry thus proposed classification of lead metal powder but not massive forms of lead. This distinction was reinforced by exposure route considerations. Inhalation is a major route of lead entry into the body and is feasible to consider for lead metal powders but not for massive forms of lead. Thus, inasmuch as patterns of normal handling and use factor into classification decisions, expert judgement must be employed in an evaluation of whether particle size should be considered for purposes of classification. Given that inhalation and ingestion are the two primary exposure routes for lead metal, the fact the particle size modulates effects mediated by both routes indicates that particle size should be regarded as an intrinsic property for purposes of classification.
The risks related to use and exposure of lead and lead compounds have been discussed for years. Aiming at limiting the risks for human beings and the environment, regulations have been implemented in different areas and lead has been substituted in several products. Manufacture, use and recycling have been improved for other products. As a result of these activities a decrease of lead concentration in the environment and a decrease of lead blood levels, which is the main indicator for human exposure, have been reported.
80% of the lead produced in Europe (primary and secondary metal) is used for the production of lead acid batteries. The Berzelius Metall GmbH (http://www.berzelius.de/berzelius_en/batterieentsorgung/?navid=6) is a major collector and recycler of these accumulators in Germany. In Germany nearly 100% of lead batteries are collected and material utilization rate is > 90%, which exceeds the requirements of the Battery Directive (2006/66/EC). The manufacture and recycling process is subject to IPPC (Dir 2008/1/EC) and IED (Dir 2010/75/EU) and implementation of BREF notes is mandatory. Related to cars, life cycle emission has been reduced by 99.6% mainly due to increased battery recycling efforts (Ökoinstitut 2010 ).
Reprotoxic effects of lead-ion detected in the human body have been widely discussed and accepted and trigger a high standard of risk management in lead industry. This is also reported in the CSR in the registration framework and the voluntary risk assessment report VRAR). These documents are already providing valuable information on how risks from lead can be effectively managed, for example in the case of worker health, and industry is committed to implementing these measures. The report is also helping to identify areas where further research is needed and again industry is committed to delivering this.
On the other hand exposure to lead is still an issue. But exposure of the general population cannot be explained by the use of products containing lead metal. More bioavailable lead compounds are still in use and diffuse sources (agriculture, past pollution, contaminated food) play an imported role in human exposure. To reduce risks related to the latter completely different measures have to be implemented.
Swallowable pieces, especially those containing lead, should be kept out of reach for children. Consumer products with potential direct contact like toys (even for adults), decoration, and furniture should not contain lead. We further note that risks to children (and adults) are being addressed by various restrictions that are in progress related to the REACH regulation (eg jewellery, toys etc) and would not be mitigated in any way by a harmonised classification on reproductive toxicity. In most cases the related products have been imported from outside EU and there is not legal requirement to label consumer articles with related information.
We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to

adults.
We can assume that the source for lead exposure of the general population is rather diffuse than the result of contact with lead metal or lead containing articles. It is thus questionable, whether exposure of the general population will be influenced by classification of lead metal
According to a report by Fraunhofer ISI on behalf of the German UBA (UBA 2003) there is a basic need for action to reduce the environmental burden due to non-point emissions of lead. As main sources for lead burden traffic (cars) and agriculture have been identified. Reduction potentials are described for lead free brake linings and wheel weights (replacement already on-going) and measures reducing erosion of soil of agricultural areas (lead input trough mineral fertilizer and other fertilizers). These sources are in no way affected by classification or authorization since the concentrations in the fertilizers are far below concentration threshold for classification.
In the past 20 years the blood levels in the general population have been significantly fallen since the introduction of a ban of tetraethyl lead in petrol (Kemi 2007, p. 8, UBA 2007b). The average decline in children's blood lead has been approximately 5% per year between 1995 and 2007. The general population is exposed to lead principally via food. For adults more than 80% of the daily uptake of lead happens via food. The sources are dust deposition on plants and on feeding for animals. Children may take up lead via ingestion of soil and dust particles.
The comment that lead is a soft metal that can easily "rub off" on the skin in case of dermal contact is not accurate. Hand to mouth behaviour can result in elevated blood lead levels and this is highlighted in the REACH registration dossier but this is not the result of lead being "rubbed off" on to the skin but more likely the result of exposure to oxidation products on the surface of the metal. Industry studies described in the VRAR have quantitated dermal transfer of oxidation products from metallic lead objects to which consumers are likely to be exposed and determined it to be quite low (1 – 3 µg/cm2 of exposed skin). It has been estimated that of the lead that is transferred to the skin (most likely in the form of lead oxide, due to rapid oxidation of lead metal in air), only about 0.0002% of this is systemically bioavailable.

P17 Section B 2.1 Manufacture: In the EU the majority of lead placed on the market is manufactured from recycled scrap rather than from primary ores.

P17, section B 2.2, Identified uses: Please consider that aviation fuel, paints and crystal glass do not contain lead in the metallic form but lead compounds which are not subject to this classification proposal. The main application of metallic lead is in lead acid batteries (80-90%). In many applications and articles the essential lead is embedded in the object with no relevant contact for the user (machinery, weights, radiation protection, batteries).
Articles containing unwanted and also unessential lead parts with directly accessible surfaces are found more often in imported products (buttons, zippers, jewelleries).

P18, section 4.1.2, Oral absorption rate. Animal feeding studies have long demonstrated that metallic lead is far less bioavailable than soluble lead compounds and many sparingly soluble compounds (Bartrop and Meek (1979)). These observations have been confirmed by in vitro bioavailability tests that demonstrate that metallic lead is usually a 1- 2 orders of magnitude less bioavailable than soluble lead compounds (U.S EPA 2007, OSWER 9285.7-77). We further note that data specific to the uptake of lead by children is not relevant to a discussion of classification for reproductive toxicity which should be restricted to consideration of exposures to adults.
P19 Inhalation rate: We note that this section confirms our earlier comments suggesting that particle size is a significant predictor of exposure and should be considered for the purposes of classification of metals in the massive form.
P 19 Dermal Absorption: Industry studies conducted under controlled experimental conditions indicate that the dermal transfer of oxidation products from lead metal surfaced is far lower than suggested here.

**Dossier Submitter's Response**

The comments are much the same as those presented by the International Lead Association; please see Dossier submitter's responses under comment number 7 (ILA) starting on page 4.

**RAC's response**

The RAC agrees to the DS response and refers to its responses to comments 1 and 7.

| Date | Country | Organisation | Type of Organisation | Comment numb |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| | | | | **er** |
| 07/12/2012 | Germany | Aurubis AG | Company-Manufacturer | 35 |

**Comment received**

Aurubis AG is a member of the International Lead Association (ILA) and the Pb REACH Consortium. ILA has provided a consolidated response on behalf of members of the Pb REACH consortium. As a consequence, Aurubis AG fully supports and subscribes to the comments made by ILA. Further consolidated responses have been provided by Wirtschaftsvereinigung Metalle (WVM) and the European Copper Institute (ECI). Aurubis AG is a member of both associations and fully supports those comments as well.

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

**TOXICITY TO REPRODUCTION**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 04/12/2012 | Germany | EppsteinFOILS GmbH & Co.KG | Company-Downstream user | 36 |

**Comment received**

Page 24ff Chapter B 4.11.1.2: Our company is a company dealing with lead for 160 years and has not seen any impact on fertility for their present and former employees. Workers at our company and its predecessors always have been in contact with metallic lead. Upon request blood lead values - by the way today in average substantially below occupational health thresholds - are available and there are no cases of reduced fertility known. Our company would support a scientific study on male fertility in addition to those listed in table 11.
On the other hand CLH report is giving no new facts. It is a new summary on elder contemporarily available information.
Page 24 ff Chapter 4.11.1.2: The CLH report is giving no positive evidence that lead metal itself is having an impact on fertility. In addition to this the CLH report is irresponsibly mixing up facts related to lead compounds. The majority of the various studies for fertility in Table 11 are from occupational settings with a high variation range between results and often limited reliability of single results. The majority of cases in table 11 are from surroundings making exposure to lead compounds very likely (smelter, battery worker…) This is no evidence for toxicity of solid lead metal. There are to be considered difficulties to evaluate impact of lead on fertility: Fertility, especially male fertility, today is affected by many other effects than only lead.

**Dossier Submitter's Response**

The fact that risks arising from professional use (perhaps) already are well handled is not an argument for refraining to classify lead under CLP.

Regardless of how exposure occurs (via lead compounds or via lead metal); it is the lead ion that is responsible for lead toxicity in the body. In all the studies presented, the toxic effects of lead are therefore caused by the same lead ion, regardless of which lead compound was responsible for the exposure in the first place. For more regarding "read across", see dossier submitter's response under comment 7 on page 5-6.

**RAC's response**

The RAC agrees to the DS response in that it is the ion, which induces the toxic effects relevant for C&L. However, as indicated in its responses to comments 1 and 7 on the bioavailability of lead from its different physical forms RAC has concluded that the proposed C&L is applicable to lead of all its physical-chemical forms.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 05/12/2012 | United Kingdom | International Lead Association | Industry or trade association | 37 |

**Comment received**

Toxicity to Reproduction

• P21-24 Section 4.11.1.1 Non-human information We concur that the extensive information available to characterize the effects of lead upon reproduction in humans renders non-human information to secondary importance. However, it is incorrect to imply that mechanistic inferences can be drawn with ease. As described in the VRAR, there appear to be distinct mechanistic differences for the impact of lead upon semen quality parameters in humans as opposed to experimental animals such as rodents. Moreover, human exposure in many scenarios is not to metallic lead but to lead compounds and hence care needs to be taken when reading across this information for classification purposes.

**Dossier Submitter's Response:** Please see dossier submitter's response under comment 7 on page 5-6 regarding "read across".

• P21 Section 4.11.1.1 Whilst it is true that the lead cation is responsible for the adverse effects of lead compounds it is not true that it is unimportant which type of lead source is really causing the exposure. Information on relative bioavailability (e.g. relative amounts of absorption) within a related group/category of chemicals is of use in classification. The relative bioavailability of lead metal and soluble lead compounds (which the author has already indicated are selected for experimental studies due to their good oral bioavailability) should be used to examine whether classification in the same CLP category is appropriate.

**Dossier Submitter's Response:** Relative bioavailability has been discussed previously; please see dossier submitter's response on eg page 1 and 3.

• P24 Section 4.11.1.2 Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. One would have to question whether normal handling of use of lead in massive form could provide sufficient bio-available lead ion to cause similar effects. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that "under conditions in which it is reasonably expected to be used "lead in massive form can produce effects on male fertility.

**Dossier Submitter's Response:** For C&L purposes there is no need for evidence of actual effects on male fertility, the inherent properties of lead are enough to warrant classification. To determine whether a "sufficient bio-available" amount of lead is formed during "reasonably expected use" is touching upon risk assessment, which is not a part of the evaluation for C&L. The intrinsic properties of lead have a potential to cause effects on male fertility, this is sufficient for the purpose of classification. Even if the lead metal causes exposure via an oxidized surface containing lead oxide it is the lead that is the source of the exposure. If the exposure takes place via lead oxide which results in lead ions in the body it is still the lead that shall be classified.

• P29 Female fertility Whilst we recognize that data on human female fertility is limited, a dossier proposing classification for reproductive toxicity cannot explicitly exclude evaluation of effects in adult females.

**Dossier Submitter's Response:** Please see p.29 of the CLH-report (Female fertility). Excluding female fertility in the evaluation will not affect classification as classification is based on both genders and the data presented addressing male fertility is sufficient for classification.

• P29 Section 4.11.2.1 There are no animal studies investigating developmental toxicity of metallic lead. Findings reported in the dossier have all been the result of utilising soluble lead compounds with high bioavailability. Read across arguments are therefore required. It is clear that read across is not appropriate for all endpoints (probably as a result of different potency in relation to bioavailability). This is exemplified by the fact that whereas a number of soluble lead compounds were carcinogenic following oral administration in a rodent bioassay, lead metal powder did not produce the same response (Furst et al, 1976) .

**Dossier Submitter's Response:** There are robust human data describing the developmental effects of lead (Lanphear et al. (2008) etc), human data is preferred over animal data so this should not be considered a problem. Regarding "read across", see dossier submitter's response under comment 7, point 2 (page 5-6).

• P29 Section 4.11.2.2 Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10 mcg/dL. The discussion of individual studies notes effects upon MDI's and GCI's – these are not IQ impacts.
After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. However, importantly no association was observed with gestational blood lead levels.

• We do not understand why this section contains detailed discussion of the pooled analysis undertaken by Lanphear et al. These studies examined the postnatal or childhood effects of exposure to lead. It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity.

• We would therefore conclude that epidemiological data does not support the conclusion that there is sufficient human evidence to merit classification of lead metal as Repr Category 1A for developmental toxicity if this is restricted to prenatal exposures. This is especially the case when considering classification of metallic lead (in massive form) which as we have indicated previously has significantly lower bioavailability compared to soluble lead compounds.

**Dossier Submitter's Response:** This has already been discussed. Please see dossier submitter's response under comment 7 on page 5.

• P33 Section 4.11.4 The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy as the result of parental exposure. We disagree with the statement that there is no safe level for lead induced developmental neurotoxicity as we do not believe that the available data for lead metals supports such an effect.

**Dossier Submitter's Response:** Same as above.

• P34 Section 4.11.5 We disagree with the conclusion that there is sufficient human evidence to prove the toxicity of metallic lead in all physical forms. Animal studies require read across from lead in a more bioavailable form and human developmental studies are confounded by subsequent postnatal exposure. We believe that the points we have made during this consultation merit discussion at RAC, specifically those related to the relative bioavailability when grouping or reading across between chemicals and the role the physical form a substance is placed on the market should have upon classification. We do not necessarily believe that this is a discussion on risk but more of bioavailability, and the effect this may have on the likelihood the effect may occur under reasonably expected use. It is important also to recognise that when processing the metal in massive form, exposures resulting from production of vapour or dust will not be to the metal itself but to metal oxides.
We would argue that the on-going debate on nanomaterial's provides further evidence that the statement made in this dossier that "different physical forms thus all reflect the manifestations of the substances intrinsic properties" is not correct in all instances. We believe that consideration of the physical form in which a substance is placed on the market (and thus the likelihood that a specific effect could be manifested under normally expected use) is common to all metals in the massive form and needs to be considered in the context of classification and labelling decisions.

• P35 Justification of Chosen Specific Concentration Limit We are surprised that this section refers to "newly update CLP guidelines". The guidelines were only published on 20th November, sometime after the public consultation on the CLH report was initiated. We do not believe that it was appropriate to start a public consultation of a document that includes reference to methodology for

assessing SCL before guidelines had been published and were available to all stakeholders.

**Dossier Submitter's Response:** This has been discussed previously. Please see dossier submitter´s response under comment 31 on page 38 and under comment 37 on page 45.

• We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence, as is the case being proposed for lead.

**Dossier Submitter's Response:** Please see dossier submitter's response on the next page.

• As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labelling. This in itself eliminates one of the advantages of having a globally harmonised classification and labelling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.

**Dossier Submitter's Response:** Noted, but this argument has nothing to do with the CLH-proposal and has no relevancy here.

• An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the hazard presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.

**Dossier Submitter's Response:** Noted, and we understand your concern. We would like to pass on the discussion regarding setting of a SCL to RAC for discussion.

Notwithstanding the comments above, as indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects. Whilst one may be able to propose extrapolation of effects of exposure during early childhood to theoretical prenatal effects on the foetus we believe that the available evidence does not support this.

**Dossier Submitter's Response:** This has been discussed previously. Please see dossier submitter's response under comment 7 on page 5.

Calculation of a SCL is not as straight forward as the CLH report indicates and there are likely many difficulties in evaluating developmental toxicity (pre-natal) potency and calculating an ED10 for metallic lead from effects observed in epidemiological evidence on childhood IQ resulting from exposure to different forms of lead. While there could be reasons for extrapolation of the hazardous properties of metallic lead from data available on soluble lead compounds, the expected potency of the effects is likely to be quite different and difficult to estimate (as illustrated by quite different estimates of relative bioavailability).
These difficulties are highlighted by the approach taken in the report. For example blood lead-external administered dose calculations employed are at significant variance with the basic toxicokinetics of lead. Multiple biokinetic models are available to predict the relationship between specific lead exposures and levels of lead in blood (VRAR, 2008) and should be employed in place of the inaccurate and simplistic toxicokinetic assumptions in the present proposal. Also the document further indicates that the ED10 is the lowest dose that produces reprotoxic effects when in fact it should be more precisely and quantitatively defined (Muller et al., 2012) as "the effective dose with a

10% effect level above the background".
We therefore believe that the calculations utilised to assign a specific concentration limit of 0.03% are severally flawed and not an appropriate methodology. We believe that there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ and that an alternative starting point for quantifying an SCL for potential reproductive effects such as birth weight in offspring, obstetric outcomes or paternal semen quality should be utilised.

**Dossier Submitter's Response:** We agree that our approach to calculate the $ED_{10}$ can be discussed, and there may be more complex models that can be used for calculating a more finely tuned $ED_{10}$. Unfortunately, there is no specific guidance on how to set a SCL based on human data. However, whatever model is chosen for the calculations there will be inaccuracies and the resulting SCL could be discussed. Our "$ED_{10}$"-calculation should be seen as an indication, where the take-home-message is that lead is highly potent; in the range of many orders of magnitude more potent than what is required for assigning a SCL lower than the generic concentration limit of 0.3%.

The dossier submitter would like to pass on further discussions regarding the setting of an appropriate SCL based on human data to RAC.

• P36 Section 4.11.6 We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.
We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

**Dossier Submitter's Response:** As discussed previously, the developmental effects of lead occur after both pre- and post natal exposure, see dossier submitter's response on page 5. Bioavailability has also been discussed previously; please see dossier submitter's response on page 1.

---
*ECHA's comment: The literature list below was submitted as attachment.*

Literature Cited
Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env. Health 34: 280-285.
Bonde, J.P., Joffe, M., Apostoli, P., Dale, A., Kiss, P., Spano, M., Caruso, F., Giwercman, A., Bisanti, L., Porru, S., Vanhoorne, M., Comhaire, F., Zschiesche, W. (2002). Sperm Count And Chromatin Structure In Men Exposed To Inorganic Lead: Lowest Adverse Effect Levels. Occup Environ Med 59: 234-242.
Bornschein, R.L., Grote, J., Mitchell, T., Succop, P.A., Dietrich, K.N., Krafft, K.M., Hammond, P.B.

(1989). Effects Of Prenatal Lead Exposure On Infant Size At Birth. In Lead Exposure and Child Development: An International Assessment. Smith, M.A., Grant, L.D. and Sors, A. I (eds), Kluwer Academic Publishers.
Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.
Furst, A., Schlauder, M., Sasmore, D. (1976 ) Tumorigenic Activity of Lead Chromate. Cancer Res 36:1779-1783
ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)
Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN, Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899
Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.
Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory approach to assess the potency of substances toxic to the reproduction 16

Regul Toxicol Pharmacol: 63(1):97-105
OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media
Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.
Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71.
Strőmberg U et al (2008) Yearly measurements of blood lead in Swedish children since 1978: The declining trend continues in the petrol free period 1995-2007, Env Res 107 (3), 332-335
U.S. Environmental Protection Agency (2007). Estimation of the relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77.

**Dossier Submitter's Response**

Comments have been inserted directly under each relevant section.

**RAC's response**

The RAC agrees to the DS response in that it is the ion, which induces the toxic effects relevant for C%L. However, RAC concludes that lead is bioavailable in all forms and classification for reproductive toxicity should apply to all forms.
Regarding the C&L as such RAC refers to its response to comment 7 on the CLP-criteria for developmental toxicity.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 05/12/2012 | Finland | | MemberState | 38 |

**Comment received**

We support the proposed classification Repr. 1A; H360DF according to CLP. We also fully agree with the dossier submitter's justification as to why physical form or particle size should not have an influence on classification of metallic lead. Also the suggested specific concentration limit of 0.03 % is supported.

**Dossier Submitter's Response**

Your support is appreciated.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | | MemberState | 39 |

**Comment received**

p.25, Table 11, Jockenhövel et al. (1990), column 2 should read:
The mean seminal fluid lead concentration in infertile men was 11.18 +/- 0.62 µg/dL and 5.61 +/- 0.53 µg/dL in fertile men.

column 3 should supposedly read:
The semen lead levels in the infertile groups were significantly higher (p=<0.006) than in fertile men.

p.25, Table 11, Lerda (1992), column 3 should read:
Semen volume, sperm count & percentage of live sperm were lower in the exposed group than the controls.

p.26, Table 11, Hu et al. (1992), column 3 should read:
Lead workers had a high rate of teratospermia and decrements in sperm density & motility

p.26, Table 11, Dawson et al. (1998), column 3 should read:
Significant differences were observed between high and low sperm groups for semen lead levels (p=0.01).

p.27, Table 11, El-Zohairy et al. (1996), column 3 should read:
Infertile subjects in both groups had similar sperm motility, higher level of males with lower sperm count and slightly greater proportions of abnormal sperm but concluded Pb had little impact on reproductive function.

p.27, Table 11, Wildt et al. (1983), column 3 should supposedly read:
No differences between groups on sperm count, over-all sperm morphology, prostatic function and vesicular function. Lead exposed men had normal sperm count & higher number of live spermatozoa than controls.

**Dossier Submitter's Response**

You are correct, thank you for pointing out these mistakes. The robust study summaries are copied directly from the Chemical Safety Report (2010) submitted by Industry. Something must have gone wrong when converting the format and unfortunately we didn't notice that some of the text had been misplaced before you pointed it out to us.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | BSB Recycling GmbH | Company-Manufacturer | 40 |

**Comment received**

P24, section B 4.11.1.2, Male fertility: Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that "under conditions in which it is reasonably expected to be used "lead in massive form can produce effects on male fertility.

P29, section B 4.11.2.2, Developmental toxicity: Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10 µg/dL. The discussion of individual studies notes effects upon MDI's and GCI's – these are not IQ impacts.
After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels.
It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during

pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity.

P33, section B 4.11.4, Summary and discussion of reproductive toxicity: The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy or as the result of parental exposure. We would question the statement that there is no safe level for lead induced developmental neurotoxicity as available data suggest that no effect levels can be defined for the effects of prenatal exposures

P35, section 4.11.5, Justification of Chosen Specific Concentration Limit: The "newly update CLP guidelines" the CLH report refers to, was only published after the beginning of the public consultation. We do not regard it as appropriate to include in a public consultation reference to new methodology before it had been published and made available to all stake holders.
We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence.
As indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects.
As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other Region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labeling. This in itself eliminates one of the advantages of having a globally harmonised classification and labeling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.
An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.

P36 Section 4.11.6, Conclusion on classification and labeling: We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this is not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are

positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.
We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

**Dossier Submitter's Response**

These comments have all been discussed previously. Please see dossier submitter's responses under comment number 7 and comment number 37.

**RAC's response**

The RAC supports the resonse of the DS and refers to its responses to comments 1, 7 and 37.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Denmark | | MemberState | 41 |

**Comment received**

Page 35-36: Justification of Chosen SCL:
The dossier submitter proposes an SCL of 0.03% as lead is placed in the high potency group for reproductive toxicants. However, due to the extreme potency of lead we suggest that the SCL may be even lower and that further evaluation of the appropriate SCL is undertaken. The guidance for the application of the CLP criteria states that, "For substances with an ED10 more than 10 fold below 4 mg/kg bw/day, meaning an ED10 below 0.4 mg/kg bw/day, a 10-fold lower SCL should be used. For even more potent substance the SCL should be lowered with a factor of 10 for every factor of 10 the ED10 is below 4 mg/kg bw/day".

The exposure level required to produce a lead blood level associated with significant impairment of the IQ (10 µg/dL), is estimated to range from 8.3 µg/kg to 20.8 µg/kg for worst-case and best-case scenarios, respectively. Although not directly comparable with an ED10 value, these levels are many fold below 4 mg/kg bw/day, suggesting that the appropriate SCL should be even lower than 0.03%.

**Dossier Submitter's Response**

The dossier submitter would like to pass on this question to RAC for discussion.

**RAC's response**

Please see the responses to comment 7 and 17.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Berzelius Stolberg (BBH) | Company-Manufacturer | 42 |

**Comment received**

P21-24 Section 4.11.1.1 Non-human information We concur that the extensive information available to characterize the effects of lead upon reproduction in humans renders non-human information to secondary importance. However, it is incorrect to imply that mechanistic inferences can be drawn with ease. As described in the VRAR, there appear to be distinct mechanistic differences for the impact of lead upon semen quality parameters in humans as opposed to experimental animals such as rodents. Moreover, human exposure in many scenarios is not to metallic lead but to lead compounds and hence care needs to be taken when reading across this information for classification purposes.

P21 Section 4.11.1.1 Whilst it is true that the lead cation is responsible for the adverse effects of lead compounds it is not true that it is unimportant which type of lead source is really causing the exposure. Information on relative bioavailability (e.g. relative amounts of absorption) within a related group/category of chemicals is of use in classification. The relative bioavailability of lead metal and soluble lead compounds (which the author has already indicated are selected for experimental studies due to their good oral bioavailability) should be used to examine whether classification in the same CLP category is appropriate.

P22 Section 4.11.1.2 Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. One would have to question whether normal handling of use of lead in massive form could provide sufficient bio-available lead ion to cause similar effects. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that "under conditions in which it is reasonably expected to be used "lead in massive form can produce effects on male fertility.

**Dossier Submitter's Response:** According to the CLP regulation, substances shall be classified based on their intrinsic properties (hazard). Risk should not be considered.

P29 Section 4.11.2.1 There are no animal studies investigating developmental toxicity of metallic lead. Findings reported in the dossier have all been the result of utilising soluble lead compounds with high bioavailability. Read across arguments are therefore required. It is clear that read across is not appropriate for all endpoints (probably as a result of different potency in relation to bioavailability). This is exemplified by the fact that whereas a number of soluble lead compounds were carcinogenic following oral administration in a rodent bioassay, lead metal powder did not produce the same response (Furst et al, 1976) .

P29 Female fertility Whilst we recognize that data on human female fertility is limited, a dossier proposing classification for reproductive toxicity cannot explicitly exclude evaluation of effects in adult females.

P29 Section 4.11.2.2 Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10 μg/dL. The discussion of individual studies notes effects upon MDI's and GCI's – these are not IQ impacts. After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. However, no association was observed with gestational blood lead levels.
We do not understand why this section contains detailed discussion of the pooled analysis undertaken by Lanphear et al. These studies examined the postnatal or childhood effects of exposure to lead. It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity. We would therefore conclude that epidemiological data does not support the conclusion that there is sufficient human evidence to merit classification of lead metal as Repr Category 1A for developmental toxicity if this is restricted to prenatal exposures. This is especially the case when considering classification of metallic lead (in massive form) which as we have indicated previously has significantly lower bioavailability compared to soluble lead compounds.

P33 Section 4.11.4 The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy as the result of parental exposure. We disagree with the statement that there is no safe level for lead induced developmental neurotoxicity as we do not believe that the available data for lead metals supports such an effect.

P34 Section 4.11.5 We disagree with the conclusion that there is sufficient human evidence to prove the toxicity of metallic lead in all physical forms. Animal studies require read across from lead in a

more bioavailable form and human developmental studies are confounded by subsequent postnatal exposure. We believe that the points we have made during this consultation merit discussion at RAC, specifically those related to the relative bioavailability when grouping or reading across between chemicals and the role the physical form a substance is placed on the market should have upon classification. We do not necessarily believe that this is a discussion on risk but more of bioavailability, and the effect this may have on the likelihood the effect may occur under reasonably expected use. It is important also to recognise that when processing the metal in massive form, exposures resulting from production of vapour or dust will not be to the metal itself but to metal oxides.
We would argue that the on-going debate on nanomaterial's provides further evidence that the statement made in this dossier that "different physical forms thus all reflect the manifestations of the substances intrinsic properties" is not correct in all instances. We believe that consideration of the physical form in which a substance is placed on the market (and thus the likelihood that a specific effect could be manifested under normally expected use) is common to all metals in the massive form and needs to be considered in the context of classification and labelling decisions.

P35 Justification of Chosen Specific Concentration Limit We are surprised that this section refers to "newly update CLP guidelines". The guidelines were only published on 20th November, sometime after the public consultation on the CLH report was initiated. We do not believe that it was appropriate to start a public consultation of a document that includes reference to methodology for assessing SCL before guidelines had been published and were available to all stakeholders. We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence.

As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labelling. This in itself eliminates one of the advantages of having a globally harmonised classification and labelling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.

An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.

Notwithstanding the comments above, as indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects. Whilst one may be able to propose extrapolation of effects of exposure during early childhood to theoretical prenatal effects on the foetus we believe that the available evidence does not support this.
Calculation of a SCL is not as straight forward as the CLH report indicates and there are likely many difficulties in evaluating developmental toxicity (pre-natal) potency and calculating an ED10 for metallic lead from effects observed in epidemiological evidence on childhood IQ resulting from exposure to different forms of lead. While there could be reasons for extrapolation of the hazardous properties of metallic lead from data available on soluble lead compounds, the expected potency of the effects is likely to be quite different and difficult to estimate (as illustrated by quite different estimates of relative bioavailability).

These difficulties are highlighted by the approach taken in the report. For example blood lead-external administered dose calculations employed are at significant variance with the basic toxicokinetics of lead. Multiple biokinetic models are available to predict the relationship between specific lead exposures and levels of lead in blood (VRAR, 2008) and should be employed in place of the inaccurate and simplistic toxicokinetic assumptions in the present proposal. Also the document further indicates that the ED10 is the lowest dose that produces reprotoxic effects when in fact it should be more precisely and quantitatively defined (Muller et al., 2012) as "the effective dose with a 10% effect level above the background".
We therefore believe that the calculations utilised to assign a specific concentration limit of 0.03% are severally flawed and not an appropriate methodology. We believe that there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ and that an alternative starting point for quantifying an SCL for potential reproductive effects such as birth weight in offspring, obstetric outcomes or paternal semen quality should be utilised.

P36 Section 4.11.6 We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.
We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

---
ECHA's comment:

**Dossier Submitter's Response**

The majority of these comments have been discussed previously; please see dossier submitter's response under comment number 37.

**RAC's response**

RAC supports the DS responses and refers to its responses to comments 1, 7 and 37.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | JL Goslar GmbH | Company-Downstream user | 43 |

**Comment received**

Toxicity to Reproduction

- P21-24 Section 4.11.1.1 Non-human information We concur that the extensive information

available to characterize the effects of lead upon reproduction in humans renders non-human information to secondary importance. However, it is incorrect to imply that mechanistic inferences can be drawn with ease. As described in the VRAR, there appear to be distinct mechanistic differences for the impact of lead upon semen quality parameters in humans as opposed to experimental animals such as rodents. Moreover, human exposure in many scenarios is not to metallic lead but to lead compounds and hence care needs to be taken when reading across this information for classification purposes.

- P21 Section 4.11.1.1 Whilst it is true that the lead cation is responsible for the adverse effects of lead compounds it is not true that it is unimportant which type of lead source is really causing the exposure. Information on relative bioavailability (e.g. relative amounts of absorption) within a related group/category of chemicals is of use in classification. The relative bioavailability of lead metal and soluble lead compounds (which the author has already indicated are selected for experimental studies due to their good oral bioavailability) should be used to examine whether classification in the same CLP category is appropriate.

- P22 Section 4.11.1.2 Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. One would have to question whether normal handling of use of lead in massive form could provide sufficient bio-available lead ion to cause similar effects. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that “under conditions in which it is reasonably expected to be used “ lead in massive form can produce effects on male fertility.

- P29 Section 4.11.2.1 There are no animal studies investigating developmental toxicity of metallic lead. Findings reported in the dossier have all been the result of utilising soluble lead compounds with high bioavailability. Read across arguments are therefore required. It is clear that read across is not appropriate for all endpoints (probably as a result of different potency in relation to bioavailability). This is exemplified by the fact that whereas a number of soluble lead compounds were carcinogenic following oral administration in a rodent bioassay, lead metal powder did not produce the same response (Furst et al, 1976) .

- P29 Female fertility Whilst we recognize that data on human female fertility is limited, a dossier proposing classification for reproductive toxicity cannot explicitly exclude evaluation of effects in adult females.

- P29 Section 4.11.2.2 Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10 µg/dL. The discussion of individual studies notes effects upon MDI’s and GCI’s – these are not IQ impacts.

- After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. However, no association was observed with gestational blood lead levels.

- We do not understand why this section contains detailed discussion of the pooled analysis undertaken by Lanphear et al. These studies examined the postnatal or childhood effects of exposure to lead. It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity.

- We would therefore conclude that epidemiological data does not support the conclusion that there is sufficient human evidence to merit classification of lead metal as Repr Category 1A for developmental toxicity if this is restricted to prenatal exposures. This is especially the case when considering classification of metallic lead (in massive form) which as we have indicated previously has significantly lower bioavailability compared to soluble lead compounds.

- P33 Section 4.11.4 The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy as the result of parental exposure. We disagree with the statement that there is no safe level for lead induced developmental neurotoxicity as we do not believe that the available data for lead metals supports such an effect.

- P34 Section 4.11.5 We disagree with the conclusion that there is sufficient human evidence to prove the toxicity of metallic lead in all physical forms. Animal studies require read across from lead in a more bioavailable form and human developmental studies are confounded by subsequent postnatal exposure. We believe that the points we have made during this consultation merit discussion at RAC, specifically those related to the relative bioavailability when grouping or reading across between chemicals and the role the physical form a substance is placed on the market should have upon classification. We do not necessarily believe that this is a discussion on risk but more of bioavailability, and the effect this may have on the likelihood the effect may occur under reasonably expected use. It is important also to recognise that when processing the metal in massive form, exposures resulting from production of vapour or dust will not be to the metal itself but to metal oxides.
We would argue that the on-going debate on nanomaterial's provides further evidence that the statement made in this dossier that "different physical forms thus all reflect the manifestations of the substances intrinsic properties" is not correct in all instances. We believe that consideration of the physical form in which a substance is placed on the market (and thus the likelihood that a specific effect could be manifested under normally expected use) is common to all metals in the massive form and needs to be considered in the context of classification and labelling decisions.

- P35 Justification of Chosen Specific Concentration Limit We are surprised that this section refers to "newly update CLP guidelines". The guidelines were only published on 20th November, sometime after the public consultation on the CLH report was initiated. We do not believe that it was appropriate to start a public consultation of a document that includes reference to methodology for assessing SCL before guidelines had been published and were available to all stakeholders.

- We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence.

- As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labelling. This in itself eliminates one of the advantages of having a globally harmonised classification and labelling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.

- An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.

Notwithstanding the comments above, as indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects. Whilst one may be able to propose extrapolation of effects of exposure during early childhood to theoretical prenatal effects on the foetus we believe that the available evidence does not support this. Calculation of a SCL is not as straight forward as the CLH report indicates and there are likely many difficulties in evaluating developmental toxicity (pre-natal) potency and calculating an ED10 for metallic lead from effects observed in epidemiological evidence on childhood IQ resulting from exposure to different forms of lead. While there could be reasons for extrapolation of the hazardous properties of metallic lead from data available on soluble lead compounds, the expected potency of the effects is likely to be quite different and difficult to estimate (as illustrated by quite different estimates of relative bioavailability).
These difficulties are highlighted by the approach taken in the report. For example blood lead-external administered dose calculations employed are at significant variance with the basic toxicokinetics of lead. Multiple biokinetic models are available to predict the relationship between specific lead exposures and levels of lead in blood (VRAR, 2008) and should be employed in place of the inaccurate and simplistic toxicokinetic assumptions in the present proposal. Also the document further indicates that the ED10 is the lowest dose that produces reprotoxic effects when in fact it should be more precisely and quantitatively defined (Muller et al., 2012) as "the effective dose with a 10% effect level above the background".
We therefore believe that the calculations utilised to assign a specific concentration limit of 0.03% are severally flawed and not an appropriate methodology. We believe that there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ and that an alternative starting point for quantifying an SCL for potential reproductive effects such as birth weight in offspring, obstetric outcomes or paternal semen quality should be utilised.

- P36 Section 4.11.6 We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.

We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

Literature Cited

Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env.

Health 34: 280-285.
Bonde, J.P., Joffe, M., Apostoli, P., Dale, A., Kiss, P., Spano, M., Caruso, F., Giwercman, A., Bisanti, L., Porru, S., Vanhoorne, M., Comhaire, F., Zschiesche, W. (2002). Sperm Count And Chromatin Structure In Men Exposed To Inorganic Lead: Lowest Adverse Effect Levels. Occup Environ Med 59: 234-242.
Bornschein, R.L., Grote, J., Mitchell, T., Succop, P.A., Dietrich, K.N., Krafft, K.M., Hammond, P.B. (1989). Effects Of Prenatal Lead Exposure On Infant Size At Birth. In 15
Lead Exposure and Child Development: An International Assessment. Smith, M.A., Grant, L.D. and Sors, A. I (eds), Kluwer Academic Publishers.
Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.
Furst, A., Schlauder, M., Sasmore, D. (1976 ) Tumorigenic Activity of Lead Chromate. Cancer Res 36:1779-1783
ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)
Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN, Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899
Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.
Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory approach to assess the potency of substances toxic to the reproduction Regul Toxicol Pharmacol: 63(1):97-105
OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media
Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.
Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71. 16
U.S. Environmental Protection Agency (2007). Estimation of the relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77

**Dossier Submitter's Response**

These comments have all been discussed previously. Please see dossier submitter's responses under comment 7 and 37.

**RAC's response**

RAC supports the DS responses and refers to its responses to comments 1, 7 and 37.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | Metallwerk Dinslaken GmbH & Co.KG | Company-Manufacturer | 44 |

**Comment received**

Toxicity to Reproduction

☐ P21-24 Section 4.11.1.1 Non-human information We concur that the extensive information available to characterize the effects of lead upon reproduction in humans renders non-human information to secondary importance. However, it is incorrect to imply that mechanistic inferences can be drawn with ease. As described in the VRAR, there appear to be distinct mechanistic differences for the impact of lead upon semen quality parameters in humans as opposed to experimental animals such as rodents. Moreover, human exposure in many scenarios is not to metallic lead but to lead compounds and hence care needs to be taken when reading across this information for classification purposes.

☐ P21 Section 4.11.1.1 Whilst it is true that the lead cation is responsible for the adverse effects of lead compounds it is not true that it is unimportant which type of lead source is really causing the

exposure. Information on relative bioavailability (e.g. relative amounts of absorption) within a related group/category of chemicals is of use in classification. The relative bioavailability of lead metal and soluble lead compounds (which the author has already indicated are selected for experimental studies due to their good oral bioavailability) should be used to examine whether classification in the same CLP category is appropriate.

☐ P22 Section 4.11.1.2 Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. One would have to question whether normal handling of use of lead in massive form could provide sufficient bio-available lead ion to cause similar effects. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that "under conditions in which it is reasonably expected to be used " lead in massive form can produce effects on male fertility.

☐ P29 Section 4.11.2.1 There are no animal studies investigating developmental toxicity of metallic lead. Findings reported in the dossier have all been the result of utilising soluble lead compounds with high bioavailability. Read across arguments are therefore required. It is clear that read across is not appropriate for all endpoints (probably as a result of different potency in relation to bioavailability). This is exemplified by the fact that whereas a number of soluble lead compounds were carcinogenic following oral administration in a rodent bioassay, lead metal powder did not produce the same response (Furst et al, 1976) .

☐ P29 Female fertility Whilst we recognize that data on human female fertility is limited, a dossier proposing classification for reproductive toxicity cannot explicitly exclude evaluation of effects in adult females.

☐ P29 Section 4.11.2.2 Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10
discussion of individual studies notes effects upon MDI's and GCI's – these are not IQ impacts.

☐ After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. However, no association was observed with gestational blood lead levels.

☐ We do not understand why this section contains detailed discussion of the pooled analysis undertaken by Lanphear et al. These studies examined the postnatal or childhood effects of exposure to lead. It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity.

☐ We would therefore conclude that epidemiological data does not support the conclusion that there is sufficient human evidence to merit classification of lead metal as Repr Category 1A for developmental toxicity if this is restricted to prenatal exposures. This is especially the case when considering classification of metallic lead (in massive form) which as we have indicated previously has significantly lower bioavailability compared to soluble lead compounds.

☐ P33 Section 4.11.4 The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy as the result of parental exposure. We disagree with the statement that there is no safe level for lead induced developmental neurotoxicity as we do not believe that the available data for lead metals supports such an effect.

☐ P34 Section 4.11.5 We disagree with the conclusion that there is sufficient human evidence to prove the toxicity of metallic lead in all physical forms. Animal studies require read across from lead in a more bioavailable form and human developmental studies are confounded by subsequent postnatal exposure. We believe that the points we have made during this consultation merit discussion at RAC, specifically those related to the relative bioavailability when grouping or reading across between chemicals and the role the physical form a substance is placed on the market should have upon classification. We do not necessarily believe that this is a discussion on risk but more of

bioavailability, and the effect this may have on the likelihood the effect may occur under reasonably expected use. It is important also to recognise that when processing the metal in massive form, exposures resulting from production of vapour or dust will not be to the metal itself but to metal oxides.
We would argue that the on-going debate on nanomaterial's provides further evidence that the statement made in this dossier that "different physical forms thus all reflect the manifestations of the substances intrinsic properties" is not correct in all instances. We believe that consideration of the physical form in which a substance is placed on the market (and thus the likelihood that a specific effect could be manifested under normally expected use) is common to all metals in the massive form and needs to be considered in the context of classification and labelling decisions.
☐ P35 Justification of Chosen Specific Concentration Limit We are surprised that this section refers to "newly update CLP guidelines". The guidelines were only published on 20th November, sometime after the public consultation on the CLH report was initiated. We do not believe that it was appropriate to start a public consultation of a document that includes reference to methodology for assessing SCL before guidelines had been published and were available to all stakeholders.

☐ We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence.
☐ As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labelling. This in itself eliminates one of the advantages of having a globally harmonised classification and labelling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.
☐ An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.
Notwithstanding the comments above, as indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects. Whilst one may be able to propose extrapolation of effects of exposure during early childhood to theoretical prenatal effects on the foetus we believe that the available evidence does not support this.

Calculation of a SCL is not as straight forward as the CLH report indicates and there are likely many difficulties in evaluating developmental toxicity (pre-natal) potency and calculating an ED10 for metallic lead from effects observed in epidemiological evidence on childhood IQ resulting from exposure to different forms of lead. While there could be reasons for extrapolation of the hazardous properties of metallic lead from data available on soluble lead compounds, the expected potency of the effects is likely to be quite different and difficult to estimate (as illustrated by quite different estimates of relative bioavailability).
These difficulties are highlighted by the approach taken in the report. For example blood lead-external administered dose calculations employed are at significant variance with the basic toxicokinetics of lead. Multiple biokinetic models are available to predict the relationship between specific lead exposures and levels of lead in blood (VRAR, 2008) and should be employed in place of the inaccurate and simplistic toxicokinetic assumptions in the present proposal. Also the document further indicates that the ED10 is the lowest dose that produces reprotoxic effects when in fact it should be more precisely and quantitatively defined (Muller et al., 2012) as "the effective dose with a 10% effect level above the background".

We therefore believe that the calculations utilised to assign a specific concentration limit of 0.03% are severally flawed and not an appropriate methodology. We believe that there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ and that an alternative starting point for quantifying an SCL for potential reproductive effects such as birth weight in offspring, obstetric outcomes or paternal semen quality should be utilised.

☐ P36 Section 4.11.6 We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.

We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

Literature Cited

Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env. Health 34: 280-285.

Bonde, J.P., Joffe, M., Apostoli, P., Dale, A., Kiss, P., Spano, M., Caruso, F., Giwercman, A., Bisanti, L., Porru, S., Vanhoorne, M., Comhaire, F., Zschiesche, W. (2002). Sperm Count And Chromatin Structure In Men Exposed To Inorganic Lead: Lowest Adverse Effect Levels. Occup Environ Med 59: 234-242.

Bornschein, R.L., Grote, J., Mitchell, T., Succop, P.A., Dietrich, K.N., Krafft, K.M., Hammond, P.B. (1989). Effects Of Prenatal Lead Exposure On Infant Size At Birth. In Lead Exposure and Child Development: An International Assessment. Smith, M.A., Grant, L.D. and Sors, A. I (eds), Kluwer Academic Publishers.

Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.

Furst, A., Schlauder, M., Sasmore, D. (1976 ) Tumorigenic Activity of Lead Chromate. Cancer Res 36:1779-1783

ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)

Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN, Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899

Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.

Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory approach to assess the potency of substances toxic to the reproduction

Regul Toxicol Pharmacol: 63(1):97-105
OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media
Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.
Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71.

U.S. Environmental Protection Agency (2007). Estimation of the relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77.

**Dossier Submitter's Response**

These comments have all been discussed previously. Please see dossier submitter's responses under comment number 7 and 37.

**RAC's response**

RAC supports the DS responses and refers to its responses to comments 1, 7 and 37.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Belgium | EUROBAT | Industry or trade association | 45 |

**Comment received**

EUROBAT supports and endorses all comments submitted to this consultation by the International Lead Association (ILA).

**Dossier Submitter's Response**

Noted.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Netherlands | RIVM | National Authority | 46 |

**Comment received**

We agree with classification of metallic lead as a reproductive toxicant in line with the assessment by the Health Council of the Netherlands of this substance. However, as also indicated in the assessment of the Health Council, it is difficult to justify classification specifically for metallic lead. Therefore, some comments are provided which may help to strengthen the proposal.

No information is provided in the CLH proposal on the valency or oxidation state of lead. Metallic lead (Pb0) is considered in this proposal. However, information on toxicokinetics and human exposure discusses lead blood levels only. It is unclear and possibly unknown whether this is organic or inorganic lead and Pb0, Pb2+ or Pb4+. Please make clear which form of lead is meant when known and to which form of lead (which substance) there was external exposure.

**Dossier Submitter's Response:** In epidemiological studies it is usually not known which form(s) of lead that cause(s) the exposure.

For the epidemiologic studies, it is unclear to which lead form the workers were exposed. For the laboratory studies, it is clear that the animals were exposed to Pb2+ and not Pb0. It is unclear from the provided information which of the lead forms is determinative for the reproductive effects or whether Pb0 is transformed in the body to Pb2+. In principle, this requires a read-across justification. It is suggested to justify why exposure to metallic lead can result in effects as observed in the epidemiologic and laboratory studies. Some information on the oral absorption of metallic lead is available according to the ATSDR:

**Dossier Submitter's Response:** Larger pieces of metallic lead have indeed been proven to be bioavailable. Please see dossier submitter's responses on e.g. p1 and p3.

"Effect of Particle Size. Particle size influences the degree of gastrointestinal absorption (Ruby et al. 1999). In rats, an inverse relationship was found between absorption and particle size of lead in diets containing metallic lead particles that were ≤250 µm in diameter (Barltrop and Meek 1979). Tissue lead concentration was a 2.3-fold higher when rats ingested an acute dose (37.5 mg Pb/kg) of lead

particles that were <38 µm in diameter, than when rats ingested particles having diameters in the range of 150–250 µm (Barltrop and Meek 1979)."

**Dossier Submitter's Response:** This is very interesting. The study shows that despite a relatively large (10-20 fold) difference in particle size, the absorption only differs 2-3 fold. Thus, the absorption is not directly proportionate to the particle size.

The description of the laboratory studies is limited to the reproductive effects. This makes it difficult to asses whether the observed effects are a direct effect of the substance or secondary to other toxic effects. To strengthen the justification it is recommended to describe all effects observed in the laboratory studies.

We agree that the limitation of the classification to small particles as done by industry can be questioned. Classification is based on intrinsic hazards. Particle size of a metal may change within the supply chain as a result of metalworking. When the substance is not classified, the information regarding the reprotoxic properties is not known to the downstream user. Annex I part 1.3.4 of the CLP Regulation, already states that labelling is not required if certain criteria are fulfilled. However, classification and a SDS are required. Also the downstream consequences of the classification apply. This indicates that this problem is already addressed in the legislation and that a further exemption for the metal in massive form is not warranted.

The method for setting SCLs for reproductive toxicity not only allows an SCL of 0.03% for high potency substances but also even lower SCLs in case of ED10 values which are substantially lower than 4 mg/kg bw/day. The presented calculation uses a very simple calculation of the dose per kg bw from the blood level which does not take into account elimination, distribution and accumulation. Further, neurodevelopmental effects were based on the relation between the effects and maternal or blood cord levels, meaning in utero exposure, and not on the blood levels of a child of 12 kg bw. It is suggested to base the ED10 calculation on the blood levels in the mothers using the PBPK models used in the VRAR.

**Dossier Submitter's Response**

Thank you for your support and for presenting this additional supporting information.

**RAC's response**

Noted.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 07/12/2012 | Germany | Wieland-Werke AG | Company-Downstream user | 47 |

**Comment received**

1. Classification of lead metal is not warranted by the data. Read across arguments via various steps of assumed effects does not fulfil the CLP criteria for a reprotox 1A classification. Available data show that extrapolating or read across from reproductive toxicity on bioavailable lead salts to elemental lead (especially in the massive form) is not appropriate. For details, we refer to the comments of the International Lead Association which we fully support.
2. Motivation for the proposal of a harmonized classification of lead metal seems to be the observation that some specific consumer products (like fishing sinkers) or uses (like melting lead in the home to produce bullets and fishing weights) should be prohibited in order to avoid any intoxication. These kinds of issues can be more effectively addressed via restrictions under the REACH Regulation on a case by case basis than by classification.
3. The use of the new concept of SCL for reprotox substances is neither appropriate nor procedural correct. The updated guidance was only published in the middle of the commenting phase for this classification proposal and could therefore not be addressed appropriately. Furthermore the consequences of the SCL concept for reprotoxic substances are not discussed with respect to massive materials. Particularly bioavailability, which has to be taken into account for massive metals and alloys ("special preparations" under the REACH Regulation) for environmental endpoints within the CLP, this is not yet adequately considered for human health endpoints.

**Dossier Submitter's Response**

These comments are very similar to some of the comments submitted by the ILA, please see dossier submitter's response under comment number 7 and 37.

**RAC's response**

RAC supports the DS responses and refers to its responses to comments 1, 7 and 37.

**Physical Hazards**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 06/12/2012 | Germany | | MemberState | 48 |
| **Comment received** | | | | |
| p.16, Table 9: Vapour pressure<br>Guidance on information requirements and chemical safety assessment, Chapter R.7a: Endpoint specific guidance, 7.1.1.4 "testing for vapour pressure is not required, if the melting point is > 300°C". Therefore column 2 should read: Vapour pressure is only relevant for solids with a melting point below 300 °C (Lead melts at 326°C). | | | | |
| **Dossier Submitter's Response** | | | | |
| Noted. Thank you for this information. | | | | |
| **RAC's response** | | | | |
| Noted. | | | | |
| **Date** | **Country** | **Organisation** | **Type of Organisation** | **Comment number** |
| 06/12/2012 | Germany | Muldenhütten Recycling und Umwelttechnik GmbH | Company-Manufacturer | 49 |
| **Comment received** | | | | |
| P24, section B 4.11.1.2, Male fertility: Whilst the studies cited support classification of inorganic lead compounds in bioavailable forms (dust, vapour) with respect to effects on male fertility, exposures required to elicit such effects are relatively high (resulting in blood lead levels >45ug/dl). Occupational aerosols generally do not contain metallic lead (Spear et al., 1998) and such studies thus do not provide information specific to metallic forms of lead. There are no experimental animal studies, human epidemiological studies or anecdotal case reports indicating that "under conditions in which it is reasonably expected to be used "lead in massive form can produce effects on male fertility.<br><br>P29, section B 4.11.2.2, Developmental toxicity: Epidemiology studies on effects of prenatal exposure to lead are confounded by postnatal exposure to the children which resulted in a much greater response with respect to decrement in IQ. Moreover, these studies examined effects of exposure to lead compounds and not metallic lead. It is therefore difficult to establish with certainty the effects of prenatal exposure to metallic lead (especially when in a physical form that precludes significant bioavailability). Meta-analysis indicates (Pocock et al., 1994) that prenatal lead exposures have effects secondary in magnitude to postnatal exposures and that little effect occurs at blood levels less than 10 µg/dL. The discussion of individual studies notes effects upon MDI's and GCI's – these are not IQ impacts.<br>After adjusting for confounders, Braun et al (2012) concluded that postnatal blood lead levels at 2 years of age were most strongly associated with cognitive effects. Importantly, no association was observed with gestational blood lead levels.<br>It is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore classification for developmental toxicity essentially means adverse effects induced during pregnancy or as the result of parental exposure. The direct relevance of Lanphear data and particularly the dose response reported for postnatal exposure to children would therefore be of questionable relevance to a discussion on harmonised classification for developmental toxicity.<br><br>P33, section B 4.11.4, Summary and discussion of reproductive toxicity: The summary and discussion of developmental effects refers specifically to IQ deficits in children. We have already questioned whether this is relevant to effects during pregnancy or as the result of parental exposure. We would question the statement that there is no safe level for lead induced developmental neurotoxicity as available data suggest that no effect levels can be defined for the effects of prenatal exposures<br><br>P35, section 4.11.5, Justification of Chosen Specific Concentration Limit: The "newly update CLP guidelines" the CLH report refers to, was only published after the beginning of the public | | | | |

consultation. We do not regard it as appropriate to include in a public consultation reference to new methodology before it had been published and made available to all stake holders.
We also believe that there are inherent difficulties in applying the SCL methodology proposed in the CLP guideline to human epidemiological data as the potency groups proposed to assign SCL have only been validated against animal data. They therefore take no consideration of the greater uncertainty involved in extrapolating animal data to humans and are therefore by nature over-precautionary if the reference data is obtained from human evidence.
As indicated in previous comments our understanding is that in the context of the CLP Regulation "developmental toxicity" refers to effects on offspring via maternal exposure. The evidence provided in the section justifying specific concentration limits refers to effects on childhood IQ not prenatal/developmental effects.

As a general observation we would question the effect on the adoption of SCL methodology in the EU on world trade. No other Region applying the Globally Harmonised Scheme (GHS) has adopted analogous SCL methodology and hence mixtures placed on the market in the EU will have different and in most cases more restrictive classification and labeling. This in itself eliminates one of the advantages of having a globally harmonised classification and labeling approach, creates opportunities for confusion with downstream users and adds additional expense to companies trading in multiple regions due to the need to adopt different regional labelling and hazard communication documentation for mixtures.

An additional complication of the proposed SCL of 0.03% is the practical implications that this will have on classification and labelling of other metals, alloys and products that contain lead as a minor impurity. Whereas the generic limit of 0.3% will typically have limited impact, adoption of a SCL of 0.03% will result in many more substances ,mixtures , metals and alloys being classified (and labelled) as reproductive hazards due to the presence of metallic lead as impurity. This would significantly have damaging effects on recycling flows for a wide range of metallic and other materials and appears to be disproportional to the risks presented by these materials. Very careful consideration must therefore be given to the appropriate derivation of the SCL associated with the classification proposal.

P36 Section 4.11.6, Conclusion on classification and labeling: We disagree with the statement that "there is no safe exposure level for lead induced developmental neurotoxicity". In the context of CLP where developmental toxicity (as described in ECHAs guidelines supporting this regulation) is considered to mean "adverse effects induced during pregnancy or as a result of parental exposure" as this is not supported by any quantitative evidence. Human data on prenatal impacts of lead exposure are less than definitive. Two studies are cited in evidence of prenatal effects upon IQ. The results of the Yugoslavia study were produced by heavy lead exposures not characteristic of current EU general population studies – and even these results indicate the impact of prenatal lead exposure is much smaller in magnitude than post-natal lead exposure. Data from Mexico City are also cited, but are difficult to interpret since (as described in Lanphear et al., 2005) this study observed beneficial impacts of post-natal lead exposure upon later IQ. Earlier evaluations in five prospective studies have characterized the relationship between pre-natal lead exposure and indices of physical and mental development applied to young children. However, while subtle impacts upon developmental indices have been observed, relationships to adverse impacts upon IQ are not significant. Instead, impacts associated with post-natal lead exposure are the most stable and robust predictors of adverse effects of lead upon IQ. Not only are impacts of pre-natal lead exposure in the majority of longitudinal studies of child development not statistically significant when subjected to meta-analysis (Pocock et al. 1994, Braun et al 2012), the overall slope of the regression models are positive (i.e. higher prenatal blood leads are associated with higher IQ at later ages). The available data thus do not support the use of IQ decrements resulting from prenatal lead exposure as an appropriate metric for use in classification for reprotoxic effects. Moreover, there is no consistent quantitative information sufficient for the derivation of an ED10 indexed to prenatal exposure and impacts upon IQ for derivation of a SCL.
We therefore dispute the conclusions made in the dossier that in the context of classification and labelling of lead metal, toxicity to the developing nervous system resulting in IQ deficits is supported by sufficient evidence to merit an assignment to category 1A. Moreover, assignment to category 1 for reproductive effects becomes even more tenuous if bioavailability considerations are taken into consideration when assessing the metal in massive form.

**Dossier Submitter's Response**

| |
|---|
| These comments have been discussed previously, please see dossier submitter's responses under comment number 7 and 37. |
| **RAC's response** |
| RAC supports the DS responses and refers to its responses to comments 1, 7 and 37. |

**REFERENCES:**

Barltrop, D., F. Meek (1979). Effect of particle size on lead absorption from the gut. Arch. of Env. Health 34: 280-285.

Bonde, J.P., Joffe, M., Apostoli, P., Dale, A., Kiss, P., Spano, M., Caruso, F., Giwercman, A., Bisanti, L., Porru, S., Vanhoorne, M., Comhaire, F., Zschiesche, W. (2002). Sperm Count And Chromatin Structure In Men Exposed To Inorganic Lead: Lowest Adverse Effect Levels. Occup Environ Med 59: 234-242.

Bornschein, R.L., Grote, J., Mitchell, T., Succop, P.A., Dietrich, K.N., Krafft, K.M., Hammond, P.B. (1989). Effects Of Prenatal Lead Exposure On Infant Size At Birth. In Lead Exposure and Child Development: An International Assessment. Smith, M.A., Grant, L.D. and Sors, A. I (eds), Kluwer Academic Publishers.

Braun, J.M., Hoffman, A., Schwartz, J., Sanchez, B., Schnaas, L., Mercado-Garcia, A., Solano-Gonzalez, Bellinger D.C., Lanphear, B.P., Hu, H., Tellez-Rojo, M.M., Wright, R.O., Hernandez-Avila. (2012) Assessing windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology 33, 1040-1047.

Furst, A., Schlauder, M., Sasmore, D. (1976 ) Tumorigenic Activity of Lead Chromate. Cancer Res 36:1779-1783

ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)

Lanphear BP, Hornung R, Khoury J, Yolton K, Baghurst P, Bellinger DC, Canfield RL, Dietrich KN, Bornschein R, Greene T, Rothenberg SJ, Needleman HL, Schnaas L, Wasserman G, Graziano J, Roberts R. (2005) Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environ Health Perspectives 113: 894-899

Litovitz, T., Whitaker, N., Clark, L., White, N.C., Marsolek, M. (2010). Emerging battery ingestion hazard: Clinical Implications. Pediatrics 125: 1168-1177.

Muller, A., Blaude, M, N., Ihlemann, C., Bjorge. C., Ohlson, A., Gebel. T. (2012) A regulatory approach to assess the potency of substances toxic to the reproduction 16

Regul Toxicol Pharmacol: 63(1):97-105

OECD, 2001. Guidance Document on Transformation/Dissolution of Metals and Metals Compounds in Aqueous Media

Pocock, S.J., M. Smith, P. Baghurst (1994). Environmental lead and children's intelligence: A systematic review of the epidemiological evidence. Brit. Med. J: 309: 1189-97.

Spear, T.M., Vincent, J.H., W. Svee, N. Stanisich (1998). "Chemical Speciation of Lead Dust Associated with Primary Lead Smelting." Environ Health Perspect. 106: 565-71.

Strőmberg U et al (2008) Yearly measurements of blood lead in Swedish children since 1978: The declining trend continues in the petrol free period 1995-2007, Env Res 107 (3), 332-335

U.S. Environmental Protection Agency (2007). Estimation of the relative bioavailability of lead in soil and soil-like materials using in vivo and in vitro methods. Office of Solid Waste and Emergency Response, OSWER 9285.7-77.

UBA 2003: Einträge von Kupfer, Zink und Blei in Gewässer und Böden - Analyse der Emissionspfade und möglicher Emissionsminderungsmaßnahmen, Forschungsbericht 202 242 20/02, UBA-FB 000824, Fraunhofer ISI 2003

Kemi 2007: lead in articles:
http://www.kemi.se/Documents/Publikationer/Trycksaker/Rapporter/Report5_07_Lead_in_articles.pdf

UBA 2007: Blei im Blut:
http://www.umweltbundesamt-daten-zur-umwelt.de/umweltdaten/public/theme.do?nodeIdent=2887

Ökoinstitut 2010: End-of-Life vehicle directive 2000/53/EC Annex II: Study on analysis of costs and environmental benefits of heavy metal ban, and proposal for better regulation, November 2010

Lead CSR: chemical safety report of lead metal, LR: Berzelius Stolberg GmbH, lead REACH consortium, 2010, full document can be provided on request.

ILA Europe (2008). EU Voluntary Risk Assessment on Lead (available at http://echa.europa.eu/voluntary-risk-assessment-reports-lead-and-lead-compounds)

## ATTACHMENTS RECEIVED:

APPENDIX A LEAD REACH CONSORTIUM MEMBERS (File name: APPENDIX A-Member Companies.pdf), submitted on 06/12/2012 by International Lead Association

Lead CLH Public Consultation Executive Summary (File name: Lead CLH Report-ILA Final Comments.pdf), submitted on 06/12/2012 by International Lead Association

Lead CLH Public Consultation Executive Summary (File name: Executive Summary CLH lead.pdf), submitted on 06/12/2012 by BSB Recycling GmbH

Literature Cited (File name: Literature Cited CLH lead.pdf), submitted on 06/12/2012 by BSB Recycling GmbH *[ECHA's comment: The document is copied in the above table]*

Lead CLH Public Consultation Executive Summary (File name: Executive Summary CLH lead.pdf), submitted on 06/12/2012 by Muldenhütten Recycling und Umwelttechnik GmbH

Literature Cited (File name: Literature Cited CLH lead.pdf), submitted on 06/12/2012 by Muldenhütten Recycling und Umwelttechnik GmbH *[ECHA's comment: The document is copied in the above table]*

Lead CLH Public Consultation Executive Summary (File name: Executive Summary CLH lead.pdf), submitted on 06/12/2012 by Berzelius Stolberg (BBH)

Literature Cited (File name: Literature Cited BBH.pdf), submitted on 06/12/2012 by Berzelius Stolberg (BBH) *[ECHA's comment: The document is copied in the above table]*

Composition List - Introduction for Copper Alloys (File name: annex 1 – Introduction Copper alloys List for drinking water.pdf), submitted on 06/12/2012 by European Copper Institute

Acceptance of metallic materials used for products in contact with drinking water (File name: annex 2 - 4 MS Acceptance of metallic materials for drinking water.pdf), submitted on 06/12/2012 by European Copper Institute

Annex 4 : 15 Years of development: Copper alloys meeting the health requirements of the Drinking Water Directive (1998) (File name: annex 3 - copper alloys 15 Years of development.pdf), submitted on 06/12/2012 by European Copper Institute

SOCIO ECONOMIC ANALYSIS CHANGES IN CLASSIFICATION CUT-OFF VALUES OF LEAD – IMPACT ON THE COPPER INDUSTRY (File name: SEA-lead__CLP lead cut-off value_30112012_ECI.pdf), submitted on 06/12/2012 by European Copper Institute

Proposal for harmonised classification and labelling : LEAD (File name: public consultation_Lead_20121207.docx), submitted on 07/12/2012 by Belgium MSCA *[ECHA's comment: The document is copied in the above table under General Comments]*

Comments on the Dossier proposing harmonised Classification & Labelling (CLH) of Lead (File name: 2012-12-07_WVM_Consultation Lead Classification.pdf) submitted on 07/12/2012 by WirtschaftsVereinigung Metalle *[ECHA's comment: The document is copied in the above table under General Comments]*