

Substance Name: Lead di(acetate)

EC Number: 206-104-4

CAS Number: 301-04-2

SUPPORT DOCUMENT FOR IDENTIFICATION OF

LEAD DI(ACETATE)

**AS A SUBSTANCE OF VERY HIGH CONCERN BECAUSE OF ITS
CMR¹ PROPERTIES**

¹ CMR means carcinogenic, mutagenic or toxic for reproduction

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No 1272/20088

Substance Name(s): Lead di(acetate)

EC Number(s): 206-104-4

CAS number(s): 301-04-2

The substance is identified as substance meeting the criteria of Article 57 (c) of Regulation (EC) 1907/2006 (REACH) owing to its classification as toxic for reproduction category 1A.

Some lead salts are already placed on the candidate list of substances of very high concern, on basis of their reprotoxic effects. Inclusion of lead di(acetate) on the candidate list would prevent the risk that lead di(acetate) will be used as an alternative for the lead salts which are already on the SVHC list.

Summary of how the substance meets the criteria set out in Article 57 (c) of REACH (Toxic to Reproduction 1A).

Lead di(acetate) (EC number: 206-104-4; CAS number: 301-04-2) is covered by index number 082-005-00-8 of Regulation (EC) No 1272/2008¹ in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances), as toxic to reproduction, Repr. 1A (H360D: May damage the unborn child).

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

Registration dossiers submitted for the substance: Yes

¹ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

JUSTIFICATION

1. Identity of the substance and physical and chemical properties

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	206-104-4
EC name:	Lead di(acetate)
CAS number (in the EC inventory):	301-04-2
CAS number:	301-04-2
CAS name:	Acetic acid, lead(2+) salt (2:1)
IUPAC name:	Lead(2+) diacetate
Index number in Annex VI of the CLP Regulation	082-005-00-8
Molecular formula:	C ₄ H ₆ O ₄ Pb
Molecular weight range:	325.2869 g/mol
Synonyms:	<i>Acetic acid, lead(2++) salt</i> <i>Acetic acid, lead(2+) salt</i> <i>Lead acetate</i> <i>Plomo(II) Acetato 3-hidrato</i> <i>Lead(2+) diacetate</i> <i>Lead(II) diethanoate-3-water</i>

Structural formula:



1.2 Composition of the substance

Name: Lead di(acetate)

Description: mixed organic – inorganic salt.

Degree of purity: $\geq 80\%$ (w/w).

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
lead di(acetate) EC no: 206-104-4		$\geq 80\%$ (w/w)	

1.3 Physico-chemical properties

Table 3: Overview of physicochemical properties²

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	<i>A white to colourless crystalline solid</i>	<i>IUCLID</i>
Melting/freezing point	<i>204 °C</i>	<i>IUCLID: from Gmelin Handbook of inorganic chemistry Pb Tl. C Lfg.2 Part C p. 741</i>
Boiling point	<i>Decomposition range > 204- 236 °C</i>	<i>Boiling point not applicable as substance is a solid. Gmelin Handbook of inorganic chemistry Pb Tl. C Lfg.2 Part C p.742.</i>
Vapour pressure		Study scientifically not justified: <i>Lead di(acetate) is an inorganic metal salt, which contains lead cations and acetate anions in a crystalline matrix. The melting point of lead acetate is 204°C, followed by decomposition under atmospheric conditions. Thus, under typical atmospheric conditions, lead di(acetate) exists in the solid phase and not in the gaseous phase. Therefore, the vapour pressure, i.e. the saturation pressure above a solid or liquid, is not relevant for any hazard assessment of this substance. However, if lead di(acetate) gets in contact with water, acetic acid forms in parts, which has a vapour pressure of 20.9 hPa at 25°C (experimental database provided by EpiSuite v4.0). In consequence, testing need for vapour pressure is waived for this substance, since such testing would not provide any meaningful information on the substance itself, whereas the vapour pressure of acetic acid is provided above. Ref: letter from the joint submission registrant to NL-CA.</i>
Water solubility	<i>44.3 g/100 mL at 20 °C.</i>	<i>IUCLID: CRC Handbook of Chemistry and Physics 65th Edition B-105</i>
Partition coefficient n-octanol/water (log value)	-	<i>Waived, in view of the inorganic nature of the substance.</i>
Dissociation constant	-	<i>Waived, in view of the inorganic nature of the substance.</i>

² The references of the values reported in Table 3 are available in the technical dossier.

2 Harmonised classification and labelling

Lead di(acetate) is listed as Index number 082-005-00-8 in Regulation (EC) no 1272/2008 and classified in 3.1 as follows:

Table 4: Harmonised classification according to Annex VI, Part 3, Table 3.1 of Regulation (EC) No 1272/2008

Index No	Classification		Labelling		
	Hazard Class and Category Code#	Hazard statement Code# #	Pictogram, Signal Word Code	Hazard statement Code# #	Notes
082-005-00-8	Repr. 1A	H360Df	GHS08	H360Df	Note 1
	STOT RE 2 *	H373 **		H373 **	
	Aquatic Acute 1	H400	GHS09		
	Aquatic Chronic 1	H410	Dgr	H410	

*: The classification shall be considered as a minimum classification. See, CLP regulation Annex VI paragraph 1.2.1.

** : The classification under 67/548 EEC indicating the route of exposure has been translated into the corresponding class and category according to this Regulation, but with a general hazard statement not specifying the route of exposure as the necessary information is not available. See, CLP regulation Annex VI paragraph 1.2.2.

Hazard Class and Category Code:

Repr. 1A Toxic to Reproduction Category 1A
 STOT RE 2 Specific Target Organ Toxicity Repeated Exposure Category 2
 Aquatic Acute 1 Acute Aquatic Toxicity Category 1
 Aquatic Chronic 1 Chronic Aquatic Toxicity Category 1

Hazard statement Code:

H360Df: May damage the unborn child. Suspected of damaging fertility.
 H373: May cause damage to organs through prolonged or repeated exposure.
 H400: Very toxic to aquatic life
 H410: Very toxic to aquatic life with long lasting effects

Note 1: The concentration stated or, in the absence of such concentrations, the generic concentrations of this Regulation (Table 3.1) or the generic concentrations of Directive 1999/45/EC (Table 3.2), are the percentages by weight of the metallic element calculated with reference to the total weight of the mixture.

3 Environmental fate properties

Not relevant for this type of dossier.

4 Human health hazard assessment

See section 2 on harmonised classification and labelling.

5 Environmental hazard assessment

Not relevant for this type of dossier.

6 Conclusions on the SVHC Properties

6.1 CMR assessment

Lead di(acetate) (EC number: 206-104-4; CAS number: 301-04-2) is covered by index number 082-005-00-8 of Regulation (EC) No 1272/2008³ in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances), as toxic to reproduction, Repr. 1A (H360D: 'May damage the unborn child.'). Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

³ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

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California OEHHA Toxicity Criteria Database, <http://www.oehha.ca.gov/tcdb/>, accessed 19 June 2013.

Campbell, K. I.; George, E. L.; Hall, L. L.; Stara, J. F. Dermal irritancy of metal compounds. Studies with palladium, platinum, lead, and manganese compounds. *Archives of Environmental Health* 1975, 30, (4), 168-70. (IUCLID registration)

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Kinkead E.D., Wolfe R.E, Single oral toxicity of various organic compounds. *Journal of the American College of Toxicology*; 1992; 11:713. (IUCLID registration)

Registration dossier of lead(IV) tetra acetate. ECHA, <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>, accessed June 2013. Search item used was: 546-67-8.

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Ronis, M.J.J., Badger, T.M., Shema, S.J., Roberson, P.K. and Fatima, S. (1998c). Effects On Pubertal Growth and Reproduction in Rats Exposed Continuously throughout Development. *J Toxicol Environ Health Part A* 53:327-341.

VRAR (2008). ILZRO and EBRC Consulting. Voluntary risk assessment report on lead and some inorganic lead compounds (VRAR); human health section. Final draft, d.d. 4 March 2008.

ANNEX I. SUPPLEMENTARY INFORMATION ON HUMAN HEALTH EFFECTS

It is noted that only few studies performed with lead di(acetate) are reported in the IUCLID file. Additional studies performed with lead (IV) (tetra)acetate and other lead salts have been found. The studies described in this report originate from the IUCLID file for lead di(acetate) from the registrant and from the Voluntary risk assessment lead and lead compounds document (VRAR, 2008). The studies are most frequently performed with lead (tetra)acetate. The lead ion, in which no marked difference in toxicity is expected between the Pb^{2+} and Pb^{4+} ion, is considered to cause the effects discussed within this report.

Studies with experimental animals have utilised soluble lead compounds such as lead acetate or lead nitrate. Occupational and general population studies monitor exposure to mixed forms of lead, often of unknown speciation. However, on the assumption that the lead ion released by these compounds to varying extents will behave similarly to that released by soluble or mixed environmental exposures, an assessment can be made of the toxicokinetics and health effects potentially associated with these substances (VRAR, 2008). It should be noted that next to the test animal data adverse effects of lead on human health are frequently reported and well known, which are the most important basis for the classification Repr. 1A (Hazard statement: H360: May damage fertility or the unborn child; Specific effect: H360Df - May damage fertility. May damage the unborn child).

I.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

No data available on lead di(acetate).

I.2 Acute toxicity

I.2.1 Non-human information

I.2.1.1 Acute toxicity: oral

Lead acetate is not toxic to Sprague-Dawley rats following acute oral administration. Male and female rats were dosed via gavage at five dose levels in an OECD study (equivalent or similar to OECD Guideline 401). The oral LD50 for lead di(acetate) was found to be 4665 (3153 -6900) and 5610 mg/kg bw for male and female rats, respectively. It is reasonable to assume that the toxicity of lead salts is triggered by the lead cation and not the corresponding anion. The toxicity data from lead di(acetate) is therefore also used for other soluble lead salts.

I.2.1.2 Acute toxicity: inhalation

No data available on lead di(acetate).

I.2.1.3 Acute toxicity: dermal

No data available on lead di(acetate).

I.2.1.4 Acute toxicity: other routes

No data available on lead di(acetate).

I.2.2 Human information

No data available on lead di(acetate).

I.3 Irritation

I.3.1 Skin irritation

No signs of skin irritation were observed in a study with albino rabbits (n=6) exposed to lead dichloride. Test performance is equivalent or similar to OECD 404. Irritation to skin was observed in none of the animals tested. Read-across approach is applied for lead di(acetate) based on the fact that the toxicity of lead salts is caused by the lead cation and not by the acetate anion. Furthermore, the toxicity of lead di(acetate) may reasonably be considered to be determined by the bioavailability of lead. As a first surrogate for bioavailability, the water solubility of a test substance may be used. Lead di(acetate) and lead dichloride are "soluble" to "very soluble" in water (443 g/L at 20°C and 10 g/L at 20°C/pH 4.2, respectively). Based on the result of lead dichloride it is assumed that lead di(acetate) is not irritating to skin.

I.3.2 Eye irritation

Lead di(acetate) was tested in an *in-vitro* bovine corneal opacity and permeability study (BCOP) according to the OECD guideline (OECD 437; GLP) in 2010. A mean corrected *in vitro* irritation score (IVIS) of 76.6 was calculated and staining in two eyes out of the five tested eyes was observed. The two staining eyes had the highest score and it was not known if the staining influenced the score. The registrant considers lead acetate as a severe eye irritant under the conditions of this study.

I.4 Corrosivity

No data available on lead di(acetate).

I.5 Sensitisation

In a mouse local lymph node assay (LLNA, equivalent or similar to OECD 429) conducted with lead di(acetate) at three test levels of 2.5, 5 and 10%, SI indices of 0.7, 0.8, and 1.0 were calculated. No concentration dependent increase was observed. The stimulation index is > 3. Therefore, it was concluded that lead di(acetate) is not a skin sensitiser.

I.6 Repeated dose toxicity

No data available on lead di(acetate).

I.7 Mutagenicity

No data available on lead di(acetate).

I.8 Carcinogenicity

No data available on lead di(acetate).

I.9 Toxicity for reproduction

I.9.1 Developmental toxicity

I.9.1.1 Non-human information

General.

A huge amount of data, mostly from literature, is available about effects on reproduction after exposure to lead ions. A voluntary risk assessment report on lead and some inorganic lead compound has been prepared by ILZRO and EBRC consulting group under contract to the LDAI lead risk assessment working group (VRAR, final draft march 2008). In this document, in the human health section, a summary is given of the effects of lead exposure. A few studies are described, which were also reported in the registration dossier of lead(IV) tetra acetate (ECHA site).

In a study (Ronis et al. 1998b) the effects of lifetime lead exposure on the development of the reproductive system and the underlying endocrine effects were examined. Rats were exposed to lead acetate in drinking water at 0.05%, 0.15% and 0.45% from gestational day 5. The exposure of the dams was continued until weaning and the offspring were exposed through the drinking water until sacrifice at age 21, 35, 55, and 85 days. A significant dose-response decrease in birth-weight and crown-to-rump length in all lead exposed litters was observed. Male secondary sex organ development and female vaginal opening were delayed with increasing lead dose, with statistically significant delays appearing to begin at 0.15% lead acetate.

In the second study (Ronis et al., 1998c) an assessment has been performed on the reproductive, endocrine, and growth effects of developmental lead exposure. Rats were exposed to 0.6% (502 mg/kg/day) lead acetate in drinking water ad libitum during different developmental periods. The study goal was to determine if lead effects were a result of continuous exposure to the lead ion of a secondary to disrupted neonatal "endocrine imprinting". Rats (Sprague Dawley) were exposed to lead according to the following schedules: 1) from gestation day 5 through birth; 2) during pregnancy and lactation; 3) during lactation only; 4) from birth through adulthood; or 5) from gestation day 5 through adulthood. Developmental aspects of the reproductive system, adult sex, steroid levels and growth rates in both males and females were determined. Birth weight in all animals exposed in utero was decreased and mean body weights were significantly decreased in all lead-treated groups up to weaning. Growth curves of all lead-treated groups were significantly reduced during lactation. In male pups exposed to lead during pregnancy and lactation, from birth through adulthood or from gestation day 5, growth rates were also significantly reduced during puberty. Post pubertal growth rates were unaffected in any lead-treated group. No evidence was found for an alteration of "endocrine imprinting" by lead. Exposure during pregnancy and lactation resulted in about 10% decreases in the body weight of pups post-puberty.

I.9.2 Summary and discussion of reproductive toxicity.

Birth weight and crown-to-rump length has been affected significantly by lead acetate exposure through drinking water. Growth rates of all lead-exposed groups were significantly reduced during lactation.

I.10 Other effects

No data available on lead di(acetate).