Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A OR 1B, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): Cadmium

EC Number(s): 231-152-8

CAS Number(s): 7440-43-9

Submitted by: Swedish Competent Authority (Swedish Chemicals Agency)

CONTENTS

TABLES & FIGURES

ABBREVIATIONS

AC	Article Category (use descriptor according to REACH)
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
CSA	Chemical Safety Assessment
CEC	Cation Exchange Capacity
CI	Confidence Interval
DU	Downstream User
EB	Electron Beam
EBPVD	Electron Beam Physical Vapor Deposition
ERC	Environmental Release Category (use descriptor according to REACH)
ESR	Existing Substances Regulation
ICdA	Internal Cadmium Association
IOEL	Indicative Occupational Exposure Limit
β2M	β2-microglobulin
NHANES	National Health and Nutrition Examination Survey
Ni-Cd	Nickel-Cadmium
PC	Product Category (use descriptor according to REACH)
PROC	Process Category (use descriptor according to REACH)
PVD	Physical Vapor Deposition
RAR	Risk Assessment Report
RBP	Retinol-Binding Protein
RLE	Production method for cadmium (roasting leaching electrolysis)
SCOEL	Scientific Expert Group on Occupational Exposure Limits
SMC	Swedish Mammography Cohort
SU	Sector of Use (use descriptor according to REACH)
TWI	Tolerable weekly intake

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A OR 1B, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): Cadmium

EC Number(s): 231-152-8

CAS number(s): 7440-43-9

- The substance is proposed to be identified as substance meeting the criteria of Article 57 (a) of Regulation (EC) 1907/2006 (REACH) owing to its classification as carcinogen category 1B.
- It is proposed to also identify the substance as substance of equivalent concern according to Article 57 (f), owing to the adverse effects on kidney and bone tissues after prolonged exposure (classification STOT RE1).

Summary of how the substance meets the criteria set out in Article 57(a) and 57(f) of REACH.

Carcinogen 1B

Cadmium (non-pyrophoric) is listed as Index number 048-002-00-0 and cadmium (pyrophoric) is listed as Index number 048-011-00-X in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as carcinogen, Carc. 1B (H350: May cause cancer). The corresponding classification in Annex VI, part 3, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I to Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is carcinogen, Carc. Cat. 2, R45 (May cause cancer).

Equivalent level of concern

According to REACH Article 57(f), substances for which there is scientific evidence of probable serious effects to human health or the environment, which give rise to an equivalent level of concern to CMR or PBT/vPvB substances and which are identified on a case-by-case basis, may be included in Annex XIV in accordance with the procedure laid down in Article 58.

Cadmium has the ability to cause a large number of toxic effects as is evident from the harmonized classification. It is thus clear that cadmium may cause many different serious health effects in addition to the ability to cause cancer. Adverse effects on multiple organs after repeated exposure to cadmium, in particular on ***kidney*** and ***bone***, motivated the classification as STOT RE Category 1, and it is in particular effects on kidney and bone that justify the equivalent level of concern.

A significant part of the European population is today exposed to levels of cadmium that may cause effects on kidney and bone. In non-smokers, food is the main intake route and it is therefore important to reduce all input of cadmium to foodstuff. The input of cadmium to soil is dominated by

deposition from air, which therefore must be reduced, and in order to achieve this all uses of cadmium and cadmium compounds should, wherever possible, be substituted.

Already 25 years ago it was acknowledged within EU that cadmium exposure constitutes a problem for human health and the environment and new action should be taken at Community level to control and reduce cadmium pollution (see: The Council Resolution of 25 January 1988 on a Community action programme to combat environmental pollution by cadmium (*Official Journal C 030, 04/02/1988 P. 0001 – 0001)).* Major elements of the strategy for cadmium control in the interests of the protection of human health and the environment included for example:

- limitation of the uses of cadmium to cases where suitable alternatives do not exist;
- stimulation of research and development: - of substitutes and technological derivatives, in particular, encouragement to the development of further alternatives to the use of cadmium in pigments, stabilizers and plating;
- development of a strategy designed to reduce cadmium input in soil;
- combatting significant sources of airborne and water pollution.

Cadmium is a toxic metal that ranks 7 on the US Agency for Toxic Substances & Disease Registry's priority list of hazardous substances (www.astdr.cadmiumc.gov), a prioritization of substances based on a combination of their frequency, toxicity, and potential for human exposure. As a pollutant of worldwide concern, cadmium has been reviewed by the United Nations Environment Program, and included on the list of chemical substances considered to be potentially dangerous at the global level.

To assess whether a substance can be identified as SVHC based on REACH Article 57(f) the hazardous properties of the substance, the potential impact on health and the potential impacts on society as a whole have to be compared to those effects elicited by CMR (or PBT/vPvB) substances. The following factors that are characteristic for most of the CMRs have been taken into account:

- Severity of health effects
- Irreversibility of health effects
- Delay of health effects
- Uncertainties on safe exposure
- Societal concern and impairment of quality of life

Severity of health effect: The severity of health effects due to exposure to cadmium is dependent on the concentration attained in body tissues and organs. Kidney effects range from indications of minor tubular and glomerular dysfunction (measured by the presence of proteins in the urine) to an increased risk of end stage renal disease, which necessitates dialysis treatment for survival. The effects on bone range from disturbances on bone tissue homeostasis to actual bone fractures, which especially for older people are considered quite serious and can contribute to a premature death. In a population-based study in patients aged 65 or older the risk of mortality in hip fracture patients was 3-fold higher than in the general population and included every major cause of death (Panula et al 2011). The quality of life for affected individuals is clearly impaired (for example after a hip fracture), but may also have consequences for society as a whole if many individuals are affected. When comparing with CMR substances, it should be acknowledged that also effects caused by these substances vary in severity.

Irreversibility of health effects: According to the EU RAR (ECB 2007) some controversy exists as to the reversibility of renal effects of cadmium both in the general population and in workers. The (ir)reversibility of tubular proteinuria after reduction or cessation of exposure depends on the intensity of exposure and/or the severity of the tubular damage. It was concluded that, as for inhalation exposure, incipient tubular effects associated with low Cd exposure in the general population are reversible if exposure is substantially decreased. Severe tubular damage (urinary leakage of the proteins RBP or ß2M > 1,000-1,500 µg/g creatinine) is generally irreversible.

A longitudinal study on 74 inhabitants from a cadmium-polluted area in Japan (Kido et al. 1988) showed irreversible and even progression of renal dysfunction 5 years after cessation of cadmium exposure. Likewise, a study from China indicates that the negative effects on bone still remains 10 years after the population abandoned ingestion of cadmium-polluted rice (Chen et al 2009).

The biological half-life of cadmium in humans is extremely long (estimated to be 10-30 years) and the body burden of cadmium therefore increases, mainly via accumulation in the kidney, during the entire life span of an individual. All uses of cadmium and its compounds, including when present as a contaminant, contribute to this bioaccumulation in humans, which starts already in early life.

Unless exposure is substantially decreased kidney and bone effects therefore tend to be irreversible due to the continued internal exposure from stored cadmium. In that respect cadmium behaves in a way that resembles substances that are persistent and bioaccumulating in the environment.

Delay of health effects: The bioaccumulation over the life-time of an individual also affects when effects appear; in most instances the delay between first exposure and appearance of effects is very long, i.e. decades.

Uncertainties on safe exposure: There is uncertainty about identifying safe exposure levels for cadmium. Biomedical research on cadmium is intense. A search of the literature data base PubMed revealed 14 900 articles published during the last 10 years and 8700 articles during the last 5 years. Consequently, new findings on hazards and risks connected with cadmium and its compounds continuously appear. As an example, effects on bone tissue have recently been shown at exposure levels previously considered without effects. Since what can be considered as a “safe exposure level” is steadily decreasing, precautionary community wide actions are warranted.

Further, it is not clear whether an effect on bone/kidney or carcinogenesis is the critical end-point from a risk assessment point of view, although most risk assessments concerning cadmium exposure of the general population (for example the recent report from EFSA (2012)) are based on kidney effects. In the risk assessment for workers by SCOEL (2009), the proposed limit values are also based on effects on the kidney and, to some extent, bone tissue, representing the most sensitive targets of cadmium toxicity after occupational exposure. The suggested IOEL (in air) is considered to be protective against long-term local effects (respiratory effects including lung cancer). Whether this value is also protective against cancer in other tissues was not assessed. According to a paper from the Austrian Workers’ Compensation Board (Püringer 2011), the German Committee on Hazardous Substances (AGS) has recently endorsed a limit value of 16 ng Cd/m³ based on the acceptable cancer risk of 1 : 25,000, i.e. a value 250-fold lower than the IOEL suggested by SCOEL.

Societal concern and impairment of quality of life: In particular the effects on bone tissue, with increased risk for bone fractures, are a considerable public health problem causing a lot of suffering and a burden to society in terms of cost, morbidity and mortality. Osteoporotic complications are particularly prevalent in northern Europe and, statistically, every second woman in Sweden will suffer from an osteoporotic fracture during her lifetime. The incidence of hip fractures is more than seven-fold higher in Northern Europe than in the rest of Europe. The reason(s) for the large age-

standardized geographical differences is still not known, but the differences cannot be explained by differences in risk of slipping, low calcium intake, vitamin D deficiency or by inactivity. The fracture incidence has increased substantially since the 1950ies. As the number of old and very old people in the population increases, a further increase in the prevalence of fractures is to be expected.

According to a report published by the Swedish Chemicals Agency, the annual societal costs in Sweden for cadmium in soil due to human activities is estimated to approximately 4.2 billion SEK (approx. 450 million Euros) (KemI 2012). This figure is based on the estimation that 7 and 13 %, in males and females respectively, of all fractures in Sweden are caused by cadmium exposure, mainly via food, and include direct treatment and care costs for bone fractures (approx. 1.5 billion SEK), as well as a valuation of the shortening of life time and a decreased quality of life.

In conclusion

Cadmium is considered to fulfil the criteria according to Art. 57(f), i.e. there is scientific evidence of probable serious effects to human health which give rise to “equivalent level of concern”, due to;

- the adverse effects on kidney and bones, effects that depending on dose may be serious and even contribute to premature death,
- the continuous accumulation of cadmium in the body, which leads to continuous internal exposure and in practice irreversible effects once adverse effect levels are reached,
- the occurrence of adverse effects in a significant part of the general population at present exposure levels, which are primarily of anthropogenic origin,
- uncertainties in deriving a safe exposure level, and
- high societal costs in terms of health care and shortening of life time and a decreased quality of life.

Registration dossier(s) submitted for the substance? Yes

PART I

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:	231-152-8
EC name:	cadmium
CAS number (in the EC inventory):	7440-43-9
CAS number:	
CAS name:	cadmium
IUPAC name:	cadmium
Index number in Annex VI of the CLP Regulation	048-002-00-0 048-011-00-X
Molecular formula:	Cd
Molecular weight range:	112.4099
Synonyms:	Cd rod Cd stangen kadmium stangen
Structural formula	**Cd**

1.2 Composition of the substance

Name: cadmium

Degree of purity: 80-100 % (w/w). The substance is a monoconstituent substance.

The constituents and impurities as described by the “Cadmium Reach Consortium” (http://www.reach-cadmium.eu/) are shown in Table 2 and Table 3.

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
cadmium EC no.: 231-152-8	> 99.99 % (w/w)	> 95.0 — < 100 % (w/w)	

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
lead EC no.: 231-100-4	> 0.0003 % (w/w)	> 0.0001 — < 1.5 % (w/w)	
zinc EC no.: 231-175-3	> 0.002 % (w/w)	> 0.0001 — < 3.5 % (w/w)	

1.3 Physico-chemical properties

Table 4: Overview of physicochemical properties *(data from dissemination database according to REACH, Article 119)*[1]

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	Solid Form: cast; powder Colour: powder is brownish, the cast form is shiny silver Odour: odourless	From registration[1]
Melting/freezing point	In nitrogen, the powder starts melting at 309°C, in air it starts melting at 321°C. In nitrogen, the cast cadmium particles starts melting at 309°C, in air they start melting at 313°C. In nitrogen, the substance does not decompose; sublimation temperature is ca. 450°C for the powder and ca. 400°C for the cast particles. In air, the substance starts oxidizing at ca. 270°C (powder) and at ca. 470°C (cast metal).	From registration[1]
Vapour pressure	The vapour pressure of Cd is negligible at 25°C.	From registration[1]
Water solubility	The average water solubility of Cd for the powder and bar samples was 2.3 and 8.7 mg/L, respectively. Corresponding value for pure cadmium was also calculated with HSC 7.0 software. The obtained value was 5.4 mg/L.	From registration[1] **Value used for CSA:** 2.3 mg/L at 20 °C
Relative density	The density of the substance is 8.64 g/cm^3 in powder form and 8.6 g/cm^3 in particulate form.	From registration[1]
Granulometry	The D50 of the powder is 16.27 µm, the D80 is <20 µm . The D50 of the crushed cast particles is 2103 µm, the D80 is > 2380 µm.	From registration[1]
Viscosity	Viscosity of the substance was determined on molten liquid substance. The results show that the viscosity of liquid metal cadmium is increasing slowly as a function of decreasing temperature until the melting point is reached. Here, the melting point seems to be at 318.1 °C. At the melting point, the rapid increase of the viscosity ended the measurement automatically.	From registration[1]

[1] http://echa.europa.eu/information-on-chemicals

2 HARMONISED CLASSIFICATION AND LABELLING

Cadmium (non-pyrophoric) is listed as Index number 048-002-00-0 and cadmium (pyrophoric) is listed as Index number 048-011-00-X in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, as follows:

Table 5: Harmonised classification of cadmium (non-pyrophoric) Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labeling	
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram Signal Word Code(s)	Hazard Statement Code(s)
048-002-00-0	Cadmium (non-pyrophoric)	231-152-8	7440-43-9	Carc. 1B Muta. 2 Repr. 2 Acute Tox. 2 STOT RE 1 Aquatic Acute 1 Aquatic Chronic 1	H350 H341 H361fd H330 H372 H400 H410	GHS06 GHS08 GHS09 Dgr	H350 H341 H361fd H330 H372 H410

Table 6: Harmonised classification of cadmium (pyrophoric) Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labeling	
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram Signal Word Code(s)	Hazard Statement Code(s)
048-011-00-X	Cadmium (pyrophoric)	231-152-8	7440-43-9	Carc. 1B Muta. 2 Repr. 2 Acute Tox. 2 STOT RE 1 Aquatic Acute 1 Aquatic Chronic 1 Pyr. Sol.1	H350 H341 H361fd H330 H372 H400 H410 H250	GHS06 GHS08 GHS09 Dgr	H350 H341 H361fd H330 H372 H410

H350: May cause cancer.
H341: May cause genetic defects.
H361fd: May damage fertility. May damage the unborn child.
H330: Fatal if inhaled.
H372: Causes damage to organs through prolonged or repeated exposure.
H400: Very toxic to aquatic life.
H410: Very toxic to aquatic life with long lasting effects.
H250: Catches fire spontaneously if exposed to air.

Table 7: Harmonised classification of cadmium (non-pyrophoric) according to part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification	Risk phrases	Safety phrases	Indication (s) of danger
048-002-00-0	Cadmium (non-pyrophoric)	231-152-8	7440-43-9	Carc. Cat. 2; R45 Muta. Cat. 3; R68 Repr. Cat. 3; R62 Repr. Cat. 3; R63 T+; R26 T; R48/23/25 N; R50/53	R45 R68 R62 R63 R26 R48/23/25 R50/53	S45 S53 S60 S61	T+ N

Table 8: Harmonised classification of cadmium (pyrophoric) according to part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification	Risk phrases	Safety phrases	Indication (s) of danger
048-011-00-X	Cadmium (pyrophoric)	231-152-8	7440-43-9	Carc. Cat. 2; R45 Muta. Cat. 3; R68 Repr. Cat. 3; R62 Repr. Cat. 3; R63 T+; R26 T; R48/23/25 N; R50/53 F; R17	R45 R68 R62 R63 R26 R48/23/25 R50/53 R17	S45 S53 S60 S61 S7/8 S43	T+ N

R45: May cause cancer.
R68: Possible risk of irreversible effects.
R62: Possible risk of impaired fertility.
R63: Possible risk of harm to the unborn child.
R26: Very toxic by inhalation.
R48/23/25: Toxic: danger of serious damage to health by prolonged exposure through inhalation or if swallowed.
R50/53: Very toxic to aquatic organisms; may cause long-term adverse effects in the aquatic environment.
R17: Spontaneously flammable in air.

3 ENVIRONMENTAL FATE PROPERTIES

Anthropogenic and natural sources of cadmium exposure

Cadmium is a natural element, which is present in all environmental compartments (as Cd ++). Cadmium emissions to the environment may therefore arise from both natural and anthropogenic or man-made sources. Estimates of the proportion of total cadmium emissions due to natural sources have ranged from 10% to 50%. Some of these natural emission sources include weathering and erosion of parent rocks, volcanic activity and forest fires (ICdA 2012b). The overall cadmium anthropogenic exposure is then in the range of 50 to 90 %.

In the environment cadmium is mainly associated with zinc but also with lead and copper. Anthropogenic sources include by-products of the metallurgy of these elements. The release of cadmium into the human environment occurs via emission from mining activities and metal industries (the smelting of other metals), the combustion of fossil fuels, the incineration of waste materials or inappropriate waste disposal, leaching from landfill sites and the use of cadmium-rich phosphate fertilizers and sewage sludge. These anthropogenic activities have contributed to the contamination by cadmium of the food chain. However, there are also areas with naturally elevated cadmium concentrations in soil. Because cadmium is easily taken up by many plants, plant-based food, in particular wheat, rice and potatoes, is a major source of exposure to cadmium. Another source of exposure is tobacco smoking, mainly because the absorption in the lungs is higher than in the gastrointestinal tract (KemI 2011).

When cadmium ions are present in the environment, they will interact with the environmental matrix and biota. The fate will depend on processes like dissolution, absorption, precipitation, complexation, inclusion into (soil) matrix, etc. In **freshwater** or **seawater** cadmium may occur in both suspended and dissolved forms and is partitioned over a number of chemical species. In the water, cadmium interacts with components of the water and influence the bioavailability. In **sediment**, cadmium binds to the sulphide fraction to form less soluble CdS. Due to the low solubility, cadmium will be largely bound in the sediments as long as the sediment is kept under anaerobic condition. However, if the condition turns more aerobic, due to e.g. drainage or dredging, cadmium ions may be re-mobilised into the water. In **soils**, cadmium interacts with various reactive soil surfaces (mainly adsorption). The soil pH is an important parameter that affects the speciation and the distribution of the cadmium species over the soil and the solution. Cadmium tends to be more sorbed and complexed at higher pH (pH > 7) than at lower pH. The solubility of cadmium in soil decreases with increasing pH.

Cadmium is an element and is therefore **persistent** in the environment. Cadmium is not **biomagnifying** in the aquatic food chain. However, the **bioconcentration/bioaccumulation** factors strongly increase when exposure concentrations decrease. This observation clearly shows some level of physiological regulation of uptake.

Some cadmium compounds have very low solubility and therefore release cadmium ions to a lower extent; this decreases their **bioavailability** potential. Distinction can therefore be made between cadmium compounds, as a function of their solubility. However, even cadmium forms with low solubility may be transformed into higher solubility forms due to chemical/physical transformation processes such as incineration or change of the redox potential.

Food

In a recent report from EFSA (2012) cadmium levels in food on the European market were reviewed and exposure estimated using detailed individual food consumption data. High levels of cadmium were found in algal formulations, cocoa-based products, crustaceans, edible offal, fungi, oilseeds, seaweeds and water mollusks. In an attempt to calculate lifetime cadmium dietary exposure, a middle bound overall weekly average was estimated at 2.04 µg/kg body weight and a potential 95th percentile at 3.66 µg/kg body weight. Individual dietary survey results varied between a weekly minimum lower bound average of 1.15 to a maximum upper bound average of 7.84 µg/kg bodyweight and a minimum lower bound 95th percentile of 2.01 and a maximum upper bound 95th percentile of 12.1 µg/kg body weight, reflecting different dietary habits and survey methodologies. Food consumed in larger quantities had the greatest impact on dietary exposure to cadmium. This was true for the broad food categories of grains, vegetables, and starchy roots and tubers. The review confirmed that children and adults at the 95th percentile exposure can exceed health-based guidance values (current TWI is 2.5 µg/kg bw).

Human exposure and body burden

The general population is exposed to cadmium primarily via food intake, but also via smoking, soil and dust ingestion, inhalation of ambient air and drinking water.

Three large and fairly recent studies may be used to display the "current" urinary cadmium concentrations, which reflects body burden, in the Swedish population. The results are summarized in the table below. For more information see section 9.5 in Part II of this report.

Summary of the urinary concentrations observed in three Swedish population-based studies.

	Age	*Urinary cadmium µg/g creatinine*			
	(years)	*Median and (range)*		*% >0.5µg/g*	*%>1.0 µg/g*
		All	Never-smokers	All / Never-smokers	
SEM	20-29	0.12 (0.01-0.68)	0.10 (0.02-0.68)	-	-
	50-59	0.29 (0.04-2.2)	0.24 (0.04-1.4)	20 / 4	1.8 / 0.3
WHILA	53-64	0.67 (0.13-3.6)	0.56 (0.13-3.2)	70 / 32	20 / 6
SMC	56-69	0.35 (0.05-2.4)	0.29 (0.05-1.3)	23 / 6	2.0 / 0.2

SEM; The National Swedish health-related environmental monitoring program, WHILA; Women's Helath in the Lund Area, SMC; The Swedish Mammography Cohort;

Women in the age group 50-69 years were also used to evaluate the proportion of women having urinary cadmium levels above the two predefined cutoffs of 0.5 and 1.0 µg/g creatinine. In these studies, 20%, 70% and 23% of all the women (4%, 32% and 6% in never-smokers) had urinary cadmium concentrations above 0.5 µg/g creatinine, respectively. The corresponding proportions for urinary cadmium concentrations above 1.0 µg/g creatinine were 1.8%, 20% and 2%, respectively (0.3%, 6% and 0.2% in never-smokers). Differences between studies may indicate higher exposure in Southern Sweden, but comparability of measurements may contribute.

Biomonitoring data indicate that the exposure to cadmium has not changed during the last 2-3 decades in Sweden.

As part of an EU research program **(**PHIME - Public health impact of long-term, low-level mixed element exposure in susceptible population strata), blood from 1,363 children from six European (Croatia, Czech Republic, Poland, Slovakia, Slovenia, and Sweden) and three non-European countries (China, Ecuador, and Morocco) showed remarkably small differences between the European cities (the geometric means ranged 0.11-0.17 μg/L for cadmium). The European differences were also small among 480 women (0.25-0.65 μg/L). As regards industrially polluted areas, the results clearly showed that children living in certain such areas in Europe may have cadmium and lead levels in blood that are about double those in less polluted regions (PHIME 2011).

4 HUMAN HEALTH HAZARD ASSESSMENT

In 2011, the Swedish Chemicals Agency published a report (KemI 2011) containing a human health risk assessment of cadmium from a Swedish exposure perspective (Annex 3 in KemI 2011; Authors: A Åkesson & M Vahter, Karolinska Institutet, Sweden). The summaries on different toxicity endpoints given below are primarily from this report.

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

Lung retention may be up to 20 %, especially after short-term exposure (IARC 2012).

According to (KemI 2011), a gastrointestinal absorption of cadmium ranging between 1 and 10 % seems most likely, with men and individuals with adequate iron status in the lower range and those with low iron stores and iron deficiency (mainly women) in the higher range. Newborns and small children may have an even higher absorption, independent of iron status.

Once absorbed, cadmium will bind to metallothionein, forming a cadmium–metallothionein complex that is transferred (via blood) primarily to the liver and the kidney. Metallothionein is inducible in different tissues (e.g. liver, kidney, intestine, and lung) by exposure to various agents including cadmium. When transported to the kidney, cadmium–metallothionein is readily filtered at the glomerulus, and may be efficiently reabsorbed from the filtrate in the proximal tubules. In the tubules, the protein portion is rapidly degraded to release cadmium. Cadmium accumulates in kidney tubules, and causes damage to tubular cells, especially in the proximal tubules. Absorbed cadmium is excreted very slowly, and the amounts excreted into urine and faeces are approximately equal. In humans, half-life estimates are in the range of 7–16 years (IARC 2012). According to other references (KemI 2011) it is even longer (10-30 years).

Cadmium in urine is mainly influenced by the body burden of cadmium and is generally proportional to the concentration in the kidney. There is a close relationship between the cadmium concentrations in urine and kidneys; and urinary cadmium of 1.7 to 2.5 μg/g creatinine roughly corresponds to about 50 mg/kg in the renal cortex. Because the half-life of cadmium in the body is very long urinary cadmium is highly dependent on age (KemI 2011).

4.2 Kidney toxicity

In the EU RAR of Cd and CdO (ECB 2007) it was concluded that there is ample and robust evidence of the nephrotoxic potential of cadmium. The main issue was therefore to define the dose-effect/response relationships for this endpoint as well as the health relevance of the endpoints used to establish these relationships. For workers occupationally exposed to cadmium (mainly by inhalation), a LOAEL of 5 μg Cd/g creatinine in urine was considered to constitute a reasonable estimate. The health significance of this threshold was justified by the frequent observation of irreversibility of tubular changes above this value and its association with further renal alteration. Further, it was considered plausible that the lower LOAEL (2 μg Cd/g creatinine in urine) in the general population exposed by the oral route could be the consequence of an interaction of Cd exposure with pre-existing or concurrent renal disease. It was emphasized that the interpretation of the LOAELs and the margin of safety should take into account the long half-life of cadmium and the uncertainties regarding the present hazard assessment.

According to a later risk assessment (KemI 2011), a number of studies, including the Swedish general population, show significant associations between cadmium in urine and/or blood and markers of impaired kidney function, mostly impaired tubular function, where the risk starts to increase already below 1 μg/g creatinine. It is difficult to ascertain the exact lowest effect dose for a clear adverse effect. However, also impaired glomerular filtration rate has been observed, the risk of which seems to start at 0.7 to 1.0 μg/g creatinine. That the reported associations represent causal relationships is supported by the fact that associations were observed for several different biomarkers of kidney effects, in several different populations, and in both men and women. Also, the mechanistic studies support an effect at low exposure. Thus, the observed associations, even those at very low exposure levels, may imply potentially adverse effects, which in combination with other stressors may affect the long-term health and function of the kidneys (KemI 2011).

A recent study using NHANES (National Health and Nutrition Examination Survey) data from 5426 subjects in the USA revealed that a cadmium concentration ≥ 1 μg/g creatinine in urine or ≥ 1 μg/L in blood was associated with statistically significant increased risk of albuminuria, while only the concentration of cadmium in blood and not in urine was associated with increased risk of lowered glomerular filtration rates (Ferraro et al, 2010).

There are also indications that environmental and occupational exposures to cadmium affect the development of end-stage renal disease, measured as need for renal replacement therapy (Hellström et al. 2001). Comprehensive data were available for all individuals undergoing renal replacement therapy (384 cases between 1978 and 1995, 250 men and 134 women) in a Swedish population living near a Cd battery production facility in the southeast of Sweden (Kalmar County). Based on the distance between the dwelling place, and to some extent environmental monitoring data, it was possible to identify groups with high (occupational), moderate (living within a 2 km radius of the point source), or low exposure (between 2 and 10 km) as well as a control group with no exposure (rest of the residents in the county). The incidence of renal replacement therapy (number of cases per million person-years between 20 and 79 years) was higher in the exposed groups than in the controls (201.4 versus 118.4 for genders cumulated, Mantel-Haenszel rate ratio, 1.8; 95% CI, 1.3-2.3). The age and sex adjusted rate ratio increased from 1.4 in the low exposure group to 2.3 in the high exposure group.

4.3 Bone toxicity

In the EU RAR of Cd and CdO (ECB 2007) it was concluded (based on previous extensive reviews) that it is evident that bone tissue constitutes a target organ for the general and occupational populations exposed to cadmium compounds. The hazard was considered relatively well identified both in experimental and epidemiological studies. The mechanism is, however, not fully understood and the types of bone lesions associated with cadmium exposure are not clearly identified. The most severe form of cadmium intoxication is Itai-itai disease, which comprises severe signs of osteoporosis and osteomalacia associated with renal disease in aged women.

According to a more recent risk assessment (KemI 2011), the data supporting an adverse effect of the present exposure to cadmium in Sweden on the risk of osteoporosis have increased substantially during the last few years. Only a couple of under-powered studies failed to show any association. Irrespective of whether the studies employed a decrease in the bone mineral density, increased risk of osteoporosis or increased risk of fractures, these changes seem to occur at very low urinary cadmium concentrations. Both the new Swedish (SMC) and the new American (NHANES) studies suggest that even a urinary concentration around 0.5 μg/g creatinine is associated with increased risk of osteoporosis and fractures. There are increasing data suggesting that the effect of cadmium on bone is independent of kidney damage - and recent data support that these effects occur even before the kidney damage. Furthermore, the Swedish studies showed very clear increased risk of osteoporosis and fractures even among those who never smoked. This finding suggests that dietary cadmium alone contribute to the risk (KemI 2011; Engström et al 2012).

Osteoporosis and fractures (KemI 2011)
Osteoporosis is characterized by low bone mass and microarchitectural deterioration of the skeleton, leading to fragility and increased risk of fractures. The disease is silent until the first fracture occurs. Common osteoporotic fractures are those at the hip, spine and forearm. These fractures are a considerable public health problem causing a lot of suffering and a burden to society in terms of cost, morbidity and mortality. Established or suggested risk factors for osteoporosis and fractures are female sex, old age, low body weight, early menopause, family history of osteoporosis, deficiency of Vitamin D and calcium, smoking, excessive consumption of alcohol, inactivity, several medical disorders and certain drugs.

The prevalence of osteoporotic complications, fragility fractures, is particularly high in Sweden, as in Norway and Iceland. Statistically, every other women and one out of four men in Sweden will suffer from an osteoporotic fracture during their lifetime. The incidence of hip fractures is more than seven-fold higher in Northern Europe than in the rest of Europe. In fact, it is higher in men in Scandinavia than in women in Central Europe. The reason(s) for the large age-standardized geographical differences is still not known. It is concluded that the differences cannot be explained by differences in risk of slipping, low calcium intake, vitamin D deficiency or by inactivity. The fracture incidence has increased substantially since the 1950ies. As the number of old and very old people in the population increases, a further increase in the prevalence of fractures is to be expected. Although several risk factors have been identified, they cannot fully explain the above mentioned differences, suggesting that several unknown risk factors or combinations of risk factors are involved.

How to study effects on bone in humans: The most adverse endpoint with respect to effects on bone is a fracture. A study investigating the risk of fractures in relation to biomarkers of cadmium exposure requires a large sample size in order to be adequately powered. In these studies the risk is calculated based on comparison of exposure in those who developed a fracture and those who did not. Bone mineral density (assessed by x-ray in g/cm^2) gives an estimation of the status of the

skeleton, but is not the only factor predicting the risk of fractures. The bone mineral density can be expressed as it is – a continuous variable – or by calculation of T-score or Z-score. These two scores are used to predict the risk of fractures clinically. Biochemical markers of bone remodeling are measured in serum or urine and give an indication of the activity of the continuously ongoing formation and degradation of bone tissue. Although these markers may increase our understanding of possible mechanisms involved and may also support inference with respect to causality, they cannot independently be used as markers of an adverse effect.

Fractures

Whereas several epidemiological studies have observed an association between cadmium and bone mineral density (for a review see KemI 2011), only few published studies have so far considered fracture incidence – the most adverse endpoint with respect to effects on bone.

CadmiBel: In their prospective cohort, including 506 subjects, the observed risk ratios associated with doubled urinary cadmium concentrations were 1.73 (95% CI 1.16–2.57; $P = 0.007$) for fractures in women and 1.60 (95% CI 0.94–2.72, $P = 0.08$) for height loss in men. Similar risk estimates were observed if cadmium concentrations in soil, leek and celery sampled in the relevant districts of residence were used as proxy of cadmium exposure instead of the urinary cadmium concentration (In: KemI 2011).

OSCAR: Fracture incidence was also assessed retrospectively in the Swedish OSCAR study. For fractures occurring after the age of 50 years ($n = 558$, 32 forearm fractures), the fracture hazard ratio, adjusted for sex and other relevant covariates, increased by 18% (95% CI 1.0–38%) per unit urinary cadmium (1 nmol/mmol creatinine; ~ 1 µg/g creatinine). When subjects were grouped in exposure categories, the hazard ratio reached 3.5 (90% CI 1.1–11) in the group of subjects with urinary cadmium concentrations between 2 and 4 nmol/mmol creatinine and 8.8 (90% CI 2.6–30) in the group of subjects with urinary cadmium concentrations greater than or equal to 4 nmol/mmol creatinine (mainly men). The relatively the high cadmium exposure in this study could be attributed to the inclusion of workers occupationally exposed to cadmium. Associations between cadmium and fracture risk were absent before the age of 50 (Alfvén et al 2004).

Swedish Mammography Cohort: For any first fracture (n=395) the odds ratio (OR) was 1.16 (95% CI, 0.89-1.50) comparing urinary Cd ≥0.5 µg/g creatinine with lower levels. Among never-smokers, the ORs (95% CIs) were 2.03 (1.33-3.09) for any first fracture, 2.06 (1.28-3.32) for first osteoporotic fracture, 2.18 (1.20-3.94) for first distal forearm fracture and 1.89 (1.25-2.85) for multiple incident fractures (Engström et al 2011).

Cohort of Swedish Men: In a population-based prospective cohort study, where individual cadmium intake was estimated using a food frequency questionnaire (average intake 19 µg Cd/day), dietary cadmium was associated with a statistically significant 19 % higher rate of any fracture comparing the highest Cd intake tertile with the lowest tertile (Thomas et al 2011).

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant for this dossier.

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 CMR assessment

Cadmium (non-pyrophoric) is listed as Index number 048-002-00-0 and cadmium (pyrophoric) is listed as Index number 048-011-00-X in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as carcinogen, Carc. 1B (H350: “May cause cancer”). The corresponding classification in Annex VI, part 3, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is carcinogen, Carc. Cat. 2, R45 (“May cause cancer”).

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

6.2 Substances of equivalent level of concern assessment

According to REACH Article 57(f), substances for which there is scientific evidence of probable serious effects to human health or the environment, which give rise to an equivalent level of concern to CMR or PBT/vPvB substances and which are identified on a case-by-case basis, may be included in Annex XIV in accordance with the procedure laid down in Article 58.

Cadmium has the ability to cause a large number of toxic effects as is evident from the harmonized classification. It is thus clear that cadmium may cause many different serious health effects in addition to the ability to cause cancer. Adverse effects on multiple organs after repeated exposure to cadmium, in particular on ***kidney*** and ***bone***, motivated the classification as STOT RE Category 1, and it is in particular effects on kidney and bone that justify the equivalent level of concern.

A significant part of the European population is today exposed to levels of cadmium that may cause effects on kidney and bone. In non-smokers, food is the main intake route and it is therefore important to reduce all input of cadmium to foodstuff. The input of cadmium to soil is dominated by deposition from air, which therefore must be reduced, and in order to achieve this all uses of cadmium and cadmium compounds should, wherever possible, be substituted.

Already 25 years ago it was acknowledged within EU that cadmium exposure constitutes a problem for human health and the environment and new action should be taken at Community level to control and reduce cadmium pollution (see: The Council Resolution of 25 January 1988 on a Community action programme to combat environmental pollution by cadmium (*Official Journal C 030, 04/02/1988 P. 0001 – 0001)).* Major elements of the strategy for cadmium control in the interests of the protection of human health and the environment included for example:

- limitation of the uses of cadmium to cases where suitable alternatives do not exist;

- stimulation of research and development: - of substitutes and technological derivatives, in particular, encouragement to the development of further alternatives to the use of cadmium in pigments, stabilizers and plating;
- development of a strategy designed to reduce cadmium input in soil;
- combatting significant sources of airborne and water pollution.

Cadmium is a toxic metal that ranks 7 on the US Agency for Toxic Substances & Disease Registry's priority list of hazardous substances (www.astdr.cadmiumc.gov), a prioritization of substances based on a combination of their frequency, toxicity, and potential for human exposure. As a pollutant of worldwide concern, cadmium has been reviewed by the United Nations Environment Program, and included on the list of chemical substances considered to be potentially dangerous at the global level.

To assess whether a substance can be identified as SVHC based on REACH Article 57(f) the hazardous properties of the substance, the potential impact on health and the potential impacts on society as a whole have to be compared to those effects elicited by CMR (or PBT/vPvB) substances. The following factors that are characteristic for most of the CMRs have been taken into account:

- Severity of health effects
- Irreversibility of health effects
- Delay of health effects
- Uncertainties on safe exposure
- Societal concern and impairment of quality of life

Severity of health effect

The severity of health effects due to exposure to cadmium is dependent on the concentration attained in body tissues and organs. Kidney effects range from indications of minor tubular and glomerular dysfunction (measured by the presence of proteins in the urine) to an increased risk of end stage renal disease, which necessitates dialysis treatment for survival. The effects on bone range from disturbances on bone tissue homeostasis to actual bone fractures, which especially for older people are considered quite serious and can contribute to a premature death. In a population-based study in patients aged 65 or older the risk of mortality in hip fracture patients was 3-fold higher than in the general population and included every major cause of death (Panula et al 2011). The quality of life for affected individuals is clearly impaired (for example after a hip fracture), but may also have consequences for society as a whole if many individuals are affected. When comparing with CMR substances, it should be acknowledged that also effects caused by these substances vary in severity.

Irreversibility of health effects

According to the EU RAR (ECB 2007) some controversy exists as to the reversibility of renal effects of cadmium both in the general population and in workers. The (ir)reversibility of tubular proteinuria after reduction or cessation of exposure depends on the intensity of exposure and/or the severity of the tubular damage. It was concluded that, as for inhalation exposure, incipient tubular effects associated with low Cd exposure in the general population are reversible if exposure is

substantially decreased. Severe tubular damage (urinary leakage of the proteins RBP or ß2M > 1,000-1,500 µg/g creatinine) is generally irreversible.

A longitudinal study on 74 inhabitants from a cadmium-polluted area in Japan (Kido et al. 1988) showed irreversible and even progression of renal dysfunction 5 years after cessation of cadmium exposure. Likewise, a study from China indicates that the negative effects on bone still remains 10 years after the population abandoned ingestion of cadmium-polluted rice (Chen et al 2009).

The biological half-life of cadmium in humans is extremely long (estimated to be 10-30 years) and the body burden of cadmium therefore increases, mainly via accumulation in the kidney, during the entire life span of an individual. All uses of cadmium and its compounds, including when present as a contaminant, contribute to this bioaccumulation in humans, which starts already in early life.

Unless exposure is substantially decreased kidney and bone effects therefore tend to be irreversible due to the continued internal exposure from stored cadmium. In that respect cadmium behaves in a way that resembles substances that are persistent and bioaccumulating in the environment.

Delay of health effects

The bioaccumulation over the life-time of an individual also affects when effects appear; in most instances the delay between first exposure and appearance of effects is very long, i.e. decades.

Uncertainties on safe exposure

There is uncertainty about identifying safe exposure levels for cadmium. Biomedical research on cadmium is intense. A search of the literature data base PubMed revealed 14 900 articles published during the last 10 years and 8700 articles during the last 5 years. Consequently, new findings on hazards and risks connected with cadmium and its compounds continuously appear. As an example, effects on bone tissue have recently been shown at exposure levels previously considered without effects. Since what can be considered as a “safe exposure level” is steadily decreasing, precautionary community wide actions are warranted.

Further, it is not clear whether an effect on bone/kidney or carcinogenesis is the critical end-point from a risk assessment point of view, although most risk assessments concerning cadmium exposure of the general population (for example the recent report from EFSA (2012)) are based on kidney effects. In the risk assessment for workers by SCOEL (2009), the proposed limit values are also based on effects on the kidney and, to some extent, bone tissue, representing the most sensitive targets of cadmium toxicity after occupational exposure. The suggested IOEL (in air) is considered to be protective against long-term local effects (respiratory effects including lung cancer). Whether this value is also protective against cancer in other tissues was not assessed. According to a paper from the Austrian Workers’ Compensation Board (Püringer 2011), the German Committee on Hazardous Substances (AGS) has recently endorsed a limit value of 16 ng Cd/m³ based on the acceptable cancer risk of 1 : 25,000, i.e. a value 250-fold lower than the IOEL suggested by SCOEL.

Societal concern and impairment of quality of life

In particular the effects on bone tissue, with increased risk for bone fractures, are a considerable public health problem causing a lot of suffering and a burden to society in terms of cost, morbidity and mortality. Osteoporotic complications are particularly prevalent in northern Europe and, statistically, every second woman in Sweden will suffer from an osteoporotic fracture during her lifetime. The incidence of hip fractures is more than seven-fold higher in Northern Europe than in the rest of Europe. The reason(s) for the large age-standardized geographical differences is still not known, but the differences cannot be explained by differences in risk of slipping, low calcium intake, vitamin D deficiency or by inactivity. The fracture incidence has increased substantially since the 1950ies. As the number of old and very old people in the population increases, a further increase in the prevalence of fractures is to be expected.

According to a report published by the Swedish Chemicals Agency, the annual societal costs in Sweden for cadmium in soil due to human activities is estimated to approximately 4.2 billion SEK (approx. 450 million Euros) (KemI 2012). This figure is based on the estimation that 7 and 13 %, in males and females respectively, of all fractures in Sweden are caused by cadmium exposure, mainly via food, and include direct treatment and care costs for bone fractures (approx. 1.5 billion SEK), as well as a valuation of the shortening of life time and a decreased quality of life.

In conclusion

Cadmium is considered to fulfil the criteria according to Art. 57(f), i.e. there is scientific evidence of probable serious effects to human health which give rise to “equivalent level of concern”, due to;

- the adverse effects on kidney and bones, effects that depending on dose may be serious and even contribute to premature death,
- the continuous accumulation of cadmium in the body, which leads to continuous internal exposure and in practice irreversible effects once adverse effect levels are reached,
- the occurrence of adverse effects in a significant part of the general population at present exposure levels, which are primarily of anthropogenic origin,
- uncertainties in deriving a safe exposure level, and
- high societal costs in terms of health care and shortening of life time and a decreased quality of life.

PART II

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES –CONCLUSIONS ON EXPOSURE

Conclusions:

Based on the reported information below, the following conclusions can be drawn:

- Occupational exposure occurs during several industrial and professional use scenarios, such as base metal productions, manufacturing of fabricated ferrous and non-ferrous products, manufacturing of plastic products and personal and household services.
- The function of cadmium as corrosion inhibitor for metals is based on a sacrificial release. Metals coated with cadmium are used in articles which are widely used in the society and will therefore cause uncontrolled releases to surrounding environments. The application of cadmium on the surface of an article will also lead to particulate releases due to wear.
- The recycling of batteries cannot fully exclude releases of cadmium to the environment due to losses of batteries to landfills and waste incineration.
- Cadmium alloys which are widely used in articles will not fully be recycled and will therefore end up in landfill and waste incineration plants, which causes releases to the environment.
- The general population is exposed to cadmium via food and drinking water, smoking, ingestion of soil and dust, and inhalation of ambient air. The sources for the contaminations are both natural and anthropogenic.

7 MANUFACTURE, IMPORT AND EXPORT

7.1 Manufacturers of cadmium metal

Two production methods are described, the RLE method and the Pyro method:

- The RLE process: Industrial use of cadmium-bearing solution which is electrolysed in order to produce pure cadmium metal. The process is carried out in a series of electrolytic cells, with occasional controlled exposure.

- The Pyro method: Cadmium bearing blend is heated (sometimes under reduced pressure) in order to volatilize and further condense pure cadmium metal. The process is carried out in a furnace and condensor, with occasional controlled exposure.

7.2 Quantities manufactured, import and export

The total tonnage band according to the REACH registration is 1 000 – 10 000 tonnes (17 February 2013). This is based on data from 22 registrants from Germany, Norway, Italy, Belguim, Austria, Poland, UK, Bulgaria, the Netherlands, Sweden, France and Luxembourg.

The annual world production of cadmium during 1990 to 1999 was 18 000 to 21 000 tonnes (Kirk-Othmer 2004). Most of the world's primary cadmium metal was produced in Asia and the Pacific - specifically China, Japan, and the Republic of Korea, followed by North America, Central Europe and Eurasia, and Western Europe. Secondary cadmium production takes place mainly at Ni-Cd battery recycling facilities (USGS 2012).

European countries[2] contributed to 9.3 % of world production in 2010 (Figure 1; Table 9). The Netherland was the largest European producer accounting for 28 % of the EU production, followed by Poland (22 %), Bulgaria (21 %), Germany (14 %) and Norway (14 %) (BGS 2012). The production level was stable around 2000 tonnes per annum during 2006 to 2010 (Table 9). This production level is within the "total tonnage band" registered to ECHA (see above).

The historical growth in production volumes during the years 1967 to 1982 was 0.6 %, and increased between 1982 and 1995 to 0.8 % (Kirk-Othmer 2004). The refined primary cadmium production has shown decreases in recent years as secondary recycled cadmium production has increased. Recycling of cadmium was estimated to 15-20 % of the total production, of which >11 % origin are from Ni-Cd-batteries. This trend is expected to increase in the future (Kirk-Othmer 2004).

Table 9: Primary production of cadmium in Europe 2006 to 2010 (BGS 2012)

Country	**Unit**	**2006**	**2007**	**2008**	**2009**	**2010**
The Netherlands	tonnes	524	495	530	490	580
Poland	tonnes	373	421	603	534	451
Bulgaria	tonnes	320	318	376	413	440
Germany	tonnes	490	475	420	250	300
Norway	tonnes	125	269	178	249	300
France	tonnes	90	50	-	-	-
Total	**tonnes**	**1900**	**2000**	**2100**	**1900**	**2100**

[2] 34 European countries: 27 EU countries (1 Febr. 2008) + Norway, Switzerland, Croatia, Island, Macedonia, Montenegro, Turkey.

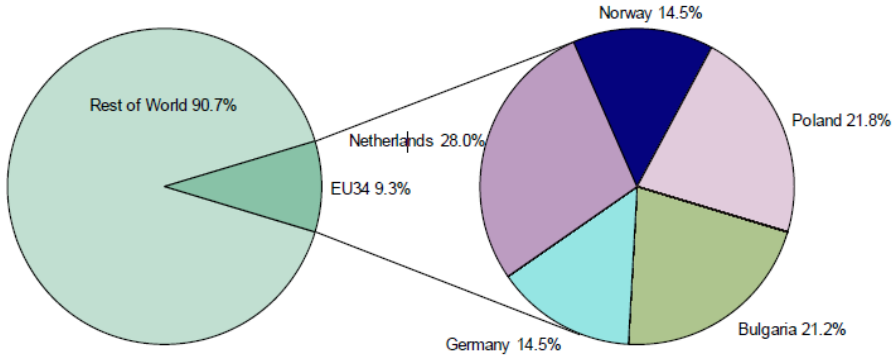

Figure 1: Production of cadmium in Europe 2010 (BGS 2012)

The cadmium metal trade in EU 2010 is dominated by Italy (high export) and Belgium (high import; **Error! Reference source not found.**).

Table 10: European import and export of cadmium metal 2006 to 2010 (BGS 2012)

Country	Unit	2006	2007	2008	2009	2010
Export						
Italy	tonnes	1	796	1633	2030	3104
France	tonnes	798	815	890	1022	763
Norway	tonnes	1064	544	816	305	606
Germany	tonnes	…	…	287	276	523
Poland	tonnes	364	368	558	590	484
Bulgaria	tonnes	369	434	374	569	474
Belgium	tonnes	298	181	442	452	459
Netherlands	tonnes	90	205	259	211	329
Total	**tonnes**	**>2984**	**>3343**	**5259**	**5455**	**6742**
Import						
Belgium	tonnes	3948	5038	5511	3439	6456
Sweden	tonnes	338	491	851	588	825
United Kingdom	tonnes	129	276	212	246	470
France	tonnes	527	771	645	455	212
Spain	tonnes	19	0	21	118	153
Netherlands	tonnes	113	437	186	50	102
Germany	tonnes	7	22	53	11	18
Italy	tonnes	30	40	49	443	3
Greece	tonnes	1	1	18	39	1
Total	**tonnes**	**5112**	**7076**	**7546**	**5389**	**8240**

Cadmium use in batteries accounted for the majority of the global consumption. The volumes for Ni-Cd batteries on the EU market reached a stable level in the late 1990's of around 13 500 tonnes/year for consumer/sealed portable nickel-cadmium batteries and 3 500 to 4 000 tonnes/year for the industrial nickel-cadmium battery market. Between 1996 and 1999 the portable Ni-Cd battery market in the EU was around 13 000 -14 000 tonnes. In the EU RAR the maximum future volume for portable batteries where assumed to be 13 500 tonnes, and 3 600 tonnes for industrial

batteries (ECB 2007). The volumes for industrial Ni-Cd batteries may increase in the future due to new market opportunities[3] (USGS 2012).

8 USES

8.1 General

The sources for cadmium are both mining and recycled alloys. Cadmium is transformed into plates, powder and different alloys (**Error! Reference source not found.**). Cadmium powder is used as a raw material for production of battery electrodes, alloys and metal coatings. The electrodes are used in Ni-Cd and Ag-Zn batteries. For metal coating the powder can be used in both the mechanical plating and the vacuum ion deposition processes. The plates are used for coating metals for anti-corrosion and/or friction reduction purposes. It is applied by the mechanical plating technique. Metal to be coated are iron, steel, aluminium and brass. The alloys are used for joining, fusing and to give special characteristics to a material.

Once cadmium metal is produced, it may be converted to an intermediate product in one country, incorporated into different semi-products/articles in another country, and finally produced and sold in an end-product/article in a third country. It is therefore, difficult to establish a geographic consumption pattern.

Nickel cadmium (Ni-Cd) batteries are the dominating end products in the world consumption of cadmium, followed by minor uses for pigments, metal coatings, stabilizers, alloys and solar cells (Figure 2).

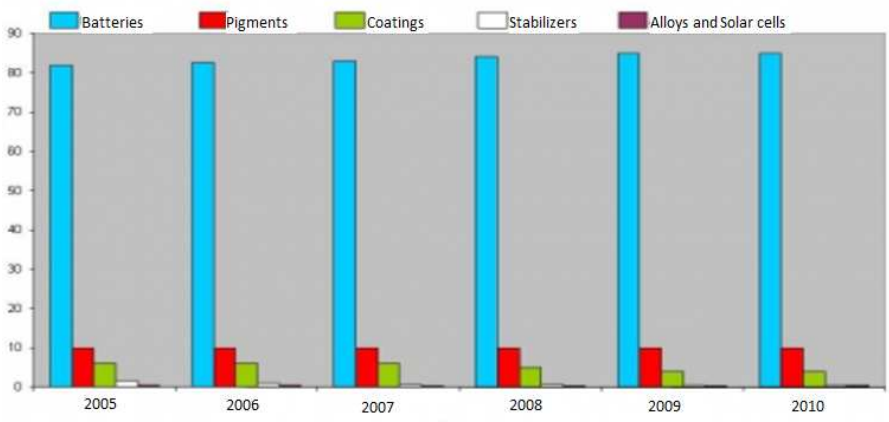

Figure 2: Trends in cadmium consumption patterns during 2005 to 2010, in per cent of the total consumption (ICdA 2013).

[3] "*Industrial-sized NiCd batteries could also be used to store energy produced by certain on-grid systems. For load leveling, excess energy produced during periods of low demand, such as night time, would be stored in a NiCd battery and later released during periods of high electricity demand, such as midday"* (USGS 2012).

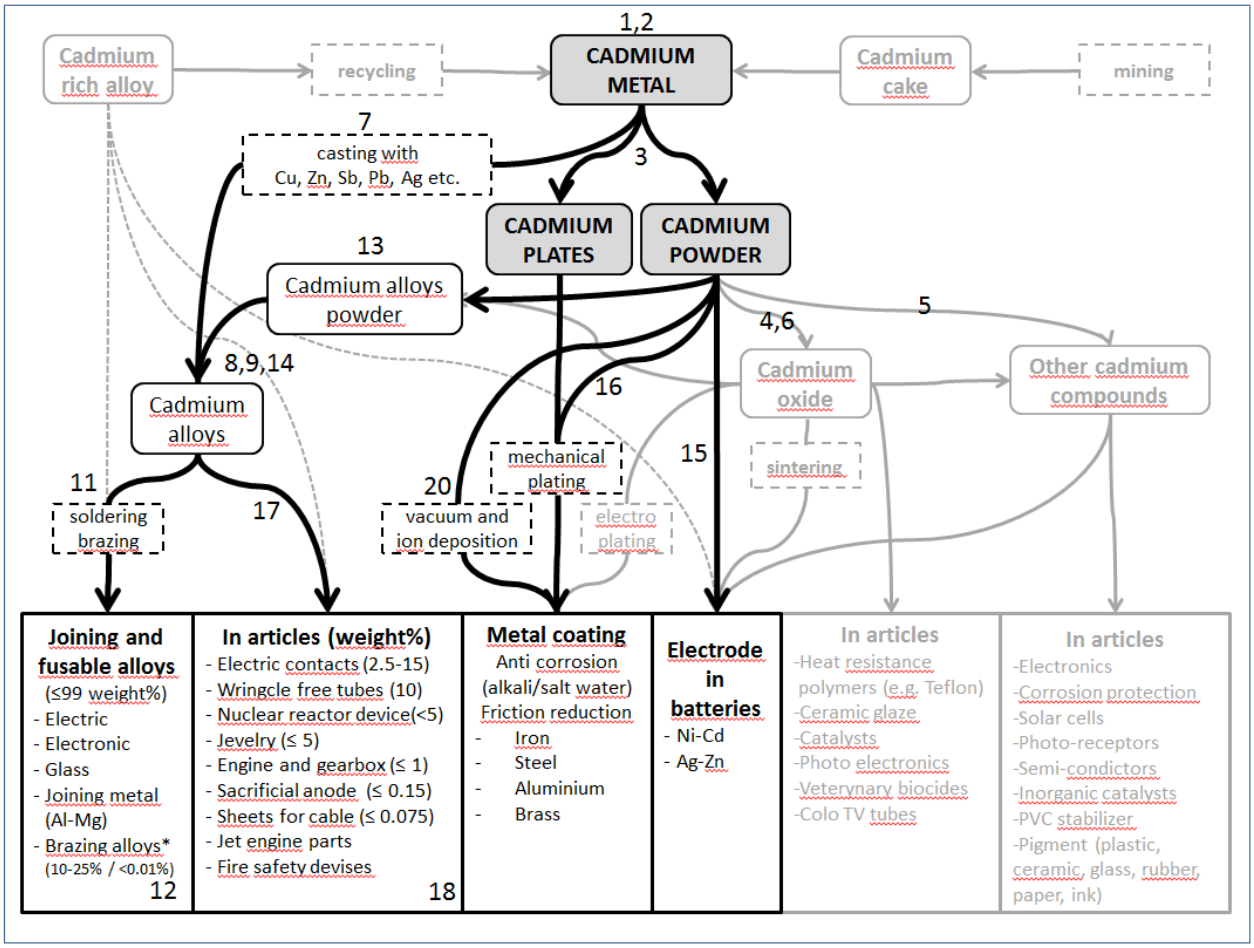

Figure 3: Overview of the cadmium downstream uses. The numbers refer to "exposure scenarios" in the registration (see section 9.1 below) (* is currently restricted under paragraph 8 of Entry 23 of Annex XVII of REACH).

The highest concentrations of cadmium are used in Ni-Cd batteries and some alloys, up to 25% (**Error! Reference source not found.**). The concentrations in coatings are less than 1%. Cadmium may occur as impurity in fertilizer, fossil fuel, cement and in different metals. The concentrations as impurities are normally in the range of 0.1 to 90 ppm. For many literature data on impurities is it unclear if it is in the form of metal.

Table 11: Concentration of different cadmium uses (US 2003, ICdA 2012b).

Product	% Cd	Use type	Comment
Ni-Cd batteries	7-25%	Intentional	Cd, CdO, $Cd(OH)_2$
Cd pigments	~1%	Intentional	Cd(Zn)S(Se)
Cd coatings	~0.2%	Intentional	Cd, CdO, Cd-Ti, Cd-Sn
Cd stabilizers	~1%	Intentional	Cd-laurate, Cd-stearate
Cd alloys *et.al.*	1-25%	Intentional	Cu-Cd, Ag-CdO

8.2 End uses of cadmium metal (excluding the intermediate applications)

8.2.1 Use in Nickel-Cadmium batteries (ICdA 2012)

A number of types of Ni-Cd cell constructions are possible. These variations in cell construction lie mostly in the nature of the electrode support utilised. For the positive electrode, three principal types are recognized - pocket plate, sintered plate and fiber plates. Negative electrode designs make use of an even broader range of materials including pocket plates, sintered nickel powder, fiber, foam and plastic bonded supports. It is the physical stability of the active material (cadmium hydroxide) in the negative electrode that permits such a wide variety of support materials.

Nickel-cadmium batteries are characterized by their resistance to electrical abuse, high cycle lives, reliability and versatility and have found a wide range of applications. The several types of cell constructions are manufactured in a wide range of size, capacity and shape and the choice of a particular battery will depend upon the application and its current load requirements. There are principally two applications types, industrial and portable batteries.

- **Industrial Ni-Cd batteries**: Nickel-cadmium batteries for industrial uses are of the open or semi-sealed type and may be of pocket plate, sintered plate or fiber structured construction. Applications for industrial batteries include railway uses such as locomotive starting, emergency braking, coach lighting and air conditioning, trackside power for signaling and warning lights. Other uses include standby power for alarm systems, emergency lighting, military communications, solar energy storage, navigation equipment, military equipment, hospital operating theatres. Semi-sealed industrial batteries are used in aeronautical applications where they are used to start engines and also to provide stand-by power for aircraft systems when the principal power source fails. After long periods of operation most vented or semi-sealed cells may require electrolyte maintenance by topping up with distilled water.

- **Portable Ni-Cd batteries**: Nickel-cadmium batteries for portable use are of the sealed type and are generally of sintered plate construction. They may be of cylindrical, button or prismatic design. Sealed nickel-cadmium batteries are in use in consumer electronic equipment such as cellular telephones, portable tools, toys, camcorders and other domestic cordless appliances. They are also used for memory back-up in computing equipment, military and civil communications, emergency lighting and many other similar applications. Sealed cells require no maintenance and may be recharged up to 2000 times.

According to information from Industry, the following attributes are unique to industrial Ni-Cd batteries:

- Superior reliability and ability to withstand mechanical and electrical abuse,
- Large operating temperature range,
- Excellent long service life (12 to 20 years), adequate cycling ability,
- Progressive aging, lends itself to accurate monitoring of aging. This makes predictive maintenance the preferred maintenance strategy. No “sudden death” syndrome,
- Low Cd metal content (8 to 10%) relative to the standard technology (Pb/acid with 70% Pb),
- Low CO2 footprint compared to the standard technology.

These unique set of performance characteristics makes this family of products the technology of choice when the safety of large assets and/or human beings is at stake. In such applications, Ni-Cd batteries are entrusted with the function of providing back-up power in case of a malfunction in the power supply (often the electrical grid). This is why industrial Ni-Cd batteries are used in safety

critical applications such as power back-up aboard commercial aircrafts and high speed trains, power back-up in networks equipment (i.e., telecom, oil and gas, IT) and power back-up in several highly critical industrial processes.

8.2.2 Cadmium coatings (ICdA 2012)

Cadmium coatings are applied to iron, steel, brass and aluminium and give high resistance to corrosion in most conditions and especially in marine and alkaline environments, and reduce risks of operating mechanisms being jammed by corrosion debris for many components in a wide range of engineering applications throughout industry.

Cadmium coatings are particularly useful in the electrical, electronic, aerospace, mining, offshore, automotive and defence industries where they are applied to bolts and other fasteners, chassis, connectors and other components industry.

Electroplating accounts for over 90% of all cadmium used in coatings but mechanical plating and vacuum or ion deposition have some commercial significance. The coating is normally specified in thickness between 5 and 25 µm depending on the severity of the atmosphere industry.

There are principally three coating methods, electroplating, mechanical plating and vacuum and ion deposition:

- **Electroplating**: Cadmium is electrodeposited on the metal article from an electrolyte solution of cadmium salts in barrels or vats. These electrolyte solutions are nearly always based on the alkaline cyanide system. Other solution types are used, such as those based on fluoroborates, but these have not proved popular as they lack the combination of brightness, covering power, throwing power and wide operating parameters of the alkaline cyanide system. When a current is passed through the electrolyte, cadmium is electrodeposited on the metal article at the cathode and cadmium from the anode goes into solution. Large or delicate articles are attached to racks and vat-plated whilst small components, such as bolts, washers, nuts, springs and clips can be vat-plated in drum cages or plated in a rotating barrel.

- **Mechanical plating**: This process uses mechanical energy to deposit metal coatings on small components by the impact of glass beads. Either cadmium or mixed-metal coatings of cadmium-tin or cadmium-zinc can be applied when glass beads, proprietary chemicals, water and metal powder are tumbled with the components in a rotating barrel. The process is suited to components such as fasteners and clips which are small enough to be plated in a barrel.

- **Vacuum and ion deposition**: Conventional thermal vapour deposition involves heating of cadmium in a vacuum until it vaporizes. Cadmium atoms then condense on the substrate to form a thin high quality coating of cadmium. Ion deposition is said to give improved coating adhesion, density and uniformity. Components such as undercarriage legs of transport aircraft, helicopter rotor parts and other high strength steel components have been coated using this method.

8.2.3 Cadmium in alloys (ICdA 2012)

Cadmium forms many binary and more complex alloys which have useful properties for many commercial applications.

Most commercial alloys containing cadmium fall into two major groups:

- Cadmium improves some feature of the alloy
- Cadmium lowers the melting point of the alloy (mainly for joining)

Alloys with special features (ICdA 2012)

- Copper-cadmium alloys, which have almost double the mechanical strength and wear resistance of pure copper, contain between 0.8 to 1.2% cadmium. Major uses include telephone drop wires, contact wire and catenary strand for railway overhead electrification, tinsel conductor for flexible telephone cords, special cables for military and aerospace uses and electrical components such as contact strips. Copper-cadmium alloys can withstand service temperatures as high as 150°C; as a result they are used in both domestic and automotive radiators and fittings.

- A zinc alloy containing 0.1% cadmium improves the mechanical properties of rolled, drawn or extruded zinc. Zinc alloys containing cadmium in the range 0.025 to 0.15% are used as sacrificial anodes in the corrosion protection of structural steelwork immersed in seawater.

- Lead alloys with up to 0.075% cadmium are sometimes used as sheaths for cables subject to cyclic stress.

- Tin-based white metal bearing alloys with up to 1% cadmium have improved tensile and fatigue strength for use in marine engines and gearboxes.

- Precious metal alloys for jewellery incorporate cadmium for improved hardness and strength. Levels of up to 5% cadmium in gold-silver-copper alloys make Greek gold, a greenish-tinged gold (this use is partly restricted in REACH, Annex XVII, entry 23).

- Silver electric contacts incorporating 10 to 15% cadmium are useful in many heavy duty electrical applications such as relays, switches and thermostats. The presence of cadmium improves resistance to material transfer and electric erosion.

- Silver-indium-cadmium alloys are used in control rods for some pressurised water reactors in nuclear power generation. These rods absorb free neutrons and so control the process. In other nuclear engineering applications, cadmium metal sheet is used for shielding by similar neutron absorption.

Joining and fusible alloys (ICdA 2012)

- Intermediate temperature soldering alloys and cadmium alloyed with silver, zinc and/or tin are often used in applications where temperature sensitivity prohibits the use of silver solders with higher tensile strength. Zinc-cadmium alloys are useful for soldering aluminium whilst cadmium-zinc-tin alloys are used for soldering magnesium.

- Cadmium as a component in quaternary silver-brazing alloys (lower temperature range of brazing alloys, together with silver, copper and zinc).

- Fusible alloys: Low temperature fusible alloys containing cadmium employ their low melting points and rapid fusing or solidifying characteristics in a variety of uses. Heat sensitive fusible links in fire safety devices or kilns and ovens can activate control mechanisms when they melt at specific temperatures. Woods metal in water sprinkler valves automatically activates the water supply as it melts.

- Proof castings in these alloys can be made from wood, plastic or plaster foundry patterns for short run dies for sheet metal and thermoplastics.

- The alloys are used to firmly mount glass lenses during grinding operations. Metal fabrication operations on complex or delicate assemblies are also easy when they are encased in a supporting jacket of metal. This technique also produces wrinkle-free bends in pipes and tubes. Similarly, jet engine turbine blades and vanes are machined whilst held by such low melting point alloys.

8.3 Identified uses in the EU (ECHA, 2012)

The registration of cadmium includes the following uses:

- Cadmium metal production - RLE
- Cadmium metal production by pyrometallurgy
- Production of chemicals (pyro)
- Production of chemicals (hydro)
- Storage of ingots-slabs in warehouses
- Additive for production of inorganic catalysts
- Melting, alloying and casting
- Cadmium casting and rolling
- Wire and rods manufacturing
- Component for brazing products
- Downstream use of Cadmium based brazing products (more details in ECHA 2012b).
- Cadmium (alloyed) powder manufacturing
- Use of fine powders for mechanical plating
- Manufacturing of Cadmium containing-alloys
- Use of cadmium in Ag alloys
- Electroplating
- Production of "targets" by EBPVD
- Component for soldering products
- Downstream use of cadmium-based soldering products
- Powders for contact materials
- Use of active powders for batteries
- PVD / coating
- Intermediate for alloys
- Downstream use of cadmium based brazing products
- Downstream use of cadmium-based soldering products

8.4 Volumes

The total international cadmium consumption is dominated by the production of Ni-Cd batteries (**Error! Reference source not found.**). Japan is the largest producer of raw material for Ni-Cd-batteries in the world (Kirl-Othmer 2004). Other relevant uses are as pigments and anti-corrosion coatings of metals. A quantification of the cadmium flow in EU[4] has been made by Lig & Held (2009).

The volume for brazing alloys, for both professional and consumer uses, was estimated to be 22 to 35 tonnes 2010 (ECHA 2012b). This amount can be expected to fall due to the REACH Annex XVII restriction on cadmium in brazing fillers which entered into force in January 2012 (ECHA 2012b).

Cadmium use is concentrated to industrialized countries with six countries accounting for 85 % of the world consumption. Japan is the leading consumer, followed by Belgium and the United States. In year 2000, an estimated 13 % of cadmium consumption in the United States came from recycled batteries and materials. However, cadmium usage in developed countries has declined in recent years owing to its toxicity (Klimasauskas 2005).

The final effect of the REACH and others legislations on global cadmium consumption has yet to be seen. If recent legislation involving cadmium dramatically reduces long-term demand, a situation could arise, similar to what has recently been seen with mercury, where an accumulating oversupply of by-product will need to be permanently stockpiled (USGS 2012).

Ni-Cd-batteries may be used in electric vehicles, hybrid electric vehicles and electric buses. However, how this usage would influence the cadmium volumes is unclear since future applications are expected to be recycled. An example of a new potential use is combinations of cadmium, calcium, copper, selenium, strontium, sulphur, and tin that can be used as substitutes for hardening lead (USGS 2012).

8.5 Recycling

In the U.S., cadmium is mainly recovered from used consumer and industrial Ni-Cd batteries. Cadmium can also be recovered from copper-cadmium alloy scrap, some complex nonferrous alloy scrap, and cadmium-containing dust from electric arc furnaces (EAF) (USGS 2012).

There are recycling systems established for used nickel-cadmium batteries. Today, there are 9 major Ni-Cd battery recycling plants located in the United States, Europe and Japan capable of recycling approximately 20 000 tonnes of industrial and consumer Ni-Cd batteries and their manufacturing scraps (ICdA 2012).

Also the plastic industry has undertaken research to determine the feasibility of recycling cadmium pigments and stabilizers from plastics (Kirk-Othmer 2004).

[4] The 27 EU member states.

8.6 Functions of the substance according to its properties; mechanisms of action

8.6.1 Ni-Cd batteries (ICdA 2012)

Cadmium is incorporated as an active electrode material in a number of rechargeable alkaline batteries or cells. The nickel-cadmium cell, with a potassium hydroxide (alkaline) electrolyte, is the most important and best known application. At the negative electrode (cathode) cadmium oxidizes to cadmium hydroxide whilst the nickel compounds are reduced to nickel hydroxide at the positive electrode (anode) according to the following reaction:

$$2\ Ni(OH)_2 + Cd(OH)_2 \leftarrow \text{charge / discharge} \rightarrow 2\ NiO(OH) + Cd + 2\ H_20$$

8.6.2 Surface coating (ICdA 2012)

Cadmium, like zinc, also provides sacrificial protection to a substrate such as steel by being preferentially corroded when the coating is damaged and small areas of the substrate are exposed. In addition to corrosion protection, cadmium coatings provide a low coefficient of friction and therefore good lubricity, predictable torque characteristics, good electrical conductivity, protection from galvanic corrosion (in particular when in contact with aluminum), and easy solderability.

8.6.3 Alloys (ICdA 2012)

Copper-cadmium alloys contain 0.8 to 1.2 % cadmium, and have almost double the mechanical strength and wear resistance compared with pure copper. Zinc containing 0.1% cadmium improves the mechanical properties of rolled, drawn or extruded zinc. Lead alloys with up to 0.075 % cadmium are sometimes used as sheaths for cables subject to cyclic stress. Silver-indium-cadmium alloys absorb free neutrons and are therefore used to control the nuclear reactions in nuclear power stations. Rods of the silver-indium-cadmium alloy absorb free neutrons and are used to control the process. In other nuclear engineering applications, cadmium metal sheet is used for shielding by similar neutron absorption.

8.6.4 Joining and fusible alloys (ICdA 2012)

Low temperature fusible alloys containing cadmium employ their low melting points (≥ 47 °C) and rapid fusing or solidifying characteristics in a variety of uses (e.g. for soldering aluminum and magnesium).

The main uses of brazing alloys were professional and industrial ones, such as tooling, heat exchangers, refrigeration, plumbing and electrical components. These uses were more widespread in southern European countries such as France, Spain, Italy and Portugal (ECHA 2012b).

9 EXPOSURE

Human exposure for cadmium can potentially occur during the whole life-cycle of the substance. Industrial and professional workers will be exposed during several scenarios where cadmium is produced, used, recycled and managed as waste.

Exposure of man via the environment occurs as a result of emissions from industrial and professional processes, and diffuse releases from private use of goods. Exposure from natural sources of cadmium needs also to be considered, and show large variation due the local/regional ground conditions. The most important sources of cadmium exposure for the general population are: (i) food and drinking water contaminated from different diffuse releases; (ii) smoking; (iii) soil and dust ingestion, and inhalation of ambient air. Vegetarians, children, smokers and people living in highly contaminated areas are identified to have the highest potential exposure.

In nonsmokers, not occupationally exposed to cadmium, food is the primary exposure source. Cadmium in food mainly originates from uptake from the agricultural soil. The soil is contaminated via the atmosphere from industrial releases and combustion of fossil fuel. Also end use of cadmium containing products will contribute to the soil contamination.

From a regulatory point of view the origin of the different cadmium exposures can be divided into three categories:

1. Anthropogenic: **Deliberate use of cadmium** as such or in mixtures or articles, for example in NiCd batteries and as anticorrosion agent for metals. Exposure of workers and also the general population via the environment,
2. Anthropogenic: Exposure from **use of substances/mixtures/articles** containing cadmium as an **impurity**, such as phosphorous fertilizer, sewage sludge, residual in zinc and fossil fuel. Mainly exposure of the general population via the environment.
3. Natural: **Natural occurring cadmium** releases from minerals in soil/sediments. Exposure of the general population.

9.1 Releases and exposure during industrial and professional uses (“Exposure scenarios”)

The following general exposure scenarios were considered relevant by ICdA (ICdA 2012). The exposure scenario numbers are shown in **Error! Reference source not found.**.

1. Cadmium metal production (RLE): Industrial use of cadmium-bearing solution [SU 3, 8, 14] which is electrolyzed in order to produce pure cadmium metal [PC 7]. The process is carried out in a series of electrolytic-cells, with occasional controlled exposure [PROC 2, 5, 8b, 9, 22, 26], [ERC 1, 2].
2. Cadmium metal production (pyro): Cadmium bearing blend is heated (sometimes under reduced pressure) [SU 3, 8, 14] in order to volatilize and further condense pure cadmium metal [PC7]. The process is carried out in a furnace and condensor, with occasional controlled exposure [PROC 2, 3, 4, 5, 22, 25, 26], [ERC 1, 2].
3. Storage ingots-slabs in warehouses: Cadmium slabs, sticks and balls [PC 7] are traded on an international scale [SU 3, 14]. Intermediate storage occurs [PROC 3, 26] at centralized warehouses [ERC 10a, 11a].

4. Production of chemicals (Pyro): Industrial use of Cadmium metal [SU 3, 8, 9, 10], primary or recycled, in the manufacture of cadmium oxide powder [PC 19, 20, 21] by the indirect process (vaporisation Cd° + oxidization to CdO) [PROC 2, 3, 22] and packaging [PROC 8, 9, 26], [ERC 1].

5. Production of chemicals (Hydro): Industrial use of cadmium metal [SU 3, 8, 9, 10], primary or recycled, in the manufacture of other inorganic cadmium-substances [PC 19, PC 20 or PC 21], [PROC 2, 3, 8b, 15] through several process routes, hydro-, pyro-, electrolytic-, with potentially drying and packaging [PROC 9, 26], [ERC 1].

6. Additive for production of inorganic catalysts: Industrial use of Cd metal [SU 3, 8, 9, 10] for the production of catalysts [PC 2, 7, 9b, 19, 20, 40]. Cadmium / CdO are constituents of many types of catalysts: it is present for its catalytic activity, and its ability to absorb catalyst poisons (a.o. S and Cl) [ERC 1, 4, 5, 6a, 6b].

7. Melting, alloying & casting: Industrial use of cadmium cathodes or slabs, primary or secondary [SU 3, 14 / PC 7]; they are melted, possibly alloyed (Al, Cu, Ni, Mg) and cast in required formats [PROC 2, 3, 8b, 22], [ERC 1, 2].

8. Production of "targets": Industrial use of cadmium cathodes, sticks or slabs [SU 3, 10, 14 / PC 7]; they are melted, possibly alloyed (Ag, …) and cast in the required article format of "targets" for PVD / EBPVD or other sputtering techniques [PROC 2, 3, 5, 8b, 9, 15, 22], [ERC 1, 2, 4].

9. Cadmium sheet casting & rolling: Industrial use of cadmium cathodes or slabs [SU 3, 14, 15], pure or alloyed, [PC7] by the casting and rolling process [PROC 23] to fabricate sheets and coils [AC 2, 3, 7], [ERC 2, 5].

10. Wire & rods: Cadmium metal sheet [SU 3, 14, 15] is further industrially processed [PROC 6, 21, 24] to wire format [SU 0 (Nace 25.9.3)], [ERC 2, 5].

11. Component for welding / brazing / soldering products: Industrial use of cadmium metal containing wire/rod [SU 3, 14, 15, 0 (Nace 25.9.3)]; it is prepared according specifications for use [PROC 5, 22] as brazing, soldering component [PC 7, 38], [ERC 2, 5].

12. DU of Cd-based brazing / soldering products: Professional use [SU 14, 15, 18, 19, 22, 0 (Nace 25.9.3)] of cadmium-based wires and rods, alloyed or not, [PC 7, 38] for use as brazing and soldering sticks [PROC 21, 25], [ERC 5, 10a, 11a]. The main uses of brazing alloys are professional and industrial uses, such as tooling, heat exchangers, refrigeration, plumbing and electrical components (ECHA 2012b).

13. Cadmium (alloyed) powder manufacturing: Industrial use [SU 3, 9, 14] of cadmium, pure or alloyed, in the production of cadmium powder/dust [PC 7, 14] by different metallurgical techniques [PROC 3, 8b, 9, 27a, 27b]. Main applications of the product are batteries, electronics, corrosion protection …[ERC 1, 2].

14. Powders for electrical contacts: Industrial use [PROC 5, 7, 8b, 13, 15] of cadmium powders [SU 3, 9, 14, 16, 0 (Nace C27.2)], pure or slightly alloyed [PC 7]; they are mechanically plated for assuring electrical contacts [ERC 4, 5].

15. Active powders for batteries: Industrial use [PROC 5] of cadmium powders [SU 3, 9, 14, 16, 0 (Nace C27.2)], pure or slightly alloyed (Pb, Bi, In, Mn, …), passivated or not [PC 7]; they are mixed with appropriate electrolyte and fed as active components of batteries.[ERC 3, 5].

16. Fine powders for mechanical plating: Industrial and professional use [SU 3, 14, 15, 0 (Nace C25.6.1)] of cadmium powder, pure or slightly alloyed, passivated or not, for mechanical coating (sherardizing) [PC 7, 14] of steel articles [AC 1, 2, 7] in closed bins [PROC 3, 8b ,9 , 24], [ERC 2, 5].

17. Manufacturing of cadmium containing Ag-alloys: Industrial use [SU 3, 10, 14] of cadmium as minor alloying element in metallic matrices (Al ..) for the production of several alloys [PC 7], by melting and mixing at elevated temperature [PROC 2, 9, 22]. The alloy is used for a variety of metal products [AC 7] [ERC 1, 2, 5].

18. DU of cadmium containing Ag-alloys: Industrial use [SU 3, 14, 15, 0 (Nace C24.5.3)] of cadmium containing Al-alloy slabs and ingots [PC 7] by transformation processes (PROC 6, 8, 14, 22, 25, 26) to fabricate cast pieces and articles (AC 1, 2, 3, 7), [ERC 3, 5].

19. Electroplating: Industrial use [SU 3, 15, 0 (Nace C25.6.1)] of cadmium which is deposited [PC 7, 14] from a Cadmium-rich solution as a metallic coating for corrosion inhibition [PROC 3, 8b, 9, 13, 21] during a batch electrochemical process [ERC 2, 5].

20. PVD / coating: Industrial use of cadmium-based "targets" [SU 3, 15, 0 (Nace C25.6.1)] for coating various substrates by PVD / EBPVD or other sputtering techniques [PROC 1, 2], [EC 1, 2, 4].

9.2 Releases during the service life

Release of cadmium during service life from anthropogenic sources includes products and materials to which cadmium has deliberately been added to impart a specific chemical, mechanical or physical property and products or materials in which cadmium is naturally present as a residual or impurity element. In general, the cadmium content in products or materials in which cadmium is present as a deliberate additive is greater than the levels in the products or materials in which cadmium is present as a residual or unintentional impurity (ICdA 2012b).

The emission rates from coatings during normal service life of 10-25 years are estimated to be 50% (Morrow 1996 in ICdA 2012b). 25% of coating is lost based on abrasive mechanisms (WS Atkins 1998 in ICdA 2012b). There are different cadmium coatings usages in different geographical areas (ICdA 2012b).

Cadmium can be released from automotive applications such as steering columns and disk brake parts due to abrasive conditions. Cadmium may also be used as protective coatings on fasteners. Some of the fastener applications would be subject to abrasion, but only on a limited basis. Fasteners might be torqued to a certain applied load level, but during their useful service life only disassembled and reassembled a few times. In the aircraft applications area, landing gear are frequently subjected to abrasion conditions and a heavy cadmium coating is utilized for this application to ensure that landing gear always may be safely raised and lowered during aircraft operation. Ammunition applications also result in abrasion and wear as well as railroad applications (ICdA 2012).

9.3 Releases during the waste life stage

The Ni-Cd battery recycling system will not collect 100% of the batteries on the market. It can be expected that Ni-Cd batteries (mainly portable) to some extent end up in landfills or are incinerated which cause releases of cadmium into the environment (ICdA 2012b).

9.4 Release from natural sources

Cadmium is a naturally occurring metallic element, one of the components of the earth's crust and present everywhere in our environment. Cadmium emissions to the environment may therefore arise from both natural and anthropogenic or man-made sources. Estimates of the proportion of total cadmium emissions due to natural sources have ranged from 10% to 50%. Some of these natural emission sources include weathering and erosion of parent rocks, volcanic activity and forest fires (ICdA 2012b).

Natural cadmium will also indirectly causes releases, via anthropogenic uses of a wide range of materials for industrial and consumer purposes. Cadmium is sometimes found in high concentrations in phosphate **fertilizers** (marine phosphates and phosphorites). It has also been reported at fairly low levels in **iron** and **steel** because all of the raw materials (iron ore, limestone, coke and scrap steel) utilized to make iron and steel usually contain residual amounts of cadmium. Virtually all **fossil fuels** contain various levels of cadmium depending on their specific type, and are a significant contributor to cadmium air pollution since they all must be combusted to be utilized. The raw materials employed to produce **cement** and **concrete** also contain residual amounts of cadmium and are a contributor to total cadmium environmental emissions. Cadmium is present as a residual element in **zinc**, **lead** and **copper** ores. However, cadmium is normally removed as a by-product during the smelting and refining processes for these metals and converted directly to cadmium metal for sale on the market. It is not generally left in zinc, lead or copper metals and alloys unless deliberately, in order to achieve an improvement in some mechanical, chemical or physical property. The tendency, in fact, in recent years has been to produce these nonferrous metals, their alloys and their compounds with lower and lower residual cadmium levels. Furthermore, deliberate cadmium additions to zinc, lead or copper alloys are generally low (<1%), and even in these cases they are seldom utilized for atmospheric exposure applications. Residual or unintentional cadmium levels in various products or materials are summarized in Table 12 (ICdA 2012b). Corrosion of cadmium from unintentional impurities in metallic materials such as irons and steels and nonferrous metals is expected to be extremely low and not to contribute significantly to overall cadmium releases due to corrosion. The presence of cadmium in and its emission into the environment from fossil fuels, cement manufacture or wear, and fertilizers do not arise from corrosion processes but represents chemical dissolution or wear/erosion processes rather than electrochemical corrosion processes (ICdA 2012b).

Table 12: Concentration of cadmium as impurities in different types of products/materials (ICdA 2012b).

Product	% Cd
Phosphate fertilizers	3 – 90 ppm
Fossil fuels	0.1 – 1.5 ppm
Cement	2.0 – 2.5 ppm
Iron and steel	0.1 – 5.5 ppm
Nonferrous metals	1 – 50 ppm

9.5 General population - current exposure

The general population is exposed to cadmium primarily via food intake, but also via smoking, soil and dust ingestion, inhalation of ambient air and drinking water.

Three large and fairly recent studies were used to display the "current" urinary cadmium concentrations in the Swedish population (KemI 2011), for a summary see Table 13.

- The National Swedish health-related environmental monitoring program (SEM), financed by the Swedish Environment Protection Agency, coordinates longitudinal monitoring of cadmium concentrations in urine (µg/g creatinine), representing long-term exposure, for younger (20-29 years of age) and middle aged (50-59 years) women in four geographical regions in Sweden. The urine sampling circulates by geographical area every second year. Results are available for the period of 2002-2009 with 2 time points for most areas (http://www.imm.ki.se/Datavard/Tidsserier/Cadmium%20in%20urine.htm).
  In total, 1458 women (n=669 women 20-29 years, n=759 women 50-59 years of age) are sampled.

- The Women's Health in the Lund Area Study (WHILA) included women, aged 54 to 63 years, living in a rural area in Southern Sweden (with no known industrial cadmium emission). During 1999, 820 women were recruited (71% participation rate). Cadmium was assessed in both blood (median, 0.38 µg/L) and urine (median 0.52 µg/L; density adjusted = 0.67 µg/g creatinine).

- Data from the Swedish Mammography Cohort (SMC). During 2003 to 2009, 2831 women in the town of Uppsala, 56-69 years of age had urines samples determined for cadmium.

Table 13: Summary of the urinary concentrations observed in three Swedish population-based studies.

	Age	*Urinary cadmium µg/g creatinine*			
	(years)	*Median and (range)*		*% >0.5µg/g*	*%>1.0 µg/g*
		All	Never-smokers	All / Never-smokers	
SEM	20-29	0.12 (0.01-0.68)	0.10 (0.02-0.68)	-	-
	50-59	0.29 (0.04-2.2)	0.24 (0.04-1.4)	20 / 4	1.8 / 0.3
WHILA	53-64	0.67 (0.13-3.6)	0.56 (0.13-3.2)	70 / 32	20 / 6
SMC	56-69	0.35 (0.05-2.4)	0.29 (0.05-1.3)	23 / 6	2.0 / 0.2

SEM; The National Swedish health-related environmental monitoring program, WHILA; Women's Helath in the Lund Area, SMC; The Swedish Mammography Cohort;

Proportion of the population with urinary cadmium above 0.5 and 1.0 µg/g creatinine

Women in the age group 50-69 years were also used to evaluate the proportion of women having urinary cadmium levels above the two predefined cutoffs of 0.5 and 1.0 µg/g creatinine. In these studies, 20%, 70% and 23% of all the women (4%, 32% and 6% in never-smokers) had urinary cadmium concentrations above 0.5 µg/g creatinine, respectively. The corresponding proportions for urinary cadmium concentrations above 1.0 µg/g creatinine were 1.8%, 20% and 2%, respectively (0.3%, 6% and 0.2% in never-smokers). Differences between studies may indicate higher exposure in Southern Sweden, but comparability of measurements may contribute.

Cadmium exposure over time

Based on a Swedish study on kidney biopsies (from 2010) assessing cadmium content in the kidneys of 109 living donors (aged 24–70 years; median 51 years), the kidney cadmium concentrations were compared to results from studies published starting in the 1970. Two earlier Swedish studies assessed kidney-cadmium in diseased people at autopsy. When comparing kidney cadmium concentrations in never-smokers in this recent study the levels were similar to or only marginally lower than those from the 1970s.

The reported concentrations in the National Swedish health-related environmental monitoring program for 2002-2009 may indicate a slight decrease in urinary cadmium with time in south-western and northern Sweden (see **Error! Reference source not found.**). However, there has been a change in analytical instrumentation and the comparability is still under investigation. In the northern area, blood cadmium concentrations 1990-1999 showed no changes over time. In Stockholm, where the samples have been analyzed with the same method and instrumentation, there is no apparent decrease over time. If anything, there may be a slight increase in the younger age group. This longitudinal series of monitoring data also seems to indicate that there is a geographical variation in urinary cadmium concentrations with lower values in northern Sweden and higher in the south. This will be further evaluated in the future.

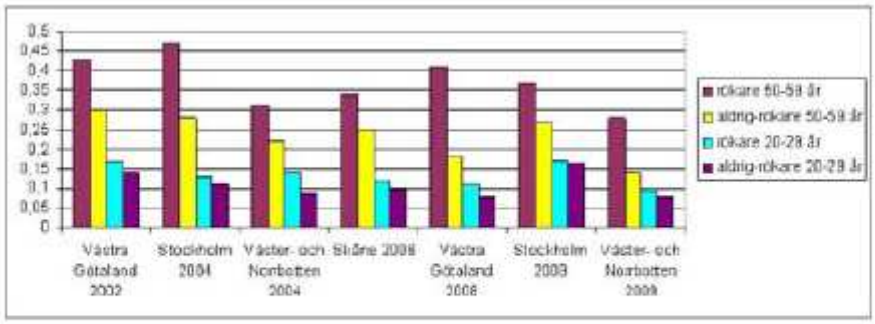

Figure 4: Urinary cadmium (µg/g creatinine) among Swedish woman, 20-29 years and 50-59 years of age, presented as the median.

In summary, the comprehensive data base on cadmium exposure based on biomarkers of exposure and measured dietary intake in Sweden shows no decrease in cadmium exposure over time during the last 2-3 decades in Sweden.

9.6 Worker exposure to cadmium

The main route of cadmium exposure in the occupational setting is via the respiratory tract, although there may be incidental ingestion of dust from contaminated hands, and food. Occupations in which the highest potential exposures occur include cadmium production and refining, Ni–Cd battery manufacture, cadmium pigment manufacture and formulation, cadmium alloy production, mechanical plating, zinc smelting, brazing with a silver–cadmium–silver alloy solder, and polyvinylchloride compounding. Although levels vary widely among the different industries, occupational exposures generally have decreased since the 1970s (IARC 2012).

Estimates of the number of workers potentially exposed to cadmium and cadmium compounds have been developed by CAREX in Europe. Based on occupational exposure to known and suspected carcinogens collected during 1990–93, the CAREX (CARcinogen EXposure) database estimates that 207 350 workers were exposed to cadmium and cadmium compounds in the European Union, with over 50% of workers employed in the construction (*n* = 32 113), manufacture of fabricated metal products (*n* = 23 541), non-ferrous base metal industries (*n* = 22 290), manufacture of plastic products not elsewhere classified (*n* = 16 493), personal and household services (*n* = 15 004), and manufacture of machinery except electrical (*n* = 13 266) (IARC 2012).

CAREX Canada estimates that 35 000 Canadians (80% males) are exposed to cadmium in their workplaces. The largest exposed group are workers in polyvinyl chloride plastic product manufacturing (*n* = 12 000), who are exposed to cadmium bearing stabilizers. Other industries in which exposure occurs include: foundries, commercial and industrial machinery manufacturing, motor vehicle parts manufacture, architectural and structural metal manufacturing, non-ferrous metal (except aluminum) production and processing, metalworking machinery manufacturing, iron and steel mills and ferro-alloy manufacturing, alumina and aluminum production and processing, and other electrical equipment and component manufacture (IARC 2012).

In the registration dossier of the lead registrant exposure assessments of the various work tasks involving cadmium are mainly from the EU RAR (ECB 2007). In addition, a few recent air measurements and urinary concentrations of exposed workers are given.

9.7 Consumer exposure

According to the EU RAR, the consumer uses of cadmium oxide and metal fall into five categories corresponding to at least 5 scenarios of exposure: Active electrode material in nickel-cadmium batteries; Pigments used mainly in plastics, glasses and ceramics, enamels and artists' paints; Use of cadmium as stabilizers for plastics or polymers; Metal plating (steel and some non-ferrous metals); Component of alloy. In the lead registration dossier, no consumer use is given and therefore also no exposure assessments. It is, however, mentioned that one new use (small in quantity) has been emerging: i.e. the use of cadmium substances in the production of photovoltaic cells. This application does not result in any direct consumer exposure.

The recent revision of Entry 23 in Annex XVII includes several new restrictions that will decrease the risk for consumers. However, given the wide range of potential uses of cadmium it cannot be completely ruled out that some consumer exposure from articles containing cadmium may still take place.

10 ALTERNATIVES

10.1 Battery

The information below has been obtained from the battery industry:

Pb/acid batteries: The Pb/acid technology fulfils approximately 90-95% of the industrial storage market needs. However the relatively short service life (3 to 5 years), the limited ability to withstand harsh temperature conditions and the different aging behaviour of lead (Pb/acid) batteries (sudden death syndrome) do not match the performance of industrial Ni-Cd batteries. They are therefore widely used as stationary and motive power batteries when reliability expectations are less severe and are usually selected due to price consideration when their performance is deemed sufficient. The ability of the Pb/acid technology to replace industrial Ni-Cd batteries is therefore considered quite limited.

Li-ion batteries: The set of characteristics of Li-ion batteries relative to Ni-Cd batteries are their high energy and power (volumetric and weight) density, as well as superior ability to cycle many thousands of times. These advantages come with a much higher price tag (2 to 3 times that of Ni-Cd) and such batteries need to be driven and monitored with advanced electronics, as they do not have the same intrinsic stability and ability to withstand abuse as industrial Ni-Cd batteries. These batteries have a good fit for cycling applications, especially when weight limitations are important, volumes are high, and the intrinsic price difference of this technology along with the cost of the required battery management system can be justified. They are not a good candidate for industrial floating uses.

***Ni/MH batteries*:** This chemistry has not been able to show clear benefits for the industrial market.

Na-S batteries: Sodium-sulphur batteries have a high energy (but low power) density making them suitable for some grid storage uses (e.g. linked to wind and solar power) as well as some other stationary applications where cycling is needed. This technology is mainly found in Japan where it fulfils a niche of the stationary market. Use in other fields has been explored, but there is very limited potential for this technology. Indeed there are several technical issues to be solved as these batteries operate at high temperatures (requiring bulky insulation) and the corrosive nature of the sodium polysulfide gives rise to limited shelf life. Currently production has been stopped due to fire incidents, pending resolution. Thus, this technology is focusing on grid related stationary uses and holds no potential to replace mission critical power back-up uses.

10.2 Metal coating

Except where the surface characteristics of a coating are critical (e.g. fasteners for aircraft), coatings of zinc or vapor-deposited aluminum can be substituted for cadmium in many plating applications (USGS 2012).

10.2.1 Anti-corrosion metal coating

Technical alternatives to cadmium electroplating have been identified for electroplated cadmium. The following alternatives was identified in a study from US 1994: electroplating (alternative

materials), chromate conversion coating, electroless plating, ion coating, mechanical plating, metallic-ceramic coating, organic coating, surface hardening, and thermal spraying (NDCEE 1994).

Electroplated aluminium has been mentioned as an alternative to cadmium plating. It is an commercially available high purity aluminum plating for corrosion control. The coating can be applied via a wet but non-aqueous process to any conductive substrate, from carbon steel to aluminum beryllium alloys and even graphite. High purity aluminum has high corrosion resistance properties, even as a thin coating. It is also highly ductile, nonembrittling, mitigates galvanic corrosion and can be used in applications up to 1,000 °F. The coating is especially useful in the aerospace industry (Vallejo 2003).

An alternative for the cadmium plating in the aircraft industry has been developed. It is based on a tin-zinc alloy (SIFCO 2012).

10.2.2 Military Electrical Connectors

Alternatives for cadmium in military electrical connectors have been assessed (Mason 2012). According to the abstract are the most promising candidate coating processes to replace cadmium and hexavalent chromium in electrical connector applications are technologies that are already being used on electrical connectors to some extent, or demonstrate both considerable promise for the application and sufficient maturity. These include:

- Electroplated aluminum (AlumiPlate®)
- Electroplated alkaline zinc-nickel (5–15% nickel in the deposit)
- Electroplated tin-zinc (at least 20% zinc in the deposit)

Future efforts will focus on these three most promising candidates. In addition, to support efforts being undertaken by electrical connector manufacturers, two EN-based technologies, both incorporating occluded particles, will also be evaluated. Coatings with both CCCs and TCPs will be considered, as available, and cadmium with CCC will be used as the control. The most promising candidate coating processes from emerging alternatives were also identified. These are technologies that show promise for electrical connector applications, but require further development for the electrical connectors employed by TARDEC. These include:

- Alloys deposited from ionic liquids
- Magnetron sputtered aluminum alloys
- Tin-indium alloys

Future efforts may consider these candidates as the technology matures and becomes more feasible for electrical connectors (Mason 2012).

10.2.3 Brazing alloys (ECHA 2012b)

New specifications for cadmium-free alloys are available on the Internet. ICdA indicates that brazing fillers which do not contain cadmium are now most commonly used in the EU. However,

brazing fillers which contain cadmium are still used in the aerospace and military sectors, and in high-speed trains, where safety and security are said to be the main drivers for non-substitution, with the quantity of cadmium involved being less than 25 tonnes per year in Europe. In relation to the identified use in high-speed trains, ICdA noted that cadmium is used in the realisation of 'aluminium cooling systems' for electrical equipment. However, it seems that this application is more relevant to soldering (<450°C) rather than brazing.

11 RISK-RELATED INFORMATION

An EU risk assessment is available for cadmium metal (ECB, 2007). It was concluded that there was a need for limiting the risks for both workers, consumers and for humans exposed via the environment. Some of these concerns have been addressed in the recent revision of entry 23 in REACH, Annex XVII.

In addition, SCOEL (Scientific Expert Group on Occupational Exposure Limits) has evaluated cadmium (and its inorganic compounds) and suggests an 8-hour time-weighted average (TWA) value of 4 μg/m^3 (respirable fraction). Further, a biological limit value in urine is suggested: 2 μg/g creatinine. It may be noted that a lower value, 1 μg/g creatinine, was used by EFSA as a reference point for their risk evaluation of cadmium in food. The suggested values for the work environment have so far not been included in the list of indicative occupational exposure limit values (the most recent directive on indicative occupational exposure limit values, 2009/161/EU, was published 17 December 2009).

In the SCOEL document, the proposed limit values are based on effects on the kidney and, to some extent, bone tissue, representing the most sensitive targets of Cd toxicity after occupational exposure. The suggested IOEL (in air) is considered to be protective against long-term local effects (respiratory effects including lung cancer).

11.1 Risk estimation in the registration

Risk for workers

According to the lead registration dossier, worker exposure to dust and fumes is controlled by a general application of local exhaust ventilation at the work place and, in specific cases, personal protection measures. Dermal exposure is prevented by the general use of specialized clothing, including specialized working gloves.

In the CSA, the suggested IOEL of 4 μg/m^3 (respirable fraction) has been used as a DNEL. Although the exposure assessments from the EU RAR in many cases are higher than this value it is claimed that the more recent measured data show that exposures, at least in most cases, are below the IOEL. In this comparison measured inhalable concentrations have been divided with a factor of 2, or sometimes 2.5, to compensate for presumed higher values in the inhalable fraction compared to the respirable fraction. Comparisons with the proposed biological limit value are also made in the CSA, showing that most, but not all, tested workers have urinary cadmium concentrations below 2 μg/g creatinine.

According to the registration dossier technical measures are taken to comply with the EU proposed indicative OEL of 4 μg respirable Cd/m^3. If compliance with the IOEL cannot be ensured in a

consistent way, protection of the worker is ensured by complementary risk reduction measures and compliance with biological indicator limit values at the individual level.

11.2 Swedish risk assessment of cadmium (KemI 2011)

In a recent report (KemI Rapport Nr 1/11) from the Swedish Chemicals Agency, health effects of cadmium in Sweden were evaluated. The summary is given below.

Summary

The main source of cadmium exposure is food, mainly food of plant origin, offal and seafood. The gastrointestinal absorption of cadmium is influenced by age, type of diet, and nutritional status, with iron status being particularly important.

Blood cadmium is localized mainly in the red blood cells and is a useful marker of ongoing exposure. Urinary cadmium is a useful biomarker of long-term exposure, as it reflects the concentration in the kidney, where cadmium is accumulating with very long half-life. It is the most frequently used biomarker of cadmium exposure. The measured concentrations need to be adjusted for variation in urine dilution, mainly by creatinine or specific gravity. In particular creatinine adjusted urinary cadmium will vary by age, body size, gender, and meat consumption. An alternative way of adjustment is by specific gravity. A critical review of the database on biomarkers of cadmium exposure provides no evidence for a decrease in cadmium exposure over time during the last 2-3 decades in Sweden.

Long-term cadmium exposure may cause various toxic effects. *The kidney* has generally been considered the critical target organ for cadmium toxicity. Circulating cadmium, after being filtered in the glomerular part of the kidney, is reabsorbed and retained in the proximal tubules causing high intracellular concentrations. A large number of studies, also in the Swedish general population, show significant association between cadmium in urine and/or blood and markers of impaired kidney function, mostly impaired tubular function. Critical review of recent studies, particularly those in Sweden, indicates that the risk of impaired function increases already below 1 μg/g creatinine in urine. In addition, cadmium exposure has been associated with impaired glomerular filtration rate, the risk of which seems to start at 0.7 to 1.0 μg/g creatinine.

There is a debate concerning the causality and the health significance of the associations between urine-based biomarkers of cadmium exposure and kidney effects (mainly tubular effects) that occur at very low cadmium concentrations. Thus, it is difficult to ascertain the exact lowest effect dose for a clear adverse effect. However, several recent mechanistic studies support effects at low exposure.

Because of the uncertainties of lowest effect dose for cadmium in the proximal tubules, the present risk assessment focuses on *bone effects of cadmium*. It is well established since long that excessive exposure to cadmium affects the metabolism of calcium, in severe cases leading to osteomalacia and osteoporosis, in addition to kidney damage (Itai-Itai disease). Data supporting adverse effects of much lower cadmium exposure on the risk of osteoporosis has increased substantially during the last few years. The effect of cadmium on bone seems to be independent of kidney damage, possibly the effects occur even before the kidney damage. Whereas several epidemiological studies have observed an association between cadmium and bone mineral density, only three published studies have so far considered fracture incidence – the most adverse endpoint with respect to effects on bone. Other studies have included markers of bone remodeling to increase the understanding of causal relationships and possible mechanisms involved. It appears that cadmium preferentially affects bone resorption.

Irrespective of whether the studies employed a *decrease in the bone mineral density, increased risk of osteoporosis or increased risk of fractures*, these changes seem to occur at very low urinary cadmium concentrations. Both a recent Swedish study (SMC) and an American study (NHANES) suggest that already a cadmium concentration in urine of around 0.5 μg/g creatinine is associated with increased risk of osteoporosis and fractures. Importantly, the Swedish studies showed increased risk of osteoporosis and fractures among those who never smoked, suggesting that dietary cadmium alone contribute to the risk. Statistically, every other women and one out of four men in Sweden will suffer from an osteoporotic fracture during their lifetime. Considering the high prevalence of osteoporotic fractures in Sweden, compared to central and southern Europe, it cannot be ruled out that the Swedish population might be more sensitive to cadmium exposure. It should be noted that even a small increase in the average exposure will result in a proportionally larger increase in the fraction of the population at risk of fractures.

Cadmium is classified as human carcinogen, mainly based on lung cancer among occupationally exposed people. Mechanistic studies support that cadmium is a carcinogen. The relationship between cadmium exposure and cancer risk has recently also been studied outside the occupational exposure and several studies show increased risks. Experimental studies also suggest that cadmium may have estrogen-like effects. Swedish epidemiological studies have been initiated and associations between estimated dietary exposure and increased risk of hormone-related cancer (endometrial cancer) have been shown. At present it is difficult to draw conclusions about the cancer risk linked to dietary exposure to cadmium, but the data are in support of the need for a precautionary approach. Knowledge on cadmium-related cardiovascular disease and diabetes do not provide sufficient information for risk assessment but also supports a precautionary approach. Two recent well performed prospective studies from Belgium and USA indicate associations between cadmium and *increased mortality* which is alarming. Still, it is difficult to judge whether the results could be affected by residual confounding. Nevertheless, these data clearly add to the concern that cadmium might exert severe effects on human health.

A number of fairly small cross-sectional studies indicate that cadmium exposure may have a negative effect of *fetal growth and child development*. Although available data does not allow quantitative health risk assessment, these effects should be born in mind.

In conclusion, a number of studies, several of which in Sweden, have shown associations between long-term low-level cadmium exposure and adverse health effects mainly in the form of kidney dysfunction, osteoporosis and fractures. Causal relationships are supported by mechanistic experimental studies. Although associations with all those effects are found at very low exposure levels, the main emphasis in this risk assessment has been put on recent data on bone effects of cadmium. Unlike the studies on subclinical kidney effects, the bone effects include several different endpoints, which are not based on urine-based biomarkers. Rather, they include clinical findings, the most severe of which are bone fractures. Thus, the data on bone effects are more suitable for evaluation of health risks at low exposure levels, i.e. levels observed in Sweden today.

Taken together, the recent comprehensive epidemiological studies strongly indicate that the effects of cadmium on bone among Swedish women starts somewhere between 0.5 and 1 μg/g creatinine in urine. A considerable part of the Swedish women have urinary cadmium concentrations in this range. Thus, it is clear that cadmium-related health effects occur at the present exposure levels in Sweden.

It should be noted that these risk levels (0.5-1 µg/g creatinine) are slightly lower than that (1 µg/g creatinine) reported in the recent EFSA risk assessment of cadmium, which was mainly based on dose-response relationship between urinary cadmium and markers of impaired renal tubular function obtained in a meta-analysis of selected, mainly Asian studies. Because of the associations with multiple health effects observed already at the present cadmium exposure in the general population, it is essential not to increase the exposure further. Compared to most other countries, the risk of fractures is very high in Sweden. In the light of this high prevalence of fractures, the population is likely to be extra sensitive to an exposure that further increases the risk. It should be noted that even a small increase in the average exposure will result in a proportionally large increase in the fraction of the population with increased risk of severe effects, such as fractures. Therefore, mitigation efforts are needed to decrease the exposure, the main part of which is through food.

11.3 Risk via food intake (EFSA 2012)

The European Food Safety Authority (EFSA) has recently updated their exposure and risk evaluation of cadmium in a scientific report (EFSA 2012), see abstract below.

ABSTRACT

Cadmium can cause kidney failure and has been statistically associated with an increased risk of cancer. Food is the dominating source of human exposure in the non-smoking population. The Joint FAO/WHO Expert Committee on Food Additives established a provisional tolerable monthly intake of 25 µg/kg body weight, whereas the EFSA Panel on Contaminants in the Food Chain nominated a tolerable weekly intake of 2.5 µg/kg body weight to ensure sufficient protection of all consumers. To better identify major dietary sources, cadmium levels in food on the European market were reviewed and exposure estimated using detailed individual food consumption data. High levels of cadmium were found in algal formulations, cocoa-based products, crustaceans, edible offal, fungi, oilseeds, seaweeds and water mollusks. In an attempt to calculate lifetime cadmium dietary exposure, a middle bound overall weekly average was estimated at 2.04 µg/kg body weight and a potential 95th percentile at 3.66 µg/kg body weight. Individual dietary survey results varied between a weekly minimum lower bound average of 1.15 to a maximum upper bound average of 7.84 µg/kg bodyweight and a minimum lower bound 95th percentile of 2.01 and a maximum upper bound 95th percentile of 12.1 µg/kg body weight reflecting different dietary habits and survey methodologies. Food consumed in larger quantities had the greatest impact on dietary exposure to cadmium. This was true for the broad food categories of grains and grain products (26.9%), vegetables and vegetable products (16.0%) and starchy roots and tubers (13.2%). Looking at the food categories in more detail, potatoes (13.2%), bread and rolls (11.7%), fine bakery wares (5.1%), chocolate products (4.3%), leafy vegetables (3.9%) and water mollusks (3.2%) contributed the most to cadmium dietary exposure across age groups. The current review confirmed that children and adults at the 95th percentile exposure could exceed health-based guidance values.

12 REFERENCES

- Alfvén T, Elinder CG, Hellström L, Lagarde F, Järup L. Cadmium exposure and distal forearm fractures. (2004) J. Bone Miner. Res. **19(6)**, 900-905.
- BGS (2012). European Mineral Statistics 2006-2010. British Geological Survey. www.bgs.ac.uk/downloads/start.cfm?id=1389.
- Chen X, Zhu G, Jin T, Åkesson A, Bergdahl IA, Lei L, Weng S, Liang Y. (2009) Changes in bone mineral density 10 years after marked reduction of cadmium exposure in a Chinese population. Environ. Res. **109**, 874-879.
- ECB (2007) European Union Risk Assessment Report: Cadmium oxide and cadmium metal. Part I –Environment. 3rd Priority List, Volume 72, EUR 22919 EN, European Chemicals Bureau. European Union Risk Assessment Report: Cadmium metal. Part II – human health. 3rd Priority List, Volume 74, EUR 22767 EN, European Chemicals Bureau.
- ECHA (2012). Cadmium uses extract from the ECHA database for registered substances (December 2012). http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ea7def6-ce71-0a3c-e044-00144f67d031/AGGR-dc6f98c8-cfef-44d8-820a-11e81d37fd80_DISS-9ea7def6-ce71-0a3c-e044-00144f67d031.html#section_3_5 .
- ECHA (2012b). The use of brazing fillers containing cadmium for safety reasons, derogation in paragraph 9 of entry 23 of Annex XVII. ECHA report, 9 November 2012.
- EFSA (2012) European Food Safety Authority. Cadmium dietary exposure in the European population. EFSA Journal 10(1), 2551.
- Engström A, Michaëlsson K, Suwazono Y, Wolk A Vahter M, Åkesson A. Long-term cadmium exposure and the association with bone mineral density and fractures in a population-based study among women. (2011) J Bone Miner. Res., **26(3)**, 486-495
- Engström A, Michaëlsson K, Vahter M, Julin B, Wolk A, Åkesson A. Associations between dietary cadmium exposure and bone mineral density and risk of osteoporosis and fractures among women. (2012) Bone, **50(6)**:1372-8.
- Ferraro PM, Costanzi S, Naticchia A, Sturniolo A, Gambaro G. Low level exposure to cadmium increases the risk of chronic kidney disease: analysis of the NHANES 1999-2006. (2010) BMC Public Health.**10**:304.
- Hellström L, Elinder CG, Dahlberg B, Lundberg M, Järup L, Persson B, Axelson O. Cadmium exposure and end-stage renal disease. (2001) Am. J. Kidney Dis. **38(5)**, 1001-8.
- IARC (2012). Cadmium and cadmium compounds. In Monographs, Vol 100C, A review of Human carcinogens, pp 121-145. http://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C-8.pdf
- ICdA (2012): The International Cadmium Association's website. http://www.reach-cadmium.eu/pg_n.php?id_menu=3 ; http://www.cadmium.org .
- ICdA (2012b) The release of cadmium to the environment due to corrosion from anthropogenic Sources, by Hugh Morrow, International Cadmium Association. http://www.chem.unep.ch/pb_and_cd/SR/Files/Submission%20NGO/ICdA/Cadmium%20Corrosion%20Paper_and_presentation2003.pdf
- KemI (2011) Kadmiumhalten måste minska–för folkhälsans skull. Rapport Nr 1/11. Bilaga 3. Health effects of cadmium in Sweden. http://www.kemi.se/Documents/Publikationer/Trycksaker/Rapporter/KemI_Rapport_1_11.pdf
- KemI (2012) Samhällsekonomisk kostnad för frakturer orsakade av kadmiumintag via maten. PM12/12 http://www.kemi.se/Documents/Publikationer/Trycksaker/PM/PM_12_12_kadmium.pdf

- Kido T, Honda R, Tsuritani I, Yamaya H, Ishizaki M, Yamada Y, Nogawa K. (1988) Progress of renal dysfunction in inhabitants environmentally exposed to cadmium. Arch. Environ. Health **43(3),** 213-217.
- Kirk-Othmer (2004). The Encyclopedia of Chemicals Technology, 5th Ed.
- Klimasauskas E. (2005). Cadmium, in Geotimes Mineral of the Month, August 2005.
- Lig R. and Held M. (2009). Cadmium flows in Europe. Online publication December 8, 2009. Revue de Métallurgie, 106 , pp 559-565 doi:10.1051/metal/2009089
- Mason R. et.al. (2012). Update on Alternatives for Cadmium Coatings on Military Electrical Connectors. In Metal finishing 2012. Concurrent Technologies Corporation (CTC). Metal Finishing DOI:10.1016/S0026-0576(10)00012-7. http://www.researchgate.net/publication/223008881_Update_on_alternatives_for_cadmium_coatings_on_military_electrical_connectors
- NDCEE (1994). Technical Alternatives to Cadmium Electroplating. National Defense Center for Environmental Excellence (NDCEE). http://infohouse.p2ric.org/ref/02/01264.pdf
- Panula J, Pihlajamäki H, Mattila VM, Jaatinen P, Vahlberg T, Aarnio P, Kivilä S-L. (2011) Mortality and cause of death in hip fracture patients aged 65 or older – a population-based study. BMC Musculoskeletal Disorders **12**:105
  PHIME (2011) Public health impact of long-term, low-level mixed element exposure in susceptible population strata Project no. FOOD-CT-2006-016253. Final report, August 2011. http://www.med.lu.se/labmedlund/amm/forskning/haelsorisker_av_metaller/phime
- Püringer J. (2011) Derived Minimal Effect Levels (DMELs): Shortcomings one year after the REACH registration deadline. (http://www.auva.at/mediaDB/884917_DMELs_Shortcomings_one_year_after.pdf)
- SCOEL/SUM/136, February 2009, For public consultation. Recommendation from the Scientific Expert group on Occupational Exposure Limits for Cd and its organic compounds.
- SIFCO (2012). Brush Plating of Tin-Zinc Alloy as an Alternative to Cadmium. Metal Finishing magazine. 03 April 2012. http://www.metalfinishing.com/download/771.
- Thomas LDK, Michaelsson K, Julin B, Wolk A, Åkesson A. (2011) Dietary cadmium exposure and fracture incidence among men: A population-based prospective cohort study. J. Bone Mineral Res. **26(7)**, 1601-1608.
- USGS (2012). Cadmium. Mineral Commodity Summaries 2012. U.S. Geological Survey. http://minerals.usgs.gov/minerals/pubs/mcs/2012/mcs2012.pdf
- Vallejo G. R. (2003). Electroplated Aluminum for Corrosion Control. Tri-Service Corrosion Conference Nov. 2003. 55 p. AMPLB/AM025636. Abstract: http://ammtiac.alionscience.com/ammt/iacdocs.do?AM025636

13 ANNEX 1. ADDITIONAL INFORMATION ON HAZARD AND RISK

In 2011, the Swedish Chemicals Agency published a report (KemI 2011) containing a human health risk assessment of cadmium from a Swedish exposure perspective (Annex 3 in KemI 2011; Authors: A Åkesson & M Vahter, Karolinska Institutet, Sweden). The summaries on different toxicity endpoints given below are primarily from this report.

13.1 Developmental toxicity

Neurotoxicity and child development

The risk assessments of Cd and CdO performed according to the Existing Substances legislation (ESR) concluded that "information is needed to better document the possible neurotoxic effects of Cd suggested in experimental animals, especially on the developing brain. The collection of this additional information should, however, not delay the implementation of appropriate control measures needed to address the concerns expressed for several other health effects including repeated dose toxicity and carcinogenicity." (ECB 2007).

A few small cross-sectional epidemiological studies indicate an adverse effect of cadmium exposure on child development, supported by experimental studies showing cadmium-induced neurotoxicity. Although available data does not allow quantitative health risk assessment, these effects should be kept in mind (KemI 2011).

A recent investigation in U.S. children, using NHANES data on approximately 2 200 individuals, suggests that low-level environmental cadmium exposure in children may be associated with adverse neurodevelopmental outcomes (Ciesielski *et al*, 2012). Median urinary cadmium (μg/L) ranged from 0.078 (age 6-7 yrs) to 0.146 (age 14-15 yrs). When comparing children in the highest quartile of urinary cadmium with those in the lowest quartile, adjusted odds ratios were 3.21 (95% CI: 1.43-7.17) for learning disabilities, 3.00 (95% CI: 1.12-8.01) for special education and 0.67 (95% CI: 0.28-1.61) for attention deficit hyperactivity disorder (ADHD). The urinary cadmium levels in U.S. children are probably similar to what can be expected within EU. For example, the median urinary level in young (age 20-29 yrs) non-smoking women in Sweden is approximately 0.1-0.2 μg/g creatinine, corresponding roughly to 0.1-0.2 μg/L. For urinary cadmium levels in Sweden, see the following link:
http://www.imm.ki.se/Datavard/Tidsserier/Cadmium%20in%20urine.htm.

A study on early-life low-level cadmium exposure in rural Bangladesh also indicates effects on child development, showing lower child intelligence, particularly in girls (Kippler et al 2012).

13.2 Endocrine effects

The significance of the estrogen-mimicking effects such as the well-characterized estrogenic responses of the endometrial lining (hypertrophy and hyperplasia) observed in animals exposed to environmentally relevant doses of cadmium, was further explored in humans. In a large population-based prospective cohort among Swedish postmenopausal women (n = 32 210) the association between dietary cadmium intake and endometrial cancer incidence, the cancer form most suited to explore potential estrogenic effects, was assessed. This is the first study exploring health effects in relation to the dietary cadmium intake, which is in contrast to smaller studies where cadmium has

been monitored in urine. Thus, based on the construction of a food-cadmium database in the cohort, a large study population was utilized and the incidence was assessed prospectively. This design reduces the selection bias that often occurs in case-control studies, but is on the other hand, dependent on the assumption that estimated dietary cadmium intake is a valid reflection of the internal dose. The average estimated cadmium intake was 15 µg/day (1.5 µg/kg bw per week). During 16 years of follow-up, 378 cases of endometroid adenocarcinoma were ascertained through computerized linkage to the Swedish Cancer Registry with virtually no loss to follow-up. The highest versus lowest percentile of cadmium intake was associated with risk of endometrial cancer, RR 1.39 (95 % confidence interval, CI, 1.04-1.85; P for trend 0.02). To reduce the influence of endogenous estrogen exposure, analyses were stratified by body mass index and by use of postmenopausal hormone use. Analyses were also stratified by smoking status because an anti-estrogenic effect of cigarette smoking is shown on circulating estrogen concentrations due to increased metabolic clearance, a reduction in relative body weight, and an earlier age at menopause. Among never-smoking, non-overweight women the RR was 1.86 (95 % CI 1.13-3.08; P for trend 0.009). A 2.9-fold increased risk (95 % CI 1.05-7.79) was observed with long-term cadmium intake consistently above the median intake in both 1987 and in 1997 in never-smoking women with low available estrogen (non-overweight and non-users of postmenopausal hormones). Although the data support the hypothesis that cadmium may exert estrogenic effects and possibly increase the risk of hormone-related cancers this needs to be confirmed by other studies. In a collaboration project between toxicologists and epidemiologists the possible mechanism of such estrogenic effect was investigated. In a rodent uterotrophic bioassay to transgenic (estrogen-receptor element) ERE-luciferase reporter mice, the animals were exposed to cadmium chloride subcutaneously for four days before puberty. Cadmium was unable to induce uterotrophic response *in vivo* and was unable to induce estrogenic responses via classical estrogen-receptor-signaling through ERE-driven genes. However, luminal epithelium height of the endometrium was significantly increased in a dose dependent manner after cadmium chloride (and estradiol treatment). It was concluded that cadmium can induce estrogen-like responses maybe via non-classical estrogen receptor- signaling pathway and that cadmium may promote tumor development in the uterus. In the same study population as for the study on endometrial cancer incidence (Swedish Mammography Cohort; a population-based prospective cohort), the association between dietary cadmium exposure and risk of overall and estrogen receptor defined (ER+ or ER-) post-menopausal breast cancer was assessed. In 55 987 postmenopausal women who completed a food frequency questionnaire at baseline in 1987 a total of 2112 incident cases of invasive breast cancer were ascertained (1626 ER+ and 290 ER-) during an average follow-up of 12.2 years. It was found that dietary cadmium was positively associated with overall breast cancer tumors. The risk ratio when comparing the highest tertile with the lowest was 1.21 (95% CI 1.07-1.36) (Julin et al 2012). These results are in line with the results of the endometrial cancer study (KemI 2011).

The mechanism of the estrogen-like effects of cadmium has been investigated in transgenic estrogen reporter mice and it was concluded that cadmium acts via a different mechanism from that of steroidal estrogens. Cadmium (chloride) significantly affected kinase phosphorylation and endogenous gene expression at low exposure levels; the lowest effect seen at 0.5 µg /kg bw (Ali et al 2012).

13.3 Overall mortality

Two recent studies from Belgium and USA indicate associations between cadmium and increased mortality which is alarming. Both studies are of high quality (prospective) and the Belgian study has even included repeated measurements of exposure. Still, it is difficult to judge whether the results could be due to confounding. For instance, low urinary creatinine excretion is associated with all-cause mortality and cardiovascular disease. Thus, adjusting a urine-based exposure marker by creatinine may result in falsely high associations between exposure and disease or mortality. Noteworthy, is that the Belgian study employed urinary cadmium per 24 hours and blood cadmium. Nevertheless, these data clearly add to the concern that cadmium might exert severe effects on human health (KemI 2011).

13.4 References

- Ali I, Damdimopoulou P, Stenius U, Adamsson A, Mäkelä SI, Åkesson A, Berglund M, Håkanson H, Halldin K. (2012) Cadmium-induced effects on cellular signaling pathways in the liver of transgenic estrogen reporter mice. Toxicol. Sci. **127(1)**, 66-75.
- Ciesielski T, Weuve J, Bellinger DC, Schwarz J, Lanphear B, Wright RO. (2012) Cadmium exposure and neurodevelopmental outcomes in U.S. children. Environ. Health Perspect. **120**, 758-763.
- ECB (2007) European Union Risk Assessment Report: Cadmium oxide and cadmium metal. Part I –Environment. 3rd Priority List, Volume 72, EUR 22919 EN, European Chemicals Bureau. European Union Risk Assessment Report: Cadmium metal. Part II – human health. 3rd Priority List, Volume 74, EUR 22767 EN, European Chemicals Bureau.
- Julin B, Wolk A, Bergkvist L, Bottai M, Åkesson A. Dietary cadmium exposure and risk of postmenopausal breast cancer: A population-based prospective cohort study. (2012) Cancer Res. **72**, 1459-1466.
- KemI (2011) Kadmiumhalten måste minska–för folkhälsans skull. Rapport Nr 1/11. Bilaga 3. Health effects of cadmium in Sweden. http://www.kemi.se/Documents/Publikationer/Trycksaker/Rapporter/KemI_Rapport_1_11.pdf
- Kippler M, Tofail F, Hamadani JD, Gardner RM, Grantham-McGregor SM, Bottai M, Vahter M. (2012) Early-life cadmium exposure and child development in 5-year-old girls and boys: A cohort study in rural Bangladesh. Environ. Health Perspect., **120(10)** 1462-1468.