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 sulphide

EC Number(s): 215-147-8

CAS Number(s): 1306-23-6

Submitted by: Swedish Competent Authority (Swedish Chemicals Agency)

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ABBREVIATIONS

ABS	Acrylonitrile-butadiene-styrene
AC	Article Category (use descriptor according to REACH)
BIPV	Building Integrated PhotoVoltaic applications
Cd-Ni battery	Cadmium-Nickel battery
CdSe	Cadmium selenide
CdTe	Cadmium telluride
CSA	Chemical Safety Assessment
CI	Confidence Interval
CI	Colour Index (in chemical name)
DSSC	Dye-sensitized solar cell
ERC	Environmental Release Category (use descriptor according to REACH)
ESR	Existing Substances Regulation
HDPE	High-density polyethylene
ICdA	International Cadmium Association
IOEL	Indicative Occupational Exposure Limit
LDPE	Low-density polyethylene
$\beta 2M$	$\beta 2$-microglobulin
NHANES	National Health and Nutrition Examination Survey
Ni-Cd	Nickel-Cadmium
PC	Product Category (use descriptor according to REACH)
PC	Polycarbonate
POM	Polyoxymethylene (Acetal)
PMMA	Poly(methyl methacrylate)
PPO	Polyphenylene oxide
PROC	Process Category (use descriptor according to REACH)
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl chloride
RAR	Risk Assessment Report
RBP	Retinol-Binding Protein
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

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- 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[1], which corresponds to classification as carcinogen category 2[2].

- 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 sulphide is listed as Index number 048-010-00-4 in Regulation (EC) No 1272/2008[3] 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).

Therefore, this classification of cadmium sulphide 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.

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[1] Classification in accordance with Regulation (EC) No 1272/2008 Annex VI, part 3, Table 3.1 List of harmonised classification and labelling of hazardous substances, OJ L 353, p.1, 31.12.2008

[2] Classification in accordance with Regulation (EC) No 1272/2008, Annex VI, part 3, Table 3.2 List of harmonised classification and labelling of hazardous substances (from Annex I to Council Directive 67/548/EEC), OJ L 353, p.1, 31.12.2008.

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

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 sulphide has the ability to cause a large number of toxic effects as is evident from the harmonized classification. It is thus clear that cadmium sulphide may cause many different serious health effects in addition to the ability to cause cancer. Adverse effects on multiple organs after repeated exposure, 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.

Since the toxic effect of all cadmium compounds are caused by the cadmium ion, the conclusions for "cadmium" are relevant for cadmium sulphide.

A significant part of the European population is today exposed to levels of cadmium (originating from cadmium metal and cadmium compounds) 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 on Cd and CdO (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 (KemI 2011). 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 16 000 articles published during the last 10 years and 9200 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 assessment from EFSA (2009, 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 recent report published by the Swedish Chemicals Agency, the Swedish annual societal economic cost of fractures caused by cadmium in food amounts to approximately 4.2 billion SEK (approx. 450 million Euros) (KemI 2013a). 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 a lower quality of life and shortened life expectancy for those who suffer fractures, mostly the elderly.

In conclusion

Cadmium sulphide 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:	215-147-8
EC name:	Cadmium sulphide
CAS number (in the EC inventory):	1306-23-6
CAS number:	Deleted CAS No. 106496-20-2; 1441148-55-5
CAS name:	Cadmium sulfide (CdS)
IUPAC name:	Cadmium sulphide
Index number in Annex VI of the CLP Regulation	048-010-00-4
Molecular formula:	CdS
Molecular weight range:	144.48
Synonyms:	Cadmium sulfide; C. P. Golden Yellow 55; Cadmium Golden 366; Cadmium Lemon Yellow 527; Cadmium Primrose 819; Cadmium Yellow 000; Cadmium Yellow 10G conc; Cadmium Yellow 892; Cadmium Yellow Conc. Deep; Cadmium Yellow Conc. Golden; Cadmium Yellow Conc. Lemon; Cadmium Yellow Conc. Primrose; Cadmium Yellow OZ dark; Cadmium Yellow Primrose 47-4100; Cadmium Yellow ST; Cadmium monosulfide; Cadmium sulfide yellow; Cadmium yellow; Cadmopur Golden Yellow N; Cadmopur Yellow; Capsebon; Ferro Lemon Yellow; Ferro Orange Yellow; Ferro Yellow; GSK; PC 108; Primrose 1466; Reckitt Yellow 12; Sicotherm Yellow L 1001
Structural formula	$Cd^{2+} S^{2-}$ Can form two crystal forms: Hexagonal (alpha-CdS) and Cubic (beta-CdS). The most widely used crystal compositions are a mixture of the two forms ("dimorphic"). Beta-CdS can be transformed into alpha-CdS by heating (750 °C, Kirk-Othmer 2004). cadmium sulphide also occurs in amorphous form (Eastaugh 2008).

1.2   Composition of the substance

Name: cadmium sulphide

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

1.3 Physico-chemical properties

Table 2: Overview of physicochemical properties *(data from dissemination database according to REACH, Article 119)*[4]

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	Solid Powder Colour: Orange ochre Odour: odourless	From registration[5]
Relative density	The density of the substance is 4.81 g/cm^3 at 22 °C.	From registration[5]
Granulometry	The D50 of the powder is 367 µm, the D80 is 607 µm.	From registration[5]
Water solubility	Experimental (pH range of 5.4 - 6.3): 12 000 µg Cd/L at 20 °C Calculated (HSC 7.0 software): 0.0006 µg Cd/L at 20 °C The calculated solubility of Cd^{2+} is much lower than the experimental solubility. The calculated solubility for cadmium sulphide is in good agreement with the literature value. The higher cadmium solubility shown in the experimental study was probably caused by the presence of $CdSO_4$ (an oxidation product of cadmium sulphide). As a conclusion: The solubility is strongly dependent on the purity of the substances used, and also on the oxidation rate of cadmium sulphide during different life-cycle stages.	From registration[5] Value used for CSA: 0.0006 µg/L

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

2   HARMONISED CLASSIFICATION AND LABELLING

Cadmium sulphide is listed as Index number 048-010-00-4 in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, as follows:

Table 3: Harmonised classification of cadmium sulphide according to Annex VI, 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)**
048-010-00-4	Cadmium sulphide	215-147-8	1306-23-6	Carc. 1B Muta. 2 Repr. 2 STOT RE 1 Acute Tox. 4* Aquatic Chronic 4	H350 H341 H361fd H372** H302 H413	GHS08 GHS07 Dgr	H350 H341 H361fd H372** H302 H413
Specific Concentration Limits and M Factors							
Concentration				**Classification**			
' C ≥ 10 % 0.1 % ≤ C < 10 %				- STOT RE1; H372 STOT RE2; H373			

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

H350:   May cause cancer
H341:   Suspected of causing genetic defects
H361fd: Suspected of damaging fertility. Suspected of damaging the unborn child
H372:   Causes damage to organs through prolonged or repeated exposure
H302:   Harmful if swallowed
H413:   May cause long lasting harmful effects to aquatic life
H373:   May cause damage to organs through prolonged or repeated exposure

Table 4: Harmonised classification of cadmium sulphide according to 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
048-010-00-4	Cadmium sulphide	215-147-8	1306-23-6	Carc. Cat. 2; R45 Muta. Cat. 3; R68 Repr. Cat. 3; R62 Repr. Cat. 3; R63 T; R48/23/25 Xn; R22 R53	R45 R68 R62 R63 R48/23/25 R22 R53	S45 S53 S61	T
Concentration Limits							
Concentration				**Classification**			
$C \geq 10\ \%$ $C \geq 10\ \%$ $0.1\ \% \leq C < 10\ \%$				Xn; R22 T; R48/23/25 Xn; R48/20/22			

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
R48/23/25:   Toxic: danger of serious damage to health by prolonged exposure through inhalation or if swallowed
R22:   Harmful if swallowed
R53:   May cause long-term adverse effects in the aquatic environment
R48/20/22:   Harmful: danger of serious damage to health by prolonged exposure through inhalation or if swallowed

3 ENVIRONMENTAL FATE PROPERTIES

3.1 Anthropogenic and natural sources of cadmium exposure

Cadmium is a **natural** element, which is present in all environmental compartments. 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 therefore occurs via emission from mining activities, metal industries (the smelting of other metals), the combustion of fossil fuels, the incineration of waste materials or inappropriate waste disposal, landfill leakage and fertilizing with cadmium-rich phosphate and sewage sludge. These anthropogenic activities have contributed to the contamination by cadmium of the food chain.

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 2012). The overall cadmium anthropogenic exposure is then in the range of 50 to 90 %.

3.2 Fate in the environment

Cadmium sulphide is thermodynamically unstable under aerobic conditions and will therefore slowly transform to more oxidized forms e.g. sulphate, hydroxide and oxide. Moisture triggers the deterioration (see section 9.3.2). The transformation products are more water soluble which means that cadmium will occur as cadmium ions (Cd^{+2}). In the environment the cadmium ion interacts 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 **sediment**, cadmium binds to the sulphide fraction to form the less soluble cadmium sulphide. 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.

3.3 Bioavailability

Cadmium sulphide has a very low solubility, compared to i.e. the oxide form. The potential for releasing cadmium ions is therefore also very low, which decreases the **bioavailability** potential.

Distinction can therefore be made between cadmium compounds, as a function of their solubility. However, cadmium sulphide will sooner or later be transformed into more soluble forms due to chemical/physical transformation processes (i.e. to cadmium oxide or sulphate). Important triggering factors are increased humidity, change of the redox potential and/or elevated temperature (waste incineration, wildfire). Cadmium sulphide in the waste water will, via sludge application, end up in agricultural soil. In the soil cadmium sulphide will be transformed into more water soluble forms (KemI 2013b).

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. 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 (KemI 2011).

The low bioavailability of cadmium sulphide, compared to i.e. cadmium oxide, is mainly relevant for occupational and possible consumer exposure to cadmium sulphide. However, the more bioavailable transformation products of cadmium sulphide are relevant for human exposure to cadmium via environmentally contaminated food (Cd^{2+} released from eg. oxide/hydroxide/sulphate).

3.4 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. The current TWI is 2.5 μg/kg bw (EFSA 2009, 2012).

3.5 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 9.6 in Part II of this report.

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

	Age (years)	Urinary cadmium µg/g creatinine		% >0.5µg/g	%>1.0 µg/g
		Median and (range)			
		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 to the differences observed.

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. Since the toxic effect of all cadmium compounds are caused by the cadmium ion, the conclusions for "cadmium" are relevant for cadmium sulphide.

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.

After absorption, cadmium is transported in the blood to the liver where cadmium induces metallothionein and forms a complex with this protein. The cadmium–metallothionein complex is released from the liver and transported in the blood to the kidneys. Metallothionein is inducible in different tissues (e.g. liver, kidney, intestine, and lung) by exposure to various agents including cadmium. In the kidneys, 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).

It should be noted that associations between low-molecular-weight proteins and cadmium in urine at very low environmental exposure levels should be interpreted with caution, given the unspecific nature of the tubular reabsorption of proteins. The close relationships between low-molecular-weight proteins and cadmium in urine might simply reflect the inter-individual variations in the tubular reabsorption capacity of proteins. There is however evidence of low-level cadmium exposure causing toxic bone effects, with decrease of bone mineral density, increase of osteoporosis and fractures (PHIME 2011).

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; $\sim$ 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 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 the SVHC identification of the substance in accordance with Articles 57 (a) and 57 (f).

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 CMR assessment

Cadmium sulphide is listed as Index number 048-010-00-4 in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labeling 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 labeling 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 sulphide 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 sulphide 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 (originating from cadmium metal and cadmium compounds) 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 on Cd and CdO (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 16 000 articles published during the last 10 years and 9200 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 assessment from EFSA (2009, 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 recent report published by the Swedish Chemicals Agency, the Swedish annual societal economic cost of fractures caused by cadmium in food amounts to approximately 4.2 billion SEK (approx. 450 million Euros) (KemI 2013a). 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 a lower quality of life and shortened life expectancy for those who suffer fractures, mostly the elderly.

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:

- Cadmium sulphide occurs in many different technical qualities/mixtures on the market[5]. It may be difficult to get access to information to identify if the substance still contains "cadmium sulphide" (according to the substances identifications rules in REACH).

- High colouring qualities and rather unique temperature stability make cadmium sulphide useful as **pigment** (e.g. glass and plastic). Its semiconducting property together with chemical/physical properties makes cadmium sulphide useful for **photoelectronic** applications (e.g. solar cells).

- A majority of the EU consumption of cadmium pigments are estimated to origin from **imported articles** (due to strong restrictions of the article production within EU).

- **Occupational exposure** of cadmium sulphide occurs during several industrial and professional use scenarios, such as base metal productions, manufacturing of fabricated electronic products, manufacturing of plastic products and paints.

- Cadmium sulphide occurs mainly at low concentrations in long life articles which are widely distributed in the society. This makes the **waste recovery difficult**.

- Residues of cadmium sulphide, mainly from pigment uses, end up in the waste streams such as solid waste and waste water sludge. **Waste management probably increase the bioavailability** of cadmium in cadmium sulphide, and causes uncontrolled releases to the environment (air and soil).

- 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 in agricultural soil are both natural and anthropogenic. Anthropogenic cadmium sulphide transforms into cadmium ions and contributes to the general cadmium exposure of humans.

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[5] Technical modifications of the crystal forms/composition of the original cadmium sulphide ("doped", "solid solution", "co-precipitation", "encapsultation").

- Shifts in the **solar cells** technology may increase the need for cadmium sulphide considerably. The waste management of solar cells may then be a potential release source in the future.

7 MANUFACTURE, IMPORT AND EXPORT

7.1 Manufacturing of cadmium sulphide

Two principle synthesis methods are described for production of cadmium sulphide, the "dry" method and the "wet" method:

- The dry method originally involved heating metallic cadmium, cadmium oxide or cadmium carbonate with sulphur in the absence of air at a temperature around 300-500 °C. The basic operating parameters for this process – time, temperature, purity, proportion of reactants and oxygen availability – will affect the results, so that the product is quite variable. A wet-grinding stage followed this, which modified the particle morphology and, hence, the final quality (e.g. colour).

- In the wet method, cadmium sulphide is formed from soluble cadmium salts and a soluble sulphide. The cadmium compound is normally the chloride, nitrate, sulphate or iodide. The soluble sulphur comes from hydrogen sulphide, barium or sodium sulphide, or a thiosulphate. As with the dry process, reaction conditions are crucial for the quality (e.g. the colour and permanence of the resulting pigment). The pH conditions also affect the results, with slightly acidic solutions sometimes being used (Eastaugh et.al. 2008).

The production for **pigment** uses is structured around a generic process which consists of dissolution of cadmium metal or cadmium oxide in acid, sulphide precipitation at about 90°C to form cubic cadmium sulphide, filtration and washing, drying, calcination at about 600°C, acid washing for removal of soluble cadmium, filtration and washing, drying, blending and grinding. The process is complicated and cost intensive, especially during the calcination (roasting) stage. The calcination converts the crystal form to the hexagonal form. Without proper control, the transformation of cubic cadmium sulphide to hexagonal cadmium sulphide would not be complete and some of the cadmium sulphide could be oxidized (Lussiez 1989). The last step is milling to a powder. When *cadmium sulphide selenides* are required CdSe is added to cadmium sulphide and the cadmium during the calcination step (Smith 2002).

It is mentioned in the literature that cadmium residues in metal scrap can be recovered by treating it with an ammonium carbonate solution and a sulphide. Cadmium will then be transformed to cadmium sulphide, and that can be precipitated (Kronberg 1995). However, it is unknown whether this technique is in use.

7.2 Quantities manufactured, imported and exported

7.2.1 General

The annual world production of cadmium during 1990 to 2012 increased from 18 000 to 23 000 tonnes (Kirk-Othmer 2004, USGS 2013). Cadmium consumption remained flat in 2012 when compared with that of 2011 creating a surplus of metal on the market (USGS 2013). 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. The production of recycled cadmium (*secondary cadmium*) takes place mainly at Ni-Cd battery recycling facilities (USGS 2012). The supply of cadmium and its compounds is not solely driven by their demand as they are derived as by-products of the mining and refining of zinc and lead.

European countries[6] contributed to 8.6 % of world production of cadmium in 2011 (Figure 1;Table 5). The Netherlands was the largest European producer accounting for 31 % of the EU production, followed by Poland (29 %), Bulgaria (24 %) and Norway (17 %) (BGS 2013). The European production level shows an increase during 2006 to 2011. This production level is within the "total tonnage band" registered to ECHA (see above).

The historical growth in production volumes of cadmium 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 % origins from Ni-Cd-batteries. This trend is expected to increase in the future (Kirk-Othmer 2004).

Japan is the largest producer of raw material for Ni-Cd-batteries in the world (Kirl-Othmer 2004).

Table 5: The European primary production of cadmium in tonnes (EU35) 2006 to 2011 (BGS 2013)

Country	2006	2007	2008	2009	2010	2011
The Netherlands	524	495	530	490	560	560
Poland	373	421	603	534	451	526
Bulgaria	320	318	376	413	389	430
Norway	125	269	178	249	300	309
France	90	50	-	-	-	-
Total	**1432**	**1553**	**1687**	**1686**	**1700**	**1825**

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[6] 35 European countries: 27 EU countries (1 Febr. 2008) + the EU associates Norway and Switzerland, and the EU candidates Croatia, Iceland, Macedonia, Montenegro, Serbia and Turkey.
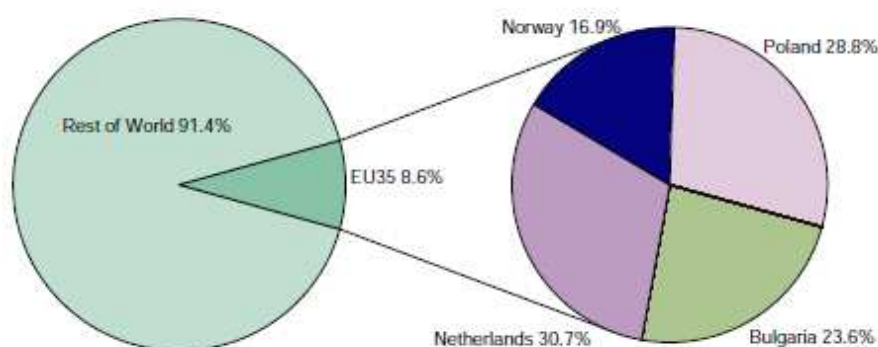
Figure 1: Production of cadmium in Europe 2011 (BGS 2013)

The cadmium metal trade in EU 2011 was dominated by Belgium and Italy (high export) (see Table 6).

Table 6: European import and export of cadmium (incl. CdO) in tonnes (based on statistics from 2007 to 2011 (BGS 2013)

EU country	EXPORT					IMPORT				
	2007	2008	2009	2010	2011	2007	2008	2009	2010	2011
Italy	796	1633	2030	3104	1722	40	49	443	3	44
France	815	890	1022	763	549	1546	1620	985	228	106
Norway	544	816	305	606	617	0	0	0	0	0
Germany	…	287	276	523	348	492	497	468	583	468
Poland	368	558	590	484	579	0	0	0	0	0
Bulgaria	434	374	569	474	421	0	0	0	0	0
Belgium	5573	4536	3982	4059	3814	5040	5520	3464	6494	6027
Netherlands	544	816	305	606	617	437	186	50	102	1
Sweden	282	398	267	315	376	513	924	625	919	1278
United Kingdom	76	54	25	2545	1441	659	550	404	740	788
Czech Republic	0	0	0	0	0	296	405	323	406	426
Spain	0	0	0	0	0	0	21	118	153	38
Greece	0	0	0	0	0	1	18	39	1	0
Total	**9432**	**10362**	**9371**	**13479**	**10484**	**9024**	**9790**	**6919**	**9629**	**9176**

The total international cadmium **consumption** is dominated by the production of Ni-Cd batteries (USGS 2012). Other relevant uses are as pigments and anti-corrosion coatings of metals. The 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 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).

7.2.2 As cadmium sulphide (CdS) – world wide

About 2000 tons of cadmium sulphide is produced annually in the world (Schulte-Schrepping et.al. 2007). A worldwide search the Internet for cadmium sulphide revealed 73-84 suppliers (Chemical Book 2013, ChemExpr 2013). China dominates with 49 suppliers[7]. According to ICdA, there are two manufacturers of **cadmium pigments** in the EU and they have pre-registered three of pigments in the tonnage band 100-1000 t/y.

Although cadmium sulphide does occur naturally no commercially viable deposit of cadmium sulphide exists.

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

Cadmium sulphide can be used as pigments. Cadmium pigments are characterized by their particular brilliant shades, high hiding power, good intensities of colour, good temperature stability (up to 1400 °C) and absolute migration resistance. Their rather unique temperature stability (compared to organic pigments) made them useful for colouring glass (see 8.3.2.2) and plastic articles and synthetic fibers (see 8.3.2.1).

The photoelectric property of cadmium sulphide makes it useful in different electric devises. One potential use under development is in a new type of solar cell technology (so-called *thin-film* solar photovoltaic material (PV)). Because it uses very little or no silicon at all, *thin-film* solar technology reduce the cost of solar modules. Furthermore, because thin-film solar PV materials can be applied to surfaces made of glass, plastic and flexible metal foils, this emerging technology can open up new range of applications that otherwise would not be possible using traditional solar cells (see 8.3.1).

8   USES

8.1   General

The sources for cadmium are both mining and recycled products. Cadmium is transformed into plates, powder and different alloys. Cadmium powder is used as a raw material for production of battery electrodes, metal coatings, alloys and other cadmium substances, such as cadmium sulphide (see Figure 3).

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[7] Note that some suppliers supply substances with different purity grades; received multiple hits.

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.

Ni-Cd batteries (Cd, CdO) are the dominating end products in the world consumption of cadmium, followed by the minor uses: **pigments (CdS) >** metal coatings (Cd) > **stabilizers (CdS) >** alloys and **solar cells (CdS)** (Figure 2). The percentage of cadmium consumed globally for Ni-Cd battery production has been increasing, while the percentages for the other traditional end uses of cadmium - specifically coatings, pigments, and stabilizers – have gradually decreased owing to environmental and health concerns (USGS 2013).

While the main use for cadmium sulphide is as pigment, it is reasonable to expect that the solar cell market will begin to consume more cadmium sulphide in the future, as the technology becomes more widely accepted and more affordable (AZom.com 2013).
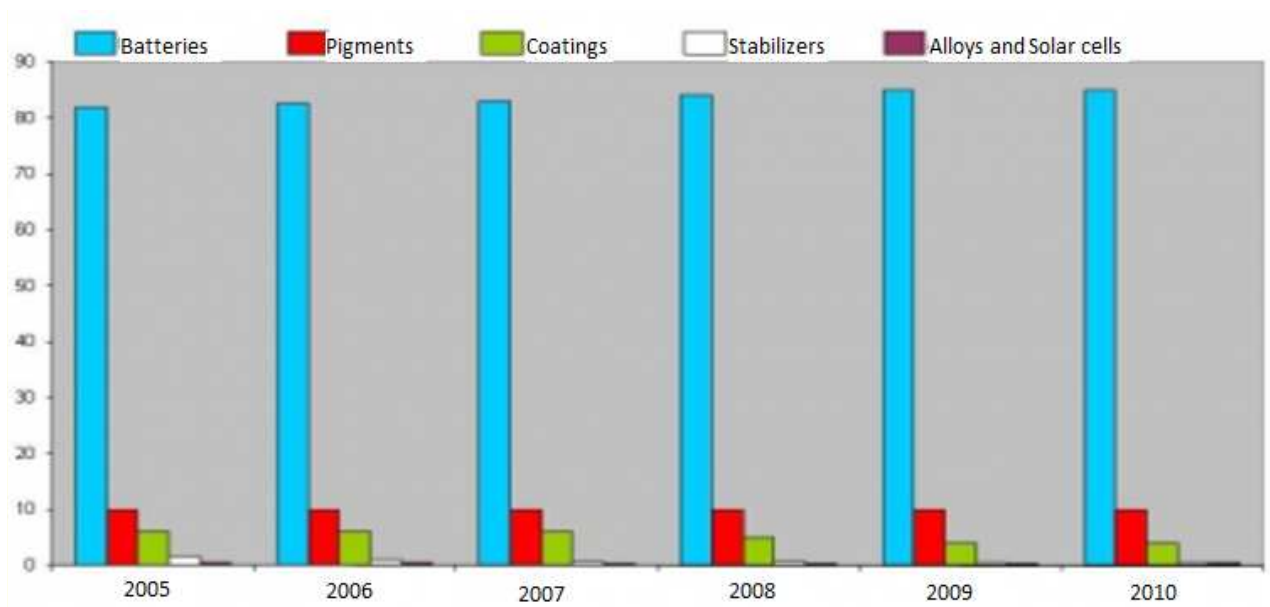
Figure 2: Trends in cadmium consumption patterns during 2005 to 2010, in per cent of the total consumption (ICdA 2013).

The annual world consumption of cadmium sulphide as **pigments** is approximately 2500 tonnes[8]. Cadmium pigments are primarily used in polymers (plastic, rubber, coating, printing ink) and ceramic glazes (Lussiez et.al. 1989) and in quality articles with a long lifetime (Klif 2013). A quantitative distribution between the different applications is shown in Table 7.

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[8] This is more than the total world production of 2000 tonnes reported by Schulte-Schrepping et.al. 2007 (section 7.2.2). The deviation may depends on data from different years.

Table 7: Applications of cadmium pigments (Smith 2002)

Polymers	90%	All grade of polymers and compounds masterbatch
Ceramics	6%	Glasses, enamels, porcelain, tile, china and glazes
Paint	3%	Oil colours, water colours, acrylics
Surface coatings	1%	Coil coatings, automotive paint, high temperature paint

8.2   Industrial & professional uses of cadmium sulphide

The industrial and professional uses of cadmium sulphide can be divided into the following groups (ICdA 2013):

- For production of inorganic cadmium compounds
- Laboratory reagent
- Cadmium production by pyrometallurgy
- For production of organic cadmium compounds
- For production of inorganic pigments
- Additive for production of frits
- Additive for production of glass
- Additive in the manufacturing of electronic components
- Use of cadmium sulphide-containing catalysts
- Component for production of PV (photovoltaic) modules
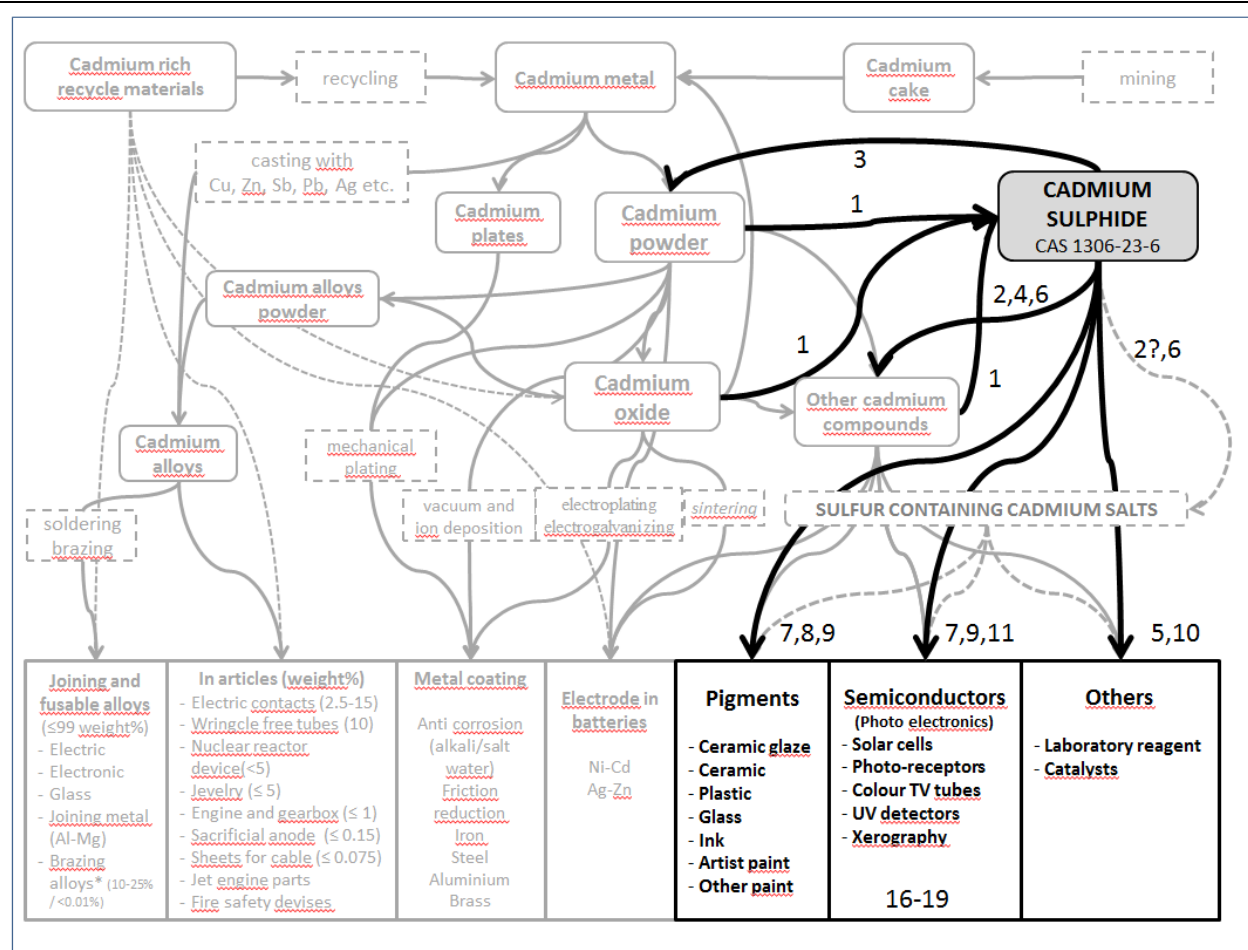
Figure 3: Overview of the cadmium downstream uses. The numbers refer to "exposure scenarios" in the registration (see section 9.1 below) (* is currently restricted under paragraph 8 of Entry 23 of Annex XVII of REACH).

The concentrations of cadmium sulphide as pigment and stabilizer in end products are in the range 0.01 to 1%. In semiconductors the concentrations of cadmium sulphide is lower, about 0.0002% (solar cells); see Table 8.

Table 8: Cadmium end product concentrations in different cadmium uses

Product	% Cd	Cadmium substance	Reference
Ni-Cd batteries	7-25%	Cd, CdO, Cd(OH)$_2$	US 2003, ICdA 2012
Cd alloys *et.al.*	1-25%	Cu-Cd, Ag-CdO	US 2003, ICdA 2012
Cd pigments	**~0.01-1%** ~1%	**CdS** Cd(Zn)S(Se)	Klif 2013 US 2003, ICdA 2012
Cd coatings	~0.2%	Cd, CdO, Cd-Ti, Cd-Sn	US 2003, ICdA 2012
Cd stabilizers	**~0.1%** ~1%	**CdS** Cd-laurate, Cd-stearate	Klif 2013 US 2003, ICdA 2012
Semiconductors **(Solar cell)**	0.0002% 0.004%	**CdS** Cd-Te	Bavarian EPA 2011

8.3 End uses of cadmium sulphide (excluding the intermediate applications)

Cadmium sulphide occurs on the market in several technical qualities. Some of the qualities are so modified that they should be considered to be different substances (according to REACH). Others are instead to be considered as mixtures. This is clear especially in the end-uses as pigments (see 8.3.2), but also the other end-uses can be expected to involve different technical qualities with unclear substance identities. The quality information from the suppliers are not always detailed enough to consider if the end-use form still contain cadmium sulphide or not.

8.3.1 Use of cadmium sulphide in semiconductors

Cadmium sulphide is a known semi-conductor material, available conventionally in crystalline form. Cadmium sulphide crystals can be used for various semi-conductor applications such as photovoltaic (PV) cells, photoconductors, phosphors and fluorescent screens, photomultipliers, radiation detectors, thin-film transistors, diodes and rectifiers, electron-beam pumped lasers, and smoke detectors, in scintillation counters, semiconductors, photoconductors. Cadmium sulphide for semiconductors are normally grown by crystalline growth by withdrawing a seed crystal from a molten pool of elemental cadmium sulphide, heated to liquid form. Cadmium sulphide can be fabricated into wafers or other materials (Kirk-Othmer 1978, Spanhel et al. 1992).

Solar cells are PV devices that convert sunlight directly into electrical power. The most common solar cell material is expensive silicon. One way of reducing the cost of solar cells is to develop low-cost thin film techniques that can deposit solar-cell-quality absorber materials on large area substrates, and to fabricate these devices using high-throughput, low-cost methods. A typical thin film PV cell has a very thin (less than 0.1 micron) polycrystalline layer called the "window" layer. The window layer's role is to form a heterojunction in combination with an "absorber" layer (e.g. CdTe). The window layer desirably is thin enough and has a wide enough bandgap to let most available light through to the absorber layer. For CIGS (Copper/Indium/Gallium/Selenide) and CdTe type solar cells, the most common material for the window layer is cadmium sulphide (Korevaar et al. 2012). Nano particles of cadmium sulphide are needed in the production of the window layer in thin film PV (Saraswathi and Manjunatha 2010). The research in **CdS**/CdTe dates back to the 1950s. Early leaders in **CdS**/CdTe cell efficiencies were GE in the 1960s, and then Kodak, Monosolar, Matsushita, and AMETEK (Wikipedia, 20 May 2013). The concentration of cadmium in a **CdS**/CdTe solar cell is about 14 g/m^2 (range 7-63). However, only 0.3 to 4% of this origins from cadmium sulphide. The total concentration of cadmium sulphide of a solar cell material is about 0.0002% (Bavarian EPA 2011).

Cadmium sulphide single crystal can be used as a **UV and IR detector** in combination with indium antimony (InSb) (Stanley 1988).

Cadmium can be used in **photoresistors** for analogue optocouplers applied in professional audio equipment (Shindengen 2013).

It is unclear if the cadmium sulphide used for semiconductors are doped. In such cases the end-use of cadmium sulphide will be as an intermediate for production of the doped cadmium sulphide.

8.3.2 Use of cadmium sulphide for pigments

Cadmium sulphide pigments occur in two **crystalline forms**: a hexagonal form, wurtzite lattices (alpha-CdS), and a cubic form (beta-CdS) (Zorll 2001). An amorphous form may also be synthesized. This phase reportedly coexists with other crystalline forms at room temperature (Eastaugh 2008). The more stable hexagonal cadmium sulphide is the only one used for high-temperature pigment applications (i.e. for thermoplastic, glass, enamel and ceramic) (Lussiez et.al. 1989).

Cadmium occurs in a number of pigments. They are all based on cadmium sulphide. Cadmium pigments are characterized by their particular brilliant shades, high hiding power, good intensities of colour, good temperature stability (up to 600°C) and "absolute" migration resistance (Zorll 2001). Cadmium sulphide is used as such as a golden yellow pigment, and in combination with other substances to create basic colours in the scale yellow-orange-red (Pritchard 1998)(see "Additives" below). Other colours that are based on yellow and red, such as green, brown, beige etc. may also contain cadmium sulphide (Klif 2013). Also mercury is used to moderate the nuance of the colour (Lussiez et.al. 1989). The mixture with mercury (cadmium mercury sulphide, CAS 1345-09-1) is said to have been developed as a result of shortage in selenium in the late 1940s. It is virtually identical in behavior and appearance to the cadmium selenide sulphides, but of lower cost (Easthaugh 2008). The pigment hue varies depending not on the arrangement of the atoms in the lattice structure, but on secondary factors relating to the structure of the colloidal aggregates, largely determined by the valence of the coagulating anions (Eastaugh 2008).

Additives can be incorporated into cadmium pigments in different ways. The most common techniques are as *solid solution* (intermediate use[9]) and *co-precipitation*. Compounding may also occur. The different techniques will influence the initial mobility of the cadmium sulphide molecule. In a *co-precipitations* pigment there are no substitutions into the cadmium sulphide crystal lattice (Eastaugh 2008). In short, in co-precipitation the different substances will be found in different crystals, as opposed to solid solutions, where the different substances will be found in the same colloidal aggregates. A *co-precipitation* should be considered as a mixture containing CdS.

$BaSO_4$ is used as **filler** in some of the commercial cadmium sulphide pigments varieties (normally 5-62%). These types of pigments are called "lithopone" pigments. Zink sulphide can also be used together with barium. The lithopones were developed due to the high cost of pure cadmium sulphide (Eastaugh 2008, Perez 2003). Even in pigments sold as pure may contain $BaSO_4$ (Perez et.al 2003). The lithopones are here considered as a cadmium sulphide mixture.

In an attempt to extend the **fire resistance,** the cadmium pigment (e.g. cadmium yellow=cadmium sulphide) was incorporated in an envelope of inert and transparent crystal materials. Such pigments are called *inclusion pigments* or *encapsulated pigments*. They consist essentially of transparent

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[9] A *solid solution* is a solid-state solution of one or more solutes in a solvent. Such a mixture is considered a solution rather than a compound when the crystal structure of the solvent remains unchanged by addition of the solutes, and when the mixture remains in a single homogeneous phase. This often happens when the two elements (generally metals) involved are close together on the periodic table; conversely, a chemical compound is generally a result of the non-proximity of the two metals involved on the periodic table. A *solid solution* with cadmium sulphide and another substance results in a new substance. Partial replacement of Cd^{2+} by Zn^{2+} ions in the lattice, produces progressively greener shades of yellow, while replacing sulphur by selenium ("sulphide/selenide pigments") gives rise to the orange, red and maroon sulphoselenides However, the exchange of ions in the lattice is considered as an intermediate use of cadmium sulphide (according to REACH).

crystals of e.g. zirconium silicate, zirconium oxide or tin oxide into which coloured compounds are included or encapsulated as a discrete phase. The production of these inclusion pigments takes place by means of heating the casing substances or their precursors and the coloured substances to be included or their precursor compounds in the presence of one or more mineralizers to temperatures up to 1400 °C. The technique was patented 1984 (Airey 1987; Kirk-Othmer 2004, Speer et al. 1991). The inclusion is here considered as a mixture of substances.

The information of the crystal formation and additives is not always available for the cadmium sulphide based pigments sold on the market (see table 11). It is therefore difficult to consider if they still contains cadmium sulphide, or if cadmium sulphide has been totally transformed into another substance.

8.3.2.1 Use of cadmium sulphide as pigments in polymers

Cadmium pigments may be used in all types of **coloured plastics** (Klif 2013). The rather unique temperature stability made them difficult to be replaced by organic pigments. Their principle use tends to be restricted to engineering polymers requiring high processing temperatures such as polyamides, Actals and PTFE (Pritchard 1998). In France, cadmium pigment is still in use in 2012 in the processing of poly Acrylonitrile Butadiene Styrene (ABS), Polymethylmethacrylate (PMMA), Polyoxymethylene (Acetal) (POM), polycarbonate and polyamide (ECHA 2012).

The concentration as pigment in polymers varies between 0.01 and 1%; the low figure for e.g. light beige and the high figure for e.g. clear warm yellow (Klif 2013).

Synthetic **textile** fibers can be coloured with cadmium sulphide during "spin dying" (or mass or dope dying) when the colorant is incorporated into the polymeric mass, prior to spinning. The melting temperature of the mass, 280 to 290 °C, is too high for many organic pigments. Cadmium sulphide[10] is among the few pigments which do not degrade during spinning (Kirk-Othmer 1978).

In the middle of the 1980's, ABS and HDPE applications were reported to account for almost 70% of the use of cadmium pigments for plastics in Europe (ECHA 2012).

8.3.2.2 Pigment uses in glass, enamel & ceramic

Cadmium sulphide is used as a colloidal yellow-orange-red colour in glass. The development of colloidal colours depends on controlled nucleation and growth of absorbing particles in glass. Coloured filter glasses can be made by precipitating cadmium sulphide crystals. Cadmium sulphide is dissolved in the glass in conjunction with a reducing agent such as tin oxide or antimony oxide. By keeping the glass at a temperature optimal for nucleation the size of the crystals, and therefore the colour, can be decided (Kirk-Othmer 1978).

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[10] As well as cadmium sulfoselenide and cadmium selenide (Kirk-Othmer 1978).

Cadmium sulphide[11] can be mixed into glazes, which when burned on ceramic articles or glass yield yellow colour. Since the ordinary cadmium sulphide pigments oxidize at temperatures above about 450°C, and decompose at temperatures above 850°C, it is necessary to use low melting glaze mixtures and frits as ingredients of the mixture (Wagner et.al. 1977). However, during the 80's, new technique has improved the thermostability of the cadmium pigments. For that the cadmium pigments[12] are encapsulated (see 8.3.2). The encapsulation technique is applicable to the whole range of cadmium pigments (incl. cadmium sulphide). The high temperature (up to 1400°C) and colouring stability allow these pigments to be considered for both underglaze and inglaze applications (Airey 1984, Airey 1987).

Cadmium pigments can be used in filter glasses and glasses used for reflectance standards (Shindengen 2013).

It is unclear if the cadmium pigments used for colouring glass occur in a *solid solution* form. In such cases the end-use of cadmium sulphide will be as an intermediate for production of the *solid solution* substance.

8.3.3 Other uses

8.3.3.1 Use of cadmium sulphide as stabilizer

Cadmium stabilizers are/were used mainly for outdoor purposes, such as plastic doors, windows and crystal clear roof windows (Klif 2013). The concentration of cadmium sulphide in such plastic materials (mainly in PVC) as stabilizer is about 0.1% (Klif 2013). cadmium sulphide improves the stability of polymers (PVC and similar materials) against heat, oxidation and UV-radiation (Kirk-Othmer 1978). cadmium sulphide can also be used as an antioxidant during processing of high-density polyethylene (HDPE) (HSDB 2012). HDPE is commonly used in the production of plastic bottles, corrosion-resistant piping, geomembranes, and plastic lumber. HDPE is commonly recycled, and has the number "2" as its recycling symbol. In 2007, the global HDPE market reached a volume of more than 30 million tons (Wikipedia).

ICdA stated that, to the best of their knowledge, there is no use within EU of cadmium compounds as stabilizers in plastics other than PVC (ECHA 2012).

8.3.3.2 Used in cathode ray tubes

Cadmium sulphide has been used in cathode ray tubes (CRTs) in older desk top computers and TV sets as a "phosphor" on the interior surface of the screen to produce light (Menad 1999).

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[11] As well as cadmium sulfoselenide that yield red colours (Wagner et.al. 1977).

[12] The only bright red colour for ceramic available is that provided by the cadmium sulphoselenide pigments. The red cadmium pigment is therefore potentially the most interesting colour for ceramics.

8.3.3.3 Used in LED illumination systems

Cadmium can be used in colour converting II-VI LEDs (in the light-emitting area) for use in solid state illumination or display systems (Shindengen 2013).

8.3.3.4 Use of Cd in printing ink

Industrial ink jet printing is a conventional coloring process for various materials (paper, glass, metal etc.). Cadmium pigments, such as Cadmium Yellow (= CdS), are now seldom used in inks, except in applications needing very high resistance properties (to light, heat, solvents, and alkali).

Cadmium pigments can be used for printing on enamels and glass, such as borosilicate and soda lime glasses (Shindengen 2013). Cadmium Yellow (= CdS) is not recommended for outdoor poster inks where they may decompose or darken under acidic atmospheric conditions (Leach and Pierce 2007).

8.4 Identified uses in the EU (ECHA, 2013)

The registration of cadmium sulphide includes the following uses:

- Raw material for production of cadmium by pyrometallurgy
- Manufacturing of organic cadmium compounds
- Manufacturing of inorganic cadmium compounds
- Manufacturing & use of inorganic pigments
- Manufacturing & use as laboratory reagent
- Manufacturing & use for production of PV modules
- Manufacturing & use of cadmium sulphide-containing catalysts
- Formulation (additive) & use in frits

8.5 Use volumes in EU

According to the REACH registration, cadmium sulphide is produced or imported by a moderate number of companies from Germany, Czech Republic, Italy, Belgium and UK. The total quantity of the annual tonnage band registered is 10 to 100 tonnes (5 May 2013). A search on the Internet for cadmium sulphide revealed 2-17 suppliers in Europe[13] (Chemical Book 2013, ChemExpr 2013).

Cadmium **pigments** and **stabilizers** were in widespread use before 1980. The use was strongly limited by the cadmium ban introduced in Sweden in 1982, in Denmark in 1983 and in the EU in 1991. In 1998, **pigments** accounted for 13% of cadmium consumption in the principal consuming countries (Scoullos et.al. 2001).

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[13] Note that some suppliers supply substances with different purity grades; received multiple hits.

Around 4 tonnes of **cadmium pigments** are used as raw material by the chemical industries in EU[14] (ECHA 2012). According to the EU RAR, the consumption of cadmium pigments, including imported articles, in EU-16 was estimated to 499 tonnes in 2003 (corresponding to 299 tonnes Cd per annum, ECHA 2012). In year 2000, the usage of cadmium in pigments in EU was about 830 tpa. Of these, about 90% where used in plastics, with only 4% in artist's colours and about 6% in colours for ceramics/glass. The primary use of cadmium sulphide is in the manufacture of brilliant red, orange and yellow pigments that are used in a range of applications, particularly engineering plastics. Although there are restrictions on the use of cadmium pigments in some plastics, many plastics are still exempted (RPA 2000).

The manufacture of polymers (such as PVC) requires **stabilizers** to prevent decomposition during both processing and use. The main use of cadmium as a PVC stabilizer is in window frames. As some countries (Sweden, Denmark, Austria, The Netherlands) have already banned this use of cadmium, and the industry has a voluntary agreement to phase out the use of new cadmium stabilizers, the overall use of cadmium in stabilizers has dropped from an EU level in 1997 of 270 tonnes per annum (tpa) to 30 tpa in 2000 (RPA 2000).

The share of **CdS**/CdTe based **solar cells** within the new *thin-layer* technology was approx. 60 % in 2009 (Bavarian EPA 2011).

A quantification of the cadmium flow in EU[15] has been made by Lig & Held (2009).

8.6 Recycling

8.6.1 Polymer uses

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

8.6.2 PV Solar cells

The PV industry is considering **recycling** of these modules at the end of their useful life. Because the metals involved are relatively rare in commerce, efforts have been undertaken to create recycling opportunities for damaged or decommissioned high performance solar panels; however, given the relative newness of this aspect of the PV solar energy industry, it is not possible to affirm with certainty that such recycling opportunities would materialize or be available at the time current

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[14] According to Eurocolour are in total about 4.1 tonnes of the pigments cadmium zinc sulphide yellow (EC232-466-8/CAS8048-07-5), cadmium sulphoselenide red (EC 261-218-1/CAS 58339-34-7) and cadmium sulphoselenide orange (EC235-758-3/CAS12656-57-4) used in plastics in the plastic industries within EU (ECHA 2012c).

[15] The 27 EU member states.

facilities are decommissioned. Absent legitimate recycling opportunities, damaged or decommissioned solar panels containing toxic metals would need to be characterized and might need to be managed as hazardous waste (Fthenakis et al. 2004).

PVs have no longer an exemption from the WEEE recycling obligations. PVs are now included under category four (Consumer Equipment and Photovoltaic Panels) and category five (small equipment with integrated PV panels). Article 5 on the directive specifies PVs in ensuring the correct treatment of all collected WEEE because of the variety of precious and rare materials such as gallium, indium and selenium used. In addition, the possible hazardous waste potential from substances such as cadmium in the thin cadmium telluride film on certain types of PV increases the need for safe and efficient hazardous waste disposal. A minimum annual collection rate of 45% will be achieved from 2016 (WEEE 2012).

The PV industry will not face the large scale recycling problem before the year 2020, today's material selection and module design may very well set a precedent for the future. The collection of spent modules is a challenge. Recycling solar panels is more complicated than that of the above products, because of the decades-long interval between installing and discarding modules, their low content of valuable materials, and their geographical dispersion. A typical photovoltaic module manufacturing facility generates a significant amount of scrap at the start of its operation but, within a few months to a year, reaches a steady-state level of production generating relatively little waste. In discussing PV recycling, it should be distinguish between near-term and future needs and capabilities. This is because of the long lapse between the start of manufacturing and decommissioning, and the corresponding differences in scale and technology. Metals from used solar panels in large centralized applications can be reclaimed in metal-smelting or refining facilities which use the glass as a fluxing agent and recover most of the metals by incorporating them into their product streams. In dispersed operations, small quantities and high transportation costs make this option relatively expensive. Separating the PV materials from the glass reduces the amount of waste generated by three orders of magnitude. Effective and economical methods of such separation have been developed that can be used in both small-scale (in-house) and large-scale recycling (Fthenakis and Moskowitz 2008).

9 EXPOSURE

Human exposure to cadmium from cadmium sulphide can potentially occur during the whole life-cycle of the substance. Industrial and professional workers will be exposed during several scenarios where cadmium sulphide 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, eg. mineral fertilizers, will contribute to the soil contamination.

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

1. <u>Anthropogenic</u>: **Deliberate use of cadmium** and its compounds 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. <u>Anthropogenic</u>: 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. <u>Natural</u>: **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 2013). The exposure scenario numbers are shown in Figure 3.

1. <u>cadmium sulphide production – Indirect and Wet</u>: Industrial use of bulk or fine chemicals [SU 8, 9] in order to **synthesize** cadmium sulphide [PC 20]. The batch or continuous processes are carried out in closed or potentially closed containers, with occasional controlled exposure at elevated temperature. Substances and mixtures are transferred into smaller containers. Solid substances are handled at ambient temperature [PROC 2, 3, 8b, 9, 22, 26]. Environmental point source exposure occurs [ERC 1]. Exposure may occur during subsequent service life.

2. <u>Production of inorganic cadmium compounds</u>: Handling of cadmium sulphide in bulk for **production** of inorganic fine chemicals, including **formulation**, in production of intermediates, laboratory chemicals and processing agents [SU 8, 9, 10][PC 19, 20, 21]. The batch or continuous processes are carried out in closed or potentially closed containers, with occasional controlled exposure at elevated temperature. Substances and mixtures are transferred into other containers [PROC 2, 3, 8b, 9, 15, 21, 22]. Environmental point source exposure occurs during substance production and formulation [ERC 1, 2, 6a]. Exposure may occur during subsequent service life.

3. <u>Use for production of cadmium by pyrometallurgy</u>: Industrial **processing** (synthesis) of cadmium sulphide in closed, continuous process with occasional controlled exposure at ambient and elevated temperature. Substances are **transferred** into dedicated facilities at elevated and ambient temperature [SU 14, 0: Nace: C24.4.5 non-ferrous metal prod.; E38.3 Materials recovery] [PC 7] [PROC 2, 8b, 9, 23, 26]. Environmental point source exposure occurs during the substance production [ERC 1].

4. <u>Component for production of organic cadmium compounds</u>: Industrial handling of cadmium sulphide in bulk for **production** of organic fine chemicals, including **formulation**, in production of intermediates, laboratory chemicals, processing agents, lubricants, pharmaceuticals, cosmetics and personal care products [SU 8, 9, 10], [PC 19, 20, 21, 24, 29, 39]. The batch or continuous processes are carried out in closed or potentially closed containers, with various degree of exposure [PROC 1, 2, 3, 4, 8b, 9, 15]. Environmental

point source exposure occurs during substance production and formulation [ERC 1, 2, 6a]. Exposure may occur during subsequent service life.

5. Use of laboratory reagent: Industrial and professional **handling** of cadmium sulphide containing products in opened or closed systems, batch or continuous, with various degree of exposure [PROC 1, 2, 3, 4, 5, 8b, 9, 15]. The laboratory reagents are used in markets sectors working with intermediates, laboratory chemicals, perfumes, fragrances, cosmetics and personal care products [SU 10, 24]. Environmental exposure occurs during formulation and the use as a processing agent. The processing agent uses occur wide dispersive in indoor & outdoor opened systems [ERC 1, 2, 4, 6a, 6b, 8a, 8d]. Exposure may occur during subsequent service life.

6. Component for production of inorganic pigments: Industrial continuous or batch **processing** in small and large scale of cadmium sulphide at elevated temperatures, with various degree of occupational exposure. **Transfer** of substances or mixtures from/to vessels at dedicated facilities [SU 8, 9, 10, 13] [PROC 1, 2, 3, 4, 5, 8b, 9, 22] [PC 9a, 9b, 9c]. Human and environmental exposure may occur during subsequent service life from articles containing pigments [ERC 1, 2, 5].

7. Additive for production of frits: Industrial continuous or batch opened and closed **processing** in small and large scale of cadmium sulphide at ambient and elevated temperatures. Industrial continuous or batch **formulation** in small and large scale at ambient and elevated temperatures, including dipping and pelettisation. **Transfer** of substances or mixtures from/to vessels. Various degree of occupational exposure [PC 19, 0, UCN R30100-R30300 raw material for intermediate products/raw material for production of glass and ceramics] [SU 10, 13][PROC 2, 3, 4, 5, 8b, 9, 13, 14, 15, 17, 22, 26]. Human and environmental exposure may occur during subsequent service life of electrical batteries, accumulators and photosensitive transistors as well as glass and ceramics. [ERC 1, 2, 3, 5][AC 3, 4, 0: Taric 854121: transistors - other than photosensitive transistors].

8. Additive for production of glass: Industrial closed continuous batch **processing** of cadmium sulphide at elevated temperatures. **Formulation** and repacking of mixtures. Various degree of occupational exposure. **Transfer** of substances or mixtures from/to vessels at dedicated facilities [PC 19, 20] [SU 10, 13, 0: Nace 23.1 Manufacture of glass and glass products] [PROC 2, 3, 4, 5, 8b, 9, 22]. Environmental exposure from industrial point sources during intermediate use, formulations and article productions [ERC 2, 3, 5, 6a]. Exposure may occur during subsequent service life of glass articles [AC 4].

9. Additive in the manufacturing of electronic components: Industrial closed mixing and blending in batch processes for **formulation**. Potentially closed processing operations at elevated temperature. High mechanical energy work-up of material containing cadmium sulphide. **Transfer** of substances or mixtures from/to vessels [PC 20] [SU 10, 13, 16, 0: Nace 26.1.1 manufacture of electronic components] [PROC 3, 5, 8b, 9, 14, 22, 24]. Environmental exposure from industrial point sources during formulations and material processing [ERC 2, 5]. Exposure may occur during subsequent service life of electronic components made by glass and ceramics [AC 2, 4].

10. Use of cadmium sulphide containing catalysts: Industrial continuous or batch opened and closed chemical and physical **processing** in small and large scale of cadmium sulphide. **Transfer** of substances or mixtures from/to vessels [PC 2, 9b, 19, 20, 40] [SU 8, 9, 10]

[PROC 1, 2, 3, 5, 8b, 9, 14]. Environmental exposure from industrial point sources during processing, formulation and use as a catalyst [ERC 1, 4, 5, 6a, 6b]. Exposure may occur during subsequent service life.

11. <u>Component for production of photovoltaic modules (PV)</u>: Industrial continuous or batch closed **processing** with no or controlled occupational exposure [SU 9, 16, 23, 24] [PROC 1, 2, 3] [PC 33]. Environmental exposure from industrial point sources during processing of semiconductors [ERC 1, 2, 5][AC 3]. Exposure may also occur at the waste management stage.

9.2   Releases and exposure during private uses

Release of cadmium during service life from anthropogenic sources includes products and materials to which cadmium sulphide has deliberately been added to impart a specific chemical, mechanical or physical property and products or materials in which cadmium sulphide is present as a residual or impurity element. The releases during private use is limited to the consumption of end use articles containing cadmium sulphide, preferable made by materials with long service life.

9.2.1 Potential for release from uses of cadmium pigments and stabilizers (Klif 2013)

Cadmium pigments and stabilizers were in widespread use before 1980. The use was strongly limited by the cadmium ban introduced in Sweden in 1982, in Denmark in 1983 and in the EU in 1991. The ban was improved with EU regulation 494/2011. Many products containing cadmium will still be in use in society e.g.:

- Lego building bricks - cadmium was used up to about 1980, but these bricks are saved from generation to generation and the real service life seems so far to be "almost" unlimited.
- Safety signs/materials - due to very high light and weather resistance cadmium is typically used for such materials. The use was allowed in EU until 2011.
- Buttons and housing/casings made of technical plastics such as PA or ABS. The use was allowed in EU until 2011.
- The use of cadmium in PVC door and windows continued to about 1990/1991. The service life of such products may reach 40 years or more. Furthermore, recycling of such product may significantly increase the in service life of cadmium stabilizers. Discussion in EU on this issue is on-going.

Many pigments especially those used in the ceramic and plastics industries are of limited colour and chemical stability. Such pigments may become **unstable** at elevated temperatures or in the presence of acids, resulting in a colour change and/or the release of toxic metals from the pigment. Cadmium sulphoselenide solid solutions are particularly unstable, which is unfortunate in that they provide an excellent range of colours from yellow through red to purple. These pigments are sensitive to temperature and atmosphere and react with lead-containing fluxes and other non-cadmium pigments giving black contamination. Despite their limitations these are the only known compounds to give bright red colours for ceramic applications (Airey 1984).

Cadmium based pigments, catalyst and stabilizers occur in **plastics and rubber** containing articles (i.e. PVC doors and windows. Releases from such products is related to wear and tear of products (e.g. if a plastic window is ground before painting). Existing information does not allow quantification, however, the quantity released can be assessed as small compared to the quantity present in the products (Klif 2013). The cadmium pigments are used in thermoplastics such as polystyrene. However, the use of these pigments in plastics could be limited because of the possible release of cadmium (Airey 1984).

ICdA stated that once enclosed in the polymer matrix – whatever this is – these substances are firmly bound into the matrix and it requires the use of acid to extract even very low levels of cadmium from the coloured polymer (ECHA 2012). However, this does not exclude releases via loss of material (e.g. grinding, wear & tear) and releases via waste incineration (see 9.3.1).

9.2.1.1 Potential for release from PV solar cells

The life-cycle **releases** of **CdS**/CdTe PV have been estimated in a life-cycle analysis (Fthenakis 2004). During the **manufacturing** of **CdS**/CdTe PV about 1% is wasted in the electrodeposition process, and about 10–30% is wasted in the vapor-transport process. In both processes, cadmium can be collected and can thereafter be safely disposed of or recycled (Fthenakis et al. 2004).

During **end use** there are no emissions of any kind generated when using PV modules, under normal conditions (Fthenakis et al. 2004).

During **waste management** releases to the aquatic environment could occur after decommissioning only if such modules end up in municipal landfills and the materials leach out. However, cadmium telluride is encapsulated between two sheets of glass and is unlikely to leach to the environment under normal conditions. No atmospheric emissions of Cd can occur under any foreseeable conditions. Under normal conditions cadmium sulphide is secured within sealed solar panels and represent no hazard to workers or the public. However, damaged solar cells may cause worker exposure and may require special handling during facility decommissioning (Fthenakis et al. 2004).

9.2.1.2 Potential for release from artistic pigments

Cadmium-containing sulphides in pigments are not thermodynamically stable under aerobic conditions. It has been observed that paintings made by cadmium based pigments show discolouration due to degradation of the pigments. This is observed especially in the lighter yellow pigments. In an artificial ageing study by light, simulating 45 years in museum conditions, the oxidation products, cadmium sulphate and cadmium oxide, where found. The study points towards the possibility that moisture treatments or even environments of high humidity may trigger the deterioration (Leone et.al. 2005).

9.3 Releases during the waste life stage

9.3.1 Potential for release from refuse incineration

Cadmium is released as a result of incineration of commercial and household waste containing cadmium-stabilized PVC plastics and products containing cadmium pigments. The slag produced contains about 8 mg/kg of cadmium while the fly ash contains approximately 200 mg/kg. These residues are sometime utilized in practical applications, e.g. in road construction, in leveling/filling material or in landfills (Scoullos et.al. 2001).

9.3.2 Potential for release from degrading pigments

Cadmium containing pigments will to some extent end up in waste water treatment sludge that is applied on agricultural soil. Cadmium-containing sulphides[16] in pigments are not thermodynamically stable under the conditions that prevail in the surface horizons of aerated agricultural soils (e.g. in Sweden). Under aerated conditions, the dissolution rate of pure cadmium sulphide is comparably high. In a soil environment containing sufficient electron acceptors such as $O_2(g)$ and $Fe(III)$, pure cadmium sulphide will be dissolved completely within one year. When sulphide-bound cadmium is supplied to soils together with an excess amount of sulphide-bound Zn, the dissolution rate of cadmium will slow down to low levels, as long as sulphide-bound Zn persists in the soil. Crystalline ZnS (such as *sphalerite*) can persist in soils for a time period of 1 to 2 decades, making cadmium sulphide dissolution slow during this period. However, most evidence suggests that most of the ZnS added in sewage sludge is amorphous, and will dissolve completely within just a few years. Further, soil samples subjected to long-term applications of sewage sludge do not show reduced cadmium solubility because of the additions of ZnS through sludge. Based on the evidence assembled, it is concluded that cadmium supplied in the form of sulphides or selenides should be considered fully available (similar to easily soluble cadmium chloride) when a time scale of 50 years is applied (KemI 2013b).

9.4 Potential for release from accidents (PV solar cells)

There is an interest in whether a **fire** in the cadmium based PV system may cause exposure of the public residents (Nieuwlaar and Alsema 1997; Fthenakis and Zweibel 2003, Bavarian EPA 2011). Current thinking is that the risk from fires in roof-mounted PV systems is minimal. Researchers conducted experiments on the release of cadmium from modules when burnt at high temperatures and found that less than 0.04% of the cadmium in modules would be released in fires (Fthenakis et al. 2004). A distribution calculation modeling carried out showed that, from a technical standpoint, a serious danger for the immediate neighborhood and the general public can be excluded when modules containing **CdS**/CdTe burn (Bavarian EPA 2011).

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[16] Referring specifically to: Cadmium sulphide (CAS 1306-23-6), Cadmium zinc sulphide yellow (CAS 8048-07-5), Cadmium sulphoselenide orange (CAS 12656-57-4), Cadmium sulphoselenide red (CAS 58339-34-7), Cadmium zinc sulphide (CAS 12442-27-2), Cadmium sulphoselenide (CAS 12626-36-7).

Releases from **broken or cracked** modules under normal operations may occur. In general, researchers have, however, concluded that such releases would result in a negligible potential for human exposures (EPRI and PIER 2003; Fthenakis and Zweibel 2003, Bavarian EPA 2011).

9.5 Potential for release from natural sources

Cadmium is a naturally occurring element, one of the components of the earth's crust and present everywhere in our environment[17]. 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 2012).

Natural cadmium will also indirectly cause 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 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 9 (ICdA 2012). 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 represent chemical dissolution or wear/erosion processes rather than electrochemical corrosion processes (ICdA 2012b).

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[17] Pure cadmium sulphide minerals are relatively rare in the nature. *Greenockite* (Scotland) and *Hawleyite* are the two recognized natural cadmium sulphide minerals. Much more commonly, cadmium sulphide occurs as a minor constituent of other sulphide minerals such as *Sphalerite* (KemI 2013b).

Table 9: Concentration of cadmium as an impurity in different types of products/materials (ICdA 2012)

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

9.6   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 10.

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

	Age (years)	Urinary cadmium µg/g creatinine			
		Median and (range)		% >0.5µg/g	%>1.0 µg/g
		All	Never-smokers	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 cut offs of 0.5 and 1.0 µg Cd/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 to the observed differences.

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 1970s. 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 (KemI 2011 and references therein).

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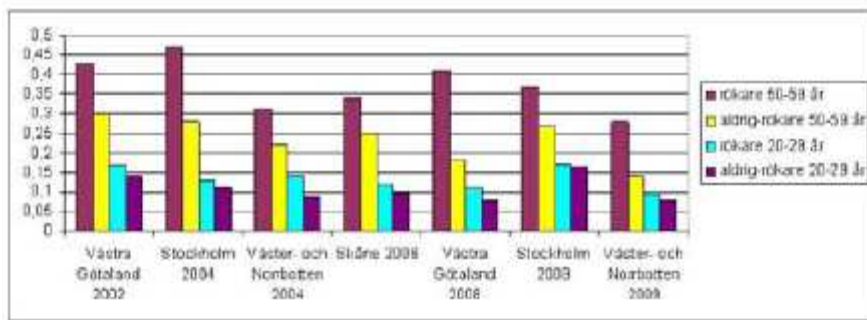
Figure 4: Urinary cadmium (µg/g creatinine) among Swedish woman, 20-29 years and 50-59 years of age, presented as the median

The estimated average *intake of cadmium via food* in Sweden has not changed in recent times. The most recent intake estimate from year 2010 is 11.2 µg Cd/person and day; earlier estimates from 1987 and 1999 were 12 µg/day and 10 µg/day (National Food Agency 2012a).

Data on the cadmium content in flour of wheat and rye in Sweden during the period 1976-2010 indicate a very slow decrease (approx. 1% per year). However, there is a dip in the time curve around year 1995 and from that year the cadmium content is slowly increasing (National Food Agency 2012b).

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 (KemI 2011).

9.7 Worker exposure to cadmium (see also the *CONFIDENTIAL ANNEX*)

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).

9.8   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 Ni-Cd 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 registration for cadmium sulphide, no consumer use is given and therefore also no exposure assessments. The use of photovoltaic solar cells, a potential new use, is not expected to result in direct consumer exposure, since cadmium sulphide is enclosed in the product.

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   Alternative - Pigments

It seems reasonable that in years to come the decline in use of cadmium pigments will continue as more environmentally-acceptable alternatives are developed (Pritchard 1998). There are many alternative pigments available on the market covering organic as well as inorganic pigments. Ultimately, the choice is a matter of costs versus colour and other characteristics like weather resistance, torsion stability and brilliance. Costs may be lower or higher depending on the substitute selected (Klif 2013). One example is cerium sulphide that can replace cadmium sulphide, mostly in plastics (USGS 2013).

After the adoption of Regulation (EU) No 494/2011, the Commission learned about niche applications (e.g. the colouring of some engineering plastics), where suitable alternatives to the use of cadmium substances, may not be available. According to this information, the cadmium substances used as pigments in these applications are: cadmium zinc sulphide Yellow (EC 232-466-8, CAS 8048-07-5), cadmium sulphoselenide Red (EC 261-218-1, CAS 58339-34-7) and cadmium sulphoselenide Orange (EC 235-758-3, CAS 12656-57-4) (ECHA 2012c).

In Sweden, the replacement of cadmium pigments in ABS and HDPE has, in the long term perspective, been performed without technical or economic implications. However, initial implications were experienced. The replacement of cadmium pigments in plastics processed at a high temperature was a problematic issue. Due to high processing temperatures ABS and PA

applications generally posed more technical problems than other thermoplastics. Initial problems with uneven colouring and decreased colour fastness with substitute pigment in HDPE were reported, e.g. in the pigmenting of HDPE boxes and crates. The use of organic pigments caused uneven colouring and warping of the products. The problems were solved by adjusting formulation and processing equipment. Cadmium pigments were generally substituted by organic pigments. They were generally more expensive than cadmium based pigments. However, organic pigments also tend to have higher colour strengths than their cadmium or inorganic equivalents. Consequently less pigment was used in the final blend (ECHA 2012).

In France, cadmium pigments in plastics are gradually replaced (by iron oxide for example), but for certain plastics as Poly Acrylonitrile Butadiene Styrene (ABS), Polymethylmethacrylate (PMMA), Polyoxymethylene (Acetal) (POM), polycarbonate (PC) and polyamide (PA), cadmium is still used (ECHA 2012).

According to ICdA, many of the pigments, sold as "substitutes" for cadmium pigments, have not the same performance in terms of heat stability and resistance to fading in outdoor use. This is particularly true of the engineering polymers which are processed at very high temperatures (perhaps up to 375°C). Also, when polymers are injection moulded, there are inevitably feed channels involved which have to be removed from the finished articles. In the case of cadmium pigments, these so-called "sprues" can be granulated and re-sued, as the pigment can withstand the processing temperature almost indefinitely. The high-performance organic pigments used as alternatives can only survive the processing temperature once, without partial breakdown to give dirty colour effects. This results in waste of both the polymer itself, and the expensive organic pigment. Inorganic pigments, in general, are also immune from migration, where the colorant can travel slowly through the organic polymer matrix and appear at the surface (ECHA 2012).

Regarding alternatives to cadmium zinc sulphide yellow (EC232-466-8/CAS8048-07-5), cadmium sulphoselenide red (EC 261-218-1/CAS 58339-34-7) and cadmium sulphoselenide orange (EC235-758-3/CAS12656-57-4), Eurocolour state that colorants with the same technical properties does not exist. Cadmium pigments provide the highest achievable values for weather resistance, light fastness, heat resistance for the converting processes and chroma. Without cadmium pigments outdoor security applications will, according to Eurocolour, become less secure due to a loss of signal colour strength (fading). Substitutes could be found with lead chromate pigments, but they are part of REACH Annex XIV. Organic red pigments in combination with UV-stabilizers cost 6 to 10 times more than the inorganic counterparts, and they still do not reach the same colour shade and weather fastness (ECHA 2012).

10.2   Alternative - Stabilizer

Barium/zinc or calcium/zinc stabilizers can replace barium/cadmium stabilizers in flexible polyvinylchloride applications (USGS 2013).

10.3 Alternative - Solar cells

10.3.1 Dye-sensitized solar cell

"Dye-sensitized solar cell" (DSSC) is a new class of low-cost thin-film solar cell that is cadmium-free. It is based on a semiconductor between a photosensitized anode and an electrolyte. Commercial applications, which were held up due to chemical stability problems, are now forecast in the "EU Photovoltaic Roadmap" to be a potential significant contributor to renewable electricity generation by 2020.

Unlike traditional silicon-based solar cells, these dye-sensitized cells require no complex manufacturing processes and the raw materials are inexpensive, leading to a lower manufacturing cost. Similar to other thin film solar cells, the DSSC is mechanically strong yet lightweight. By being mechanically robust, the dye-sensitized cells also experience higher efficiencies at higher temperatures. Conventional silicon solar cells are sensitive to the elements, resulting in protective measures being forced upon the cell such as encasing the silicon solar cell in a glass box. At higher temperatures, more electrons are produced into the conduction band of the semiconductor. As silicon solar cells are not able to dissipate the build-up, this leads to an increase in the internal temperature. For silicon solar cells, an increase in the internal temperature leads to a decrease in the efficiency rate. DSSCs are thin and mechanically robust allowing for heat to be radiated quickly and efficiently, which avoids the problem faced by traditional silicon-based solar cells. These two features make DSSCs suitable for low-density applications, such as rooftop collectors. Being a member of the thin film family of solar cells, DSSC solar cells can also be used in *Building Integrated Photovoltaic* (BIPV) applications. One very interesting advantage is that DSSCs work in low-light conditions. Due to their very favourable electrochemical kinetics, DSSCs do not share the same cut off point as other solar cells in terms of charge carrier mobility and recombination. This ensures that DSSCs will work even when the sunlight is diffuse and even when there is no direct sunlight. To develop this solar cell further, research has to both improving the efficiency rate as well as finding ways to reduce the manufacturing cost (Ponnampalam 2011).

10.3.2 Other alternative solar cells techniques

Zinc sulphide can be used as an alternative to cadmium sulphide in the *window* layers (see 8.3.1) in the copper indium gallium diselenide (CuInGaSe2)-based solar cells (Nagamani et.al. 2012).

10.4 Alternative - Spin dying

An alternative method for spin dying at lower temperature, based on aqueous media, has been developed. Organic pigments can then be used as an alternative (Sieber 2006).

10.5 Not recommended alternative substances

There is a number of, more or less specified, sulphur containing cadmium salts on the market (see Table 11). The exact use patterns for each of the substances in the table are not available. However,

many of these can be expected to be technically useful alternatives for some of the uses of the suggested SVHC.

Many of these cadmium-sulphur substances probably originate from the suggested SVHC substance, and are modified to fit different technical applications. The modifications consist of purification, additives and/or, different types of controlled crystallisation. Major additives are zinc, selenium and/or zirconium. Several of the substances are doped with aluminium, copper, manganese, europium, gold, silver, lead, chloride, and/or nickel. It is unclear if these modifications totally enter the whole content of the suggested SVHC substance into another "substance" (the "intermediate" scenario). Probably are there unmodified cadmium sulphide left in the in the modified substance.

Such substances where identified from different chemical inventory lists (covering Europe, USA, Canada, China, New Zealand and Philippines). Many of these are also on the list of preregistered substances according to REACH (see the table). Some of them are already registered according to REACH.

The substances in Table 11 can be assumed to have the same toxicological concerns as the suggested SVHC substance. They should therefore be avoided when considering alternative substances.

Table 11: Identity of sulphur containing cadmium salts. Extracts from different market inventory lists.

Type	CAS No. EC No.	Name	Inventory lists
Co-precipitation	**1345-09-1** -	**Cadmium** mercury **sulphide** (C.I. Pigment Orange 23; CI 77201; Cadmium cinnabar; Mercadmium;11-26% HgS /Eastaugh et.al. 2008).	New Zeeland 2013; DSL 2012; TSCA 2012; China 2013; Artist´s paint 2013
Co-precipitation	**1345-09-1** **-**	Calcined co-precipitate of **cadmium sulfide** and Mercuric sulfide (Pigment Orange 23; C.I. 77201).	Artist´s paint 2013
Co-precipitation	**-** -	Concentrated **CdS** plus mercury sulphide; Pigment orange 23:1; co-precipitated with BaSO$_4$; CI 77201:1	Artist´s paint 2013
Co-precipitation	**90604-89-0** -	**Cadmium** lithopone Yellow**;** Pigment Yellow 35:1; Cadmium Zinc co-precipitated with barium sulfide; CI 77205:1.	Artist´s paint 2013
Co-precipitation	**-** **-**	Mercadium Lithopone Red; Pigment red 113:1; **Cadmium sulphide**-mercuric sulfide co-precipitated on barium Sulfate.	Artist´s paint 2013
Co-precipitation	**7621-06-9** -	**Cadmium sulphide** lithophone; CdS + BaSO$_4$; Pigment Yellow 14	China 2013
Co-precipitation	**90604-90-3** -	**Cadmium-**Barium Yellow Deep**;** Pigment Yellow 37:1; co-precipitated with barium **sulfide;** *unclear chemical specification*	REACH prereg.; Artist´s paint 2013
Co-precipitation	- -	**Cadmium Green; Pigment green 14;** Intimate mixture of varying composition; Co-precipitated hydrated oxide of chromium (Viridian, PG18) with **cadmium sulphide** (PY37, PY35)	Artist´s paint 2013
Co-precipitation	**-** **-**	Cadmium-Barium Vermillion Orange**;** Concentrated **cadmium sulphide** plus Mercuric Sulfide co-precipitated with barium sulfate; ≤ 60% barium sulphate. Pigment Orange 23:1.	Artist´s paint 2013
Solid solution Doped	**68512-51-6** 270-979-9	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, aluminum and copper-doped.	REACH prereg.
Solid solution Doped	**68784-10-1** -	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, aluminum, cobalt, copper and silver-doped.	Shindengen 2013
Solid solution Doped	**68584-41-8** 271-538-3	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, aluminum and silver-doped.	REACH prereg.
Solid solution Doped	**68332-81-0** 269-773-1	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, copper and lead-doped.	REACH prereg.
Solid solution Doped	**68512-50-5** 270-978-3	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, copper and manganese-doped.	REACH prereg.

Solid solution Doped	**68584-42-9** 271-539-9	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, copper and nickel-doped.	REACH prereg.
Solid solution Doped	**68583-43-7** 271-511-6	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, copper and silver-doped.	REACH prereg.
Solid solution Doped	**68512-49-2** 270-977-8	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, copper chloride-doped.	REACH prereg.
Solid solution Doped	**68583-44-8** 271-512-1	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, nickel and silver-doped.	REACH prereg.
Solid solution Doped	**68583-45-9** 271-513-7	**Cadmium sulphide** (CdS), solid solution with zinc sulfide, silver chloride-doped.	REACH prereg.
Solid solution Doped	**101357-00-0** 309-897-6	Cadmium selenide (CdSe), solid solution with **cadmium sulphide**, zinc selenide and zinc sulfide, aluminum and copper-doped.	REACH prereg
Solid solution Doped	**101357-01-1** 309-898-1	Cadmium selenide (CdSe), solid solution with **cadmium sulphide**, zinc selenide and zinc sulfide, copper and manganese-doped.	REACH prereg.
Solid solution Doped	**101357-02-2** 309-899-7	Cadmium selenide (CdSe), solid solution with **cadmium sulphide**, zinc selenide and zinc sulfide, europium-doped.	REACH prereg.
Solid solution Doped	**101357-03-3** 309-900-0	Cadmium selenide (CdSe), solid solution with **cadmium sulphide**, zinc selenide and zinc sulfide, gold and manganese-doped.	REACH prereg.
Solid solution Doped	**101357-04-4** 309-901-6	Cadmium selenide (CdSe), solid solution with **cadmium sulphide**, zinc selenide and zinc sulfide, manganese and silver-doped.	REACH prereg.
Solid solution	**12626-36-7** 235-724-8	**Cadmium** selenide **sulphide.**	REACH prereg.
Solid solution	**12656-57-4** 235-758-3	**Cadmium sulfo**selenide orange; **CdS**/CdSe, **CdS**/CdSe/BaSO$_4$ (Se<10%; C.I. Pigment Orange 20; CI 77196).	REACH prereg., Artist´s paint 2013
Solid solution?	**-** **-**	**Cadmium-Barium Orange;** Pigment orange 20:1; **Cadmium** Seleno**sulphide** co-precipitated with barium sulfide.	Artist´s paint 2013
Solid solution	**58339-34-7** 261-218-1	**Cadmium sulfo**selenide red; CdSe/**CdS**, CdSe/**CdS**/BaSO$_4$ (Zn-CdS, Se>10%; C.I. Red 108; Pigment Red 108; CI 77202).	REACH prereg.
Solid solution	**-** **-**	**Cadmium** Barium Selenosulphite; Cadmium Barium **Sulfo**selenide; Cadmium sulphoselenide co-precipitated with barium sulphate; Pigment red 108:1.	Artist´s paint 2013
Solid solution	**8048-07-5** 232-466-8	**Cadmium** zinc **sulphide** Lemon yellow Pigment 35; 40-100% CdS/ZnS, 0-60% BaSO$_4$ (Delta colours 2005).	New Zeeland 2013; DSL 2012; TSCA 2012; Philippines 2012
Solid solution	**12442-27-2** **-**	**Cadmium** zinc **sulphide** yellow; **CdS**/ZnS/BaSO4, **CdS**/BaSO4 (C.I. Pigment yellow 35; CI 77117)	JRC 2013; REACH prereg?; New Zeeland 2013; DSL 2012; TSCA 2012; China 2013; Philippines 2012; Artist´s paint 2013

Encapsulated	102184-95-2 -	Silicic acid, zirconium salt, **cadmium pigment-**encapsulated.	JRC 2013; China 2013
Encapsulated	72968-34-4 277-135-9	Zircon, **Cadmium** Yellow.	REACH prereg., TSCA 2012; Philippines 2012
Doped. Crystal form?	72869-26-2 -	**Cadmium** Zinc **sulphide**, cobalt and copper doped, ((Cd,Zn)S).	Shindengen 2013
Doped. Crystal form?	68876-98-2 272-539-1	**Cadmium sulphide** (CdS), aluminum and copper-doped.	REACH prereg.
Doped. Crystal form?	68876-99-3 272-540-7	**Cadmium sulphide** (CdS), aluminum and silver-doped.	REACH prereg.
Doped. Crystal form?	68891-87-2 272-581-0	**Cadmium sulphide** (CdS), copper and lead-doped.	REACH prereg.
Doped. Crystal form?	68877-00-9 272-541-2	**Cadmium sulphide** (CdS), copper chloride-doped.	REACH prereg.
Doped. Crystal form?	68877-01-0 272-542-8	**Cadmium sulphide** (CdS), silver chloride-doped.	REACH prereg.
Crystal form?	11112-63-3 234-342-9	**Cadmium** selenide **sulphide.**	REACH prereg.; Shindengen 2013
Crystal form?	72828-62-7 -	Zirconium **cadmium** selenium **sulphide** red; Zircon Cadmium Red.	China 2013, Shindengen 2013
Crystal form?	99749-34-5 -	Zircon, **Cadmium** Orange.	Shindengen 2013
Crystal form?	68859-25-6 -	**Cadmium sulphide;** Pigment Yellow 37; CdS·ZnS. *Unclear chemical specification*	DSL 2012; Philippines 2012; Artist´s paint 2013
Crystal form?	12213-70-6 -	**Cadmium** selenide **sulphide,** Cd_2SeS.	Shindengen 2013
Crystal form?	12214-12-9 -	**Cadmium** selenide **sulphide,** Cd_2SeS.	Shindengen 2013
Crystal form?	71243-75-9 -	**Cadmium** selenide **sulphide,** $CdSe_{0.53}S_{0.47}$	Shindengen 2013
Crystal form?	- -	Kibeni Orange; **Cadmium** glass powder.	Artist´s paint 2013
Crystal form?	117912-89-7	$Cd_{0.55}S_{0.45}$	Shindengen 2013
Crystal form?	117912-90-0	$Cd_{0.53}S_{0.47}$	Shindengen 2013
Crystal form?	117912-91-1	$Cd_{0.52}S_{0.48}$	Shindengen 2013

11 RISK-RELATED INFORMATION

An EU risk assessment is available for cadmium metal and cadmium oxide (ECB, 2007). It was concluded that there was a need for limiting the risks for both workers, consumers (only Cd, not CdO) 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 $\mu g/m^3$ (respirable fraction). Further, a biological limit value in urine is suggested: 2 $\mu g/g$ creatinine. It may be noted that a lower value, 1 $\mu g/g$ 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

In the CSA, the suggested IOEL of 4 $\mu g/m^3$ (respirable fraction) has been used as a DNEL. Although the exposure assessments from the EU RAR (on Cd and CdO) 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 $\mu g/g$ 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 2009, 2012)

The European Food Safety Authority (EFSA) has recently updated their exposure and risk evaluation of cadmium (EFSA 2009, 2012), see summary/abstract below.

SUMMARY (EFSA 2009)
Cadmium (Cd) is a heavy metal found as an environmental contaminant, both through natural occurrence and from industrial and agricultural sources. Foodstuffs are the main source of cadmium exposure for the non-smoking general population. Cadmium absorption after dietary exposure in humans is relatively low (3–5 %) but cadmium is efficiently retained in the kidney and liver in the human body, with a very long biological half-life ranging from 10 to 30 years. Cadmium is primarily toxic to the kidney, especially to the proximal tubular cells where it accumulates over time and may cause renal dysfunction. Cadmium can also cause bone demineralisation, either through direct bone damage or indirectly as a result of renal dysfunction. After prolonged and/or high exposure the tubular damage may progress to decreased glomerular filtration rate, and eventually to renal failure. The International Agency for Research on Cancer has classified cadmium as a human carcinogen (Group 1) on the basis of occupational studies. Newer data on human exposure to cadmium in the general population have been statistically associated with increased risk of cancer such as in the lung, endometrium, bladder, and breast. Cadmium bioavailability, retention and consequently toxicity are affected by several factors such as nutritional status (low body iron stores) and multiple pregnancies, preexisting health conditions or diseases.
A health based guidance value for cadmium of 7 μg/kg body weight (b.w.) per week (Provisional Tolerable Weekly Intake (PTWI)) was established previously by the Joint FAO/WHO Expert Committee on Food Additives and endorsed by the Scientific Committee for Food. Although available data indicated that most individuals had intake levels below this PTWI, several international bodies recognised that the margin between this PTWI and the actual weekly intake of cadmium by the general population was small and in some populations may be non-existent. The Scientific Panel on Contaminants in the Food Chain (CONTAM) was asked by the European Commission to assess the risks to human health related to the presence of cadmium in foodstuffs. To provide an updated assessment of exposure from foodstuffs, about 140,000 data covering the period from 2003 to 2007 on cadmium occurrence in various food commodities were received from 20 Member States and considered by the CONTAM Panel. The highest cadmium concentrations were detected in the following food commodities: seaweed, fish and seafood, chocolate, and foods for special dietary uses. For most foods only a small percentage of the analysed samples (<5 %) exceeded the maximum level (ML), where specified. Up to 20 % of the samples were above the MLs for celeriac, horse meat, fish, bivalve molluscs other than oysters and cephalopods. Highly contaminated areas may show higher cadmium concentrations in locally produced food and the use of cadmium-containing fertilisers in agriculture increases cadmium concentrations in the crops and derived products.
To assess cadmium dietary exposure, the occurrence data and the consumption data as reported in the EFSA's Concise European Food Consumption Database were used. National food consumption dietary surveys were used to estimate the consumption pattern of specific sub-groups such as vegetarians and children. The food groups that contributed to the major part of the dietary cadmium exposure, primarily because of the high consumption, were cereals and cereal products, vegetables,

nuts and pulses, starchy roots or potatoes, and meat and meat products. The mean dietary exposure across European countries was estimated to be 2.3 µg/kg b.w. per week (range from 1.9 to 3.0 µg/kg b.w. per week) and the high exposure was estimated to be 3.0 µg/kg b.w. per week (range from 2.5 to 3.9 µg/kg b.w. per week). Due to their high consumption of cereals, nuts, oilseeds and pulses, vegetarians have a higher dietary exposure of up to 5.4 µg/kg b.w. per week. Regular consumers of bivalve molluscs and wild mushrooms were also found to have higher dietary exposures of 4.6 and 4.3 µg/kg b.w. per week, respectively. Tobacco smoking can contribute to a similar internal exposure as that from the diet. House dust can be an important source of exposure for children. Cadmium levels in urine are widely accepted as a measure of the body burden and the cumulative amount in the kidneys. The CONTAM Panel carried out a meta-analysis on a selected set of studies to evaluate the dose-response relationship between urinary cadmium and urinary beta-2-microglobulin (B2M). B2M, a low molecular weight protein, is recognized as the most useful biomarker in relation to tubular effects. A Hill model was fitted to the dose-response relationship between urinary cadmium and B2M for subjects over 50 years of age and for the whole population. From the model, a benchmark dose lower confidence limit for a 5 percent increase of the prevalence of elevated B2M (BMDL5) of 4 µg Cd/g creatinine was derived. A chemical-specific adjustment factor of 3.9, to account for inter-individual variation of urinary cadmium within the study populations, was applied, leading to a value of 1.0 µg Cd/g creatinine. Such a value was also supported by data from occupationally exposed workers and by the results of several individual studies using a variety of biomarkers.

A one-compartment model was fitted to a large data set based on non-smoking Swedish women (age range from 58 to 70 years), comprising both measurement of dietary cadmium exposure and urinary cadmium concentration to allow an estimation of the relationship between the two. The dietary cadmium exposure that corresponds to the critical urinary cadmium concentration of 1 µg/g creatinine after 50 years of exposure was then estimated using the model. In order to remain below 1 µg Cd/g creatinine in urine in 95 % of the population by age 50, the average daily dietary cadmium intake should not exceed 0.36 µg Cd/kg bw, corresponding to a weekly dietary intake of 2.52 µg Cd/kg b.w. The model calculation took into consideration the human variability in absorption rates (1–10 %) so that high absorption rates common in women of reproductive age groups due to high prevalence of low and empty iron stores as well as variations in half-life were included. Because the data used in the dose-response and kinetic modelling relate to an early biological response and a sensitive population, respectively, no adjustment or uncertainty factor was required for individual variability in susceptibility. Therefore, the CONTAM Panel established a tolerable weekly intake (TWI) for cadmium of 2.5 µg/kg b.w.

The mean exposure for adults across Europe is close to, or slightly exceeding, the TWI of 2.5 µg/kg b.w. Subgroups such as vegetarians, children, smokers and people living in highly contaminated areas may exceed the TWI by about 2-fold. Although the risk for adverse effects on kidney function at an individual level at dietary exposures across Europe is very low, the CONTAM Panel concluded that the current exposure to Cd at the population level should be reduced.

ABSTRACT (EFSA 2009)
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.

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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 (KemI 2011 and references therein)

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 (Johnson et al 2003), was further explored in humans (Åkesson et al 2008). 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 (KemI 2011).

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 (Åkesson el al 2008).

In a collaboration project between toxicologists and epidemiologists the possible mechanism of the 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 (KemI 2011).

In a further study on ovariectomized mice, estrogenic effects of cadmium administered in food or as oral intake of cadmium chloride were compared. The results suggest significantly lower absorption/retention of dietary cadmium compared to $CdCl_2$ following oral exposure. The estrogenic effects after dietary exposure of Cd were less pronounced and no increase in uterine weight was observed (Ramachandran et al 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).

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