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EUROPEAN ASSOCIATION OF METALS

International Cadmium Association

Management of the Risks Related to Chronic Occupational Exposure to Cadmium and its Compounds 2013- Revision

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2013 Revision

1. Purpose

The purpose of this document is to supply guidance to occupational medical doctors and management of plants in which cadmium and hazardous cadmium compounds are being processed, manufactured, transformed, incorporated into articles or recycled, with the purpose of bringing Cd exposure of all employees down, resulting in a urinary cadmium level below 2 µg Cd/ g creatinine.

This biomarker level is the health-based threshold proposed by the Scientific Committee on Occupational Exposure Limits (SCOEL) in 02/2010[1] to be set at EU level in an upcoming amendment to directive 98/24/EC or 2004/37/EC with the purpose of setting both an OEL (occupational exposure limit value) and a BLV (biological limit value) for cadmium and compounds for the protection of workers.

2. Structure

This Industry Guidance rests on three pillars:

1. Ensure plant cleanliness,
2. Implement collective and individual hygiene procedures,
3. Conduct medical surveillance of exposed workers, including bio-monitoring of both urinary cadmium and blood cadmium, as a safety net to detect any issue arising in pillars (1) and (2) before any adverse effect is likely to arise.

To achieve the best results, these three pillars need to be implemented concurrently.

Should equipment changes be conducted, preference should be given to equipment designs which address cleanliness performance at the onset of equipment startup, over a stepwise improvement process, which may not be able to reach the desired performance.

Should hygiene policies need to be reinforced; this can only be implemented in a stepwise, progressive manner, to ensure proper buy-in by employees and true long term behavioral changes.

Strengthened medical surveillance should be implemented swiftly; but needs to take into consideration the ability of a plant to reassign workers to non-exposed positions, should a revised (relative to the 2006 issue) biomarker-based action level increase the number of workers which ought to be displaced to a non-Cd exposed work position.

3. Ensuring plant cleanliness

Plant cleanliness, whether it is (a) eliminating cadmium deposit on surfaces or (b) ensuring inner air quality, is the foundation of any chemical risk management program.

[1] See SCOEL SUMDOC 136

3.1. Eliminating cadmium deposits on all surfaces

This involves the usual, but sometimes overlooked, requirement that floors, structures, machines, change rooms be kept tidy, so as to ensure that cadmium containing dust deposited onto surfaces cannot be remobilized by air movements into the working environment nor picked up by physical contacts.

In practical terms, adequate equipment and proper routines need to be set up so as to ensure these goals are achieved.

These routines should include, inter alia:

- *Choosing the floor coating color* which helps spotting any deposits (choose a floor coating colour which contrasts with the Cd compound being controlled),
- *Acquiring floor scrubbers*, and putting in place the adequate cleaning routines (preferably involving water spraying to avoid remobilization of dust to air),
- *Setting up negative pressure piping* with permanent/moveable click-on suction hoses,
- *Implementing regular routine addressing structure clean-up*,
- *Include machine clean-up at the end of each shift* in the shift ending procedure.
- *Handling of contaminated defect equipment* – cleaning or isolating before it is sent to the workshop

3.2. Ensuring workplace air quality

Selecting the workplace OEL:
Until recently, complying with the national OEL (be it guidance or binding) was the voluntary or mandatory strategy in countries where such an OEL did exist.

However in 2010, SCOEL gave its view as to what the EU-wide health-based OEL should be. Although as of today, EU institutions have not yet acted on this by adopting a legislative instrument, the Cadmium consortium and lead registrants of Cd and compounds brought this proposed OEL forward as the DNEL in the REACH registration dossiers of these substances.

For this reason, this DNEL becomes legally binding on Producers and Downstream Users.

The DNEL of the cadmium and compounds REACH registration dossiers is **4 µg/m3 (respirable).**

Ensuring compliance:
In order to comply with this DNEL, equipment upgrade may be required and should include, inter alia, a combination of the following adjustments:

- *Installing plant wide piping,* connected to negative pressure ventilation, along with adequate filtration before air is released to the outside atmosphere,
- *Placing machinery within negative pressure enclosures* where feasible,
- *Installing, when and where appropriate, suction heads* in places where cadmium releases occur (this should be preferred over ensuring a building-wide air circulation and replacement speed),
- C*onduct local adequate air flow studies before new equipment is installed* so as to ensure adequate air speed is obtained at the opening of each suction head,
- C*onduct section wide air flow studies when plant layout is modified*. These should cover heating and ventilation issues so as to understand and control the air flow (along with related costs) with this equipment in mind.

In cases, where it is impossible to maintain exposure at all times below the occupational exposure limit, or during intervention or particular maintenance work with risk of exposure respiratory protection devices with P3 efficiency level[1] shall be worn. It is recommended to provide blower supported devices. For tasks of up to 2 hours normal half or full masks can be used.

4. Reinforcing collective and personal hygiene procedures, including training

Even with the strictest adherence to adequate plant cleanliness practice, small particles can still occur at the workplace. It is known that once the inhalation route is placed under control through compliance with workplace air quality requirements (compliance with the DNEL), the ingestion route may become the predominant route of cadmium intake into the organism.
In order to limit this intake, plants must develop and implement the proper hygiene procedures, both at collective and individual level.

4.1. At collective level, plants need to develop several actions:

Amongst such actions, the following should be noted:

- *Conduct initial training on cadmium related risks:* how to mitigate it, the importance of complying with rules and policies,
- *Conduct refresher training on these issue on a regular basis:* preferably yearly,
- *Set up dual compartment change closets:* preferentially with separate change rooms for the city clothes side and the work clothes side, separated by a shower section,
- *Have employer supplied work clothes:* with adequate frequency of clean clothes supply (from weekly to daily depending on the area), taking into account the differing requirements of male/female employees as well as the specific requirements for the different seasons of the year. This should also include company supplied laundry service, so that dirty clothes do not find their way into the home of employees.

4.2. At individual level: several requirements need to be implemented:

Amongst these requirements, the following should be noted:

- *The requirement to comply with the above mentioned collective hygiene procedures,*
- *The requirement to take a shower after the end of each shift:* which requires that an adequate number of showers is made available, so as not to discourage employees from showering,
- *The requirement to only smoke, snack and drink in designated areas*, these activities must not occur within work areas,
- *The requirement to wash one's hands before all meals*, snacks and breaks,
- *An encouragement to stop smoking, biting nails and to avoid growing facial hair*, these being habits which favor the accumulation and transfer of cadmium into the organism,
- *The requirement to store all personal objects* (keys, cell phone, cigarette packs…) in dedicated lockers outside of the work area.

[1] for efficiency levels see EN 143

5. Strengthening medical surveillance

If all procedures indicated above are properly implemented, risks of cadmium adverse effects are controlled.

However, since cadmium is a cumulative toxicant, even minute, occasional uptakes (due to either equipment malfunction or procedural non-compliance) can be a source of cadmium accumulation for workers, which may create a risk.

It is therefore necessary to install complementary medical measures for the control of risks e.g. :

- The identification of a preexisting condition (e.g. existing kidney condition…) which renders the worker unfit to cadmium exposure,
- The identification of individuals that, in spite of general measures taken, seem still to accumulate Cd in the body. This is detected in an early stage by proper monitoring of biomarkers of Cd exposure. By these parameters, possible changes of biomarkers (subclinical) can be identified.

5.1. Identification of employees covered

All employees under a risk of exposure to cadmium, whether on a permanent basis or occasional basis, throughout their work day, are to be identified by plant management and the occupational medical doctor. The medical monitoring of employees who have been exposed to cadmium and have been removed from exposure for medical reasons needs to be continued.

5.2. "Exposure biomarkers" and their uses

Cd-B (Cd concentration in blood) is a biomarker which is influenced both by total exposure (integrated over 20 years) and recent exposure (over the past 3 months), both from ingestion and inhalation. However the variation of Cd-B over two consecutive dates if less than a year apart reflects recent exposure, and its sensitivity to recent exposure, in both directions (up or down), is quite high.

Cd-B should therefore be used to detect an equipment dysfunction or a poor implementation of hygiene policies which happened over the past 3 months.

Cd-U (Cd concentration in urine) is a biomarker which reflects total exposure of the worker over a period of 20 years. It integrates both ingestion and inhalation. There is a direct proportion between urinary clearance of cadmium and cadmium load in the kidney, which above certain levels may induce tubular dysfunction.

Cadmium half-life in the kidney is approximately 20 years. Therefore this biomarker varies quite slowly over time.

Cd-U should therefore be used to assess whether an exposed worker total exposure brings him to a situation in which his risk to develop a tubular dysfunction is increased over a non-exposed worker.

To ensure good correction for urine dilution, and ensure this indicator is meaningful, this biomarker needs to be standardized by means of a creatinine measurement.

Figure 1. Urinary RPB as a function of Cd in urine *(adapted from Chaumont et al 2011)*.

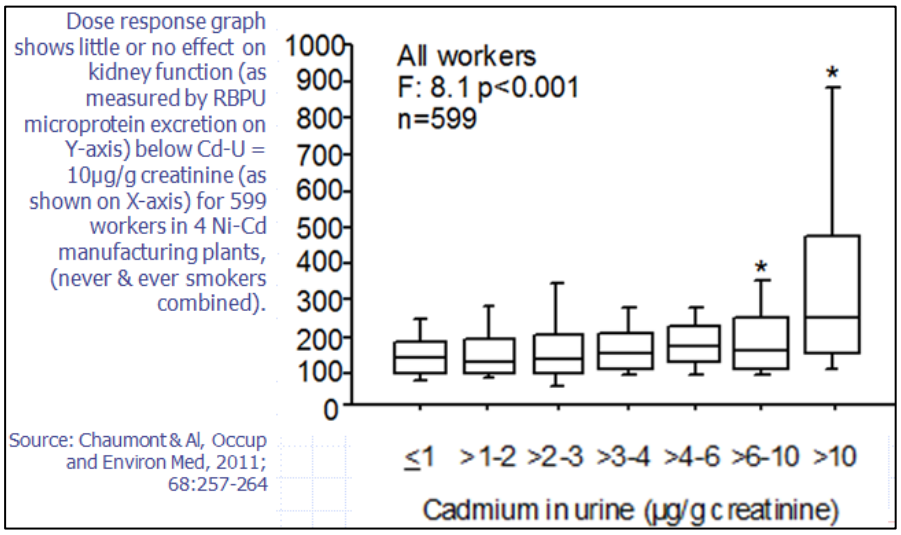


Figure 1 indicates that no degradation of the kidney tubular reabsorption (as measured by urinary RBP) function occurs if cadmium in urine is maintained below the 5 to 10 µg Cd / g creatinine level

5.3. <u>"Effect biomarkers" and their uses</u>

In order to measure the actual decrease in kidney functionality, and more specifically on tubular reabsorption, the urinary clearance of one amongst several proteins is measured.

The most commonly used proteins for this purpose are:

- Retinol binding protein (RBP)
- Alpha 1 microglobulin (α1 microglobulin also called protein HC)
- Beta 2 microglobulin (β2M)

In table 1 is the guideline given to interpret the results of microprotein excretion.

Table I. Interpretation of elevated values of urinary β_2-microglobulin (β_2-M) and retinol-binding protein (RBP) induced by occupational or environmental exposure to Cd

β_2-M or RBP in urine (µg/g creatinine)	Significance
< 300	Normal value
300 - 1,000	Incipient Cd tubulopathy (possibility of some reversal after removal of exposure if urinary Cd is not too high *i.e.* below 20 µg/g cr)
1,000-10,000	Irreversible tubular proteinuria that may accelerate the decline of glomerular filtration rate with age. At this stage glomerular filtration rate is normal or slightly impaired.
>10,000	Overt Cd nephropahy usually associated with a decreased glomerular filtration rate

Modified from Ref. 4

Source table I: Bernard A. Cadmium & its adverse effects on human health. Indian J Med Res. 2008; 128(4):557-64. Review.
Ref 4= Bernard A. Renal dysfunction induced by cadmium: biomarkers of critical effects. Biometals 2004; 17: 519-23.

5.4. <u>Using "exposure biomarkers" to conduct adequate advanced medical surveillance</u>

5.4.1. <u>Using Cd-U:</u>

- **Cd-U =< 2 µg Cd/g creatinine,** [2 µg Cd/g creatinine is a conservative threshold (and action level) based on general population studies (green zone, see Figure 2)]:
  - general medical follow-up is conducted along with regular measures of the exposure indicators Cd-U, Cd-B and the subclinical effect BI (urinary protein excretion measurement),

  - no further special action is required beyond proper implementation of the general hygiene procedures and medical surveillance.

- **2 µg Cd /g creatinine < Cd-U =<5 µg Cd/g creatinine**, [5 µg Cd/g creatinine is a 2nd threshold (and action level) based on studies at the workplace (orange zone, see Figure 2)]:
  - general medical follow-up is conducted along with regular measures of the exposure indicators Cd-U, Cd-B and the subclinical effect BI (urinary protein excretion measurement),
  - and a detailed analysis of the related workplace (by plant maintenance) along with an assessment of collective (by area supervisor) and individual hygiene procedures implementation, including training are conducted (by occupational doctor).

- **Above Cd-U > 5 µg Cd/g creatinine** (red zone, see Figure 2):
  - worker is removed from cadmium exposure.

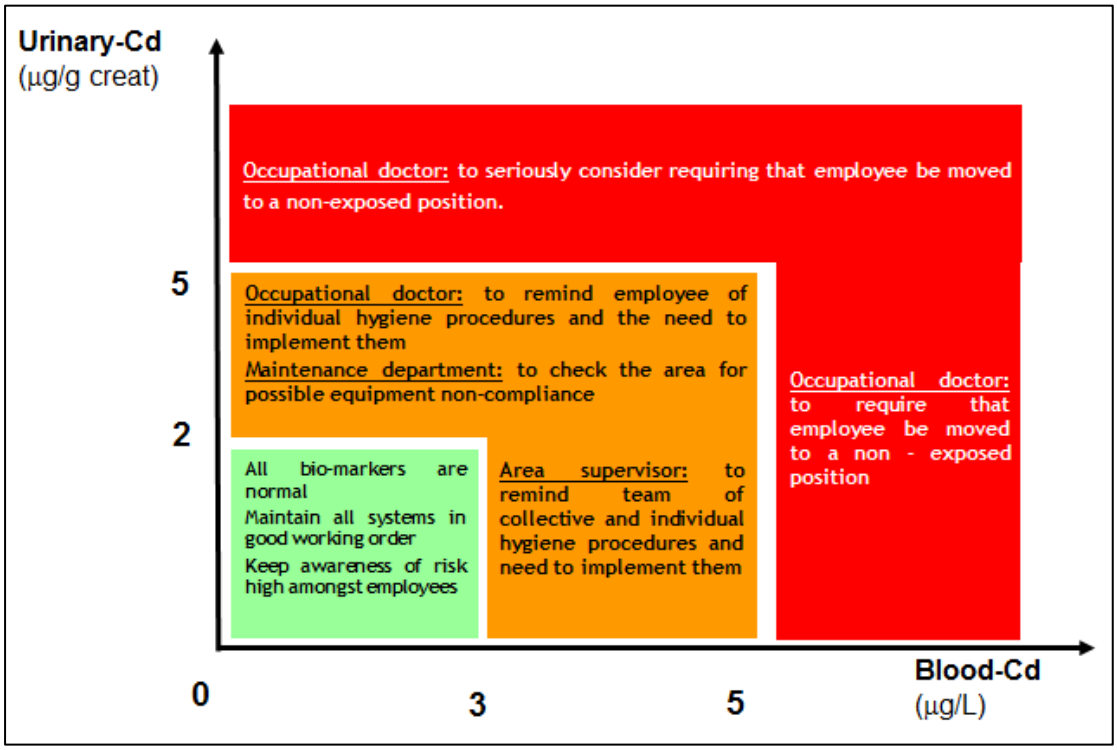
5.4.2.Using Cd-B:

As indicated under 5.2., Cd-B is function of both the Cd body burden (and as such partially proportionate to Cd-U) and of recent exposure.
Cd-B is used as a complementary biomarker mainly to identify recent accumulation (approximately within the preceding 3 months window). Cd-B is evaluated as follows:

- **A rapid increase of Cd-B towards 3 µg Cd/L or the exceedance of an action level of 3 µg Cd/L** triggers a detailed analysis of the related workplace (by plant maintenance) along with an assessment of collective (by area supervisor) and individual hygiene procedures implementation, including training (by occupational doctor),

- **A rapid increase of Cd-B towards 5 µg Cd/L or the exceedance of an action level of 5 µg Cd/L** triggers the removal of the worker from exposure.

Figure 2. Decision diagram:



5.4.3. Using the effect biomarker (β2-M, RBP or protein HC):

In all situations, if the effect biomarker is exceeding the reference value or shows a consistent pattern of increase, which may lead to approaching the reference value (300 µg/g creatinine for beta-2 microglobulin (β2-MG) and retinol binding protein (RPB), or 700 µg/mmol creatinine (=6200 µg/g creatinine) for alpha-1 microglobulin (α1-microglobulin or protein HC), the worker is removed from cadmium exposure.

6. Practical considerations

Cadmium occupational risk management programs and their medical surveillance compartment have been progressively implemented and strengthened in the EU Cd industry over the last decades. Workers that have been exposed to cadmium at earlier stages of their implementation have their situation reviewed by the supervising occupational doctor on a case by case basis. In all cases, when subclinical effect biomarkers approach or exceed the reference values (see 5.4.3.), workers are removed from exposure.

7. OCdBio[2]: Present-day exposure to Cadmium at the workplace

For the purpose of monitoring industry progress in workplace management, members of ICdA commit to report to the Association the anonymized results of exposure biomarkers monitoring.

[2] OCdBio: Observatory of Occupational Cadmium Biomarkers

These results are consolidated at industry level with the purpose of generating a complete picture of worker exposure, tracking progress towards the goal of further reducing occupational exposure of the employees that industry has set:

- **95% of European employees** subject to medical surveillance and bio-monitoring as required by their occupational medical doctor, below the urinary cadmium level of: **2 µg Cd/g creatinine by the end of 2017,**
- **98% of European employees** subject to medical surveillance and bio-monitoring as required by their occupational medical doctor, below the urinary cadmium level of: **2 µg Cd/g creatinine by the end of 2020**

This dataset allows also each site to benchmark its individual results with the overall industry distribution.

Under the OCdBio program, complementary anonymous information may also be requested from ICdA members, such as:

- biomarker distributions broken down by duration of exposure categories, in order to ensure biomarkers do go down over time within a similar duration of exposure,
- distribution of Cd-air values, to ensure workplace air quality is compliant with the DNEL,
- other information as deemed appropriate by the Association.

References:

- Bernard A (2004). Renal dysfunction induced by cadmium: biomarkers of critical effects. Biometals, 17: 519-23.
- Bernard A (2008). Cadmium & its adverse effects on human health. Indian J Med Res., 128(4):557-64. Review.
- Chaumont A, De Winter F, Dumont X, Haufroid V and Bernard A (2011). The threshold level of urinary cadmium associated with an increased urinary excretion of retinol-binding protein and β2-microglobulin: a re-assessment in a large cohort of nickel-cadmium battery workers. Occupational and environmental medicine, 68(4):257-264.
- Directive 98/24/EC of 7 april 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC)
- Directive 2004/37/EC of 29 April 2004 on the on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (Sixth individual Directive within the meaning of Article 16(1) of Council Directive 89/391/EEC)
- European standard EN 143- Respiratory protective devices - Particle filter - Requirements, testing, marking
- Scientific Expert Group on Occupational Exposure Limits (SCOEL) (2010). Recommendations from the scientific expert group on occupational exposure limits for cadmium and its inorganic compounds. SCOEL/SUM/136.