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Occupational exposure to Cadmium and Chromium(VI) through multiple sources and routes

Tutors

Prof. Daniele Martinelli
Prof. David Vernez
Prof. Florian Breider
Dott. Hasnaa Chettou

Candidate

Federica Scarpelli

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Abstract

In a context of growing attention towards chemical risk management, this thesis is part of the European PARC project (Partnership for the Assessment of Risks from Chemicals), focusing on the assessment of aggregate exposure to Cadmium (Cd) and Hexavalent Chromium (Cr(VI)), known for their toxic and carcinogenic effects. The activity mainly concerned the analysis of occupational exposure through the processing of data provided by SUVA (Swiss National Accident Insurance Fund), combining bio-monitoring and exposure modeling approaches. Specific scenarios were defined for homogeneous exposure groups (HEG), on which predictive modeling of external doses was applied. The analysis showed significant differences between occupational groups, gender, and age ranges, as well as a general trend of decreasing concentrations of Cd and Cr(VI) over time. The results obtained will be converted using PBPK models and subsequently aggregated to improve the definition of chemical risk, and finally compared with bio-monitoring data.

Keywords: Cadmium, Chromium(VI), Homogeneous exposure group, Exposure assessment, Occupational exposure, Bio-monitoring, Modeling, SUVA.

1 Introduction

1.1 Context: PARC Project

In a context where the production and use of chemicals is constantly evolving, chemical risk management represents a central challenge for the protection of human health and the environment. The European Chemicals Agency (ECHA) plays a fundamental role in implementing EU legislation on chemicals to ensure their safe use throughout Europe. In particular, ECHA is responsible for collecting and evaluating the registrations of chemicals submitted by manufacturers and importers, ensuring their compliance with the regulatory requirements established by the REACH regulation. Despite existing regulations having significantly improved chemical safety in Europe, integrating scientific advancements and innovative approaches in hazard and exposure assessment remains a complex challenge. In this context, structured collaboration between risk assessors, regulatory authorities, and the scientific community is essential to translate research innovations into effective regulatory tools. It is precisely to address these challenges and enable the transition to next-generation risk assessment that the Partnership for the Assessment of Risks from Chemicals (PARC) was developed. PARC involves around 200 institutions operating in the fields of environment and public health in 28 countries, along with three EU authorities, including the European Chemicals Agency (ECHA), the European Food Safety Authority (EFSA), and the European Environment Agency (EEA). The partnership is coordinated by ANSES (the French Agency for Food, Environmental and Occupational Health & Safety) and involves public partners from across Europe.
The project is organized into nine work packages (WP) that work to achieve three specific objectives [1]:

- develop the scientific knowledge necessary to address current and future challenges in chemical safety,
- provide new data, methods, and innovative tools to those responsible for the assessment and management of risks from chemical exposure,
- strengthen networks that bring together actors specialized in the various scientific fields that contribute to risk assessment.

The proposed thesis is the framework of WP6, which promotes innovation in chemical risk assessment by integrating next generation risk assessments. In particular, it will support activity A6.2.1, *"Aggregate exposure assessment from multiple sources and pathways for the general population and workers"*, within task T6.2 on *"Integrative exposure and risk assessment"*. The activity objectives were divided in two projects: P6.2.1a_Y1_VITO "Source-to-dose" and P6.2.1b_Y1_ANSES "Aggregate exposure". The former project aims to improve knowledge and models of chemical transfers from emission sources to exposure sources in the general environment, while the latter project aims to advance knowledge on the combination of exposures from occupational and general environments [1].

As part of activity A6.2.1, PARC gives priority to the analysis of the following families of contaminants: PFAS, heavy metals, pesticides, mycotoxins, and plasticizers. In this context, the thesis focuses on heavy metals, with particular attention to cadmium and chromium (Section 1.2).

1.2 Exposure to Cadmium and Chromium

Cadmium (Cd) and chromium (Cr) are two heavy metals widely known for their toxic effects on human health, both classified as carcinogenic to humans (group 1) by the International Agency for Research on Cancer (IARC) [19].

The choice to focus attention on Cd and Cr is based on a series of criteria. First of all, for these heavy metals there is a wide base of existing knowledge regarding human exposure, which makes it possible to develop more effective models for assessing aggregate exposure. Another important element is the availability of bio-monitoring data, which shows the presence of these contaminants in the human body, offering a starting point for analysis. Finally, Cd and Cr are relevant both in the general environment, through pathways such as food, air, or consumer products, and in the occupational environment, making an aggregate study necessary for a complete understanding of total exposure.

1.2.1 Cadmium: sources, exposure routes and health effects

Cd is a silver-white tinged lustrous metallic solid. The metal is a natural element present in the earth's crust, usually found combined with other materials such as oxygen, chlorine or sulfur and associated with zinc minerals. Cd is obtained as a by-product principally in the refining of zinc and to a lesser extent during the refining of copper and lead, from sulfide ores [26]. The element is mainly used in the production of electric batteries, as well as in the manufacture of pigments, coatings, plastic stabilizers, and welding, essentially stainless steel welding. Additionally, it is also used in cadmium plating, a process in which materials are coated with a layer of metallic Cd for protective and aesthetic purposes [16].

Cd is highly dangerous for humans, who can come into contact with it through the three main routes of exposure: inhalation, dermal contact, and ingestion. The general population can be exposed to small amounts of Cd through diet, tobacco smoking, water, and air. Exposure through diet occurs via the consumption of contaminated foods such as fruits and vegetables, which can contain toxic metals, and when ingested, they can cause long-term damage. In general, plants absorb essential metals like iron (Fe) and zinc (Zn) as nutrients for their growth; however, at the same time, other non-essential metals, such as Cd, are absorbed and accumulated in the roots and edible parts, creating a source of accumulation for consumers [9]. Another route of exposure is inhalation, especially for the smoking population. Cd is a key component of tobacco due to the tendency of *Nicotiana* species to concentrate it. The typical range of Cd in tobacco is 1-2 μg/g of dry weight, equivalent to 0.5-1 μg per cigarette. Furthermore, the oxide generated during the combustion of cigarettes is highly bio-available, with about 10% being deposited in lung tissues and another 30-40% absorbed into the systemic bloodstream. Cd levels in the blood are estimated to be 4-5 times higher in smokers compared to non-smokers [28]. Even in non-smoking populations, a small amount of Cd can be inhaled, in the form of airborne particles lifted into the air by the wind or in contaminated air, especially near emitting industries [38].

Professional exposure to Cd occurs in production and refining plants (smelters), in the production and recycling of nickel-cadmium batteries, in pigment production and formulation plants, in the production of Cd alloys, in mechanical plating, in Zn smelting, in brazing with silver solder containing Cd, and in polyvinyl chloride production factories [23].

Based on epidemiological studies and experiments, an increased incidence of lung cancer has been identified after prolonged inhalation of Cd dust, along with an increased risk of prostate and kidney cancer and chronic kidney disease [11], [25]. In particular, Cd absorbed by the body tends to accumulate in the kidneys and in the liver and, to a lesser extent, in the bones, muscles, and skin. The body burden gradually increases with age due to the long half-life of cadmium: 4-19 years in the liver and 10-20 years in the kidneys [5]. Although only a small portion is excreted in the urine, the concentration of Cd in urine is closely related to the amount accumulated in the kidneys.

Cd can be monitored through blood samples and urine tests. In particular, Cd in the blood reflects recent exposure (in the past 36 months), while urinary Cd is the main indicator used in long-term risk management, as it reflects chronic exposure and body burden.

ANSES sets a pragmatic biological limit value (BLV) for occupational populations, based on tubular toxicity, of 5 μg of Cd/g of creatinine (Kr) in urine; and a pragmatic BLV for Cd in blood of 4 μg/L. For the general population, it establishes a biological reference value (BRV) of 0.7 μg/L for non-smokers and 3 μg/L for smokers [5]. SUVA sets a biological tolerance value (BAT - Biologischer Arbeitsstoff-Toleranzwert) of 2.01 nmol Cd/mmol Kr [31].

1.2.2 Chromium: sources, exposure routes and health effects

Cr is a silver-gray metallic element, shiny, hard, and brittle, which can be highly polished. In nature, it is mainly found in its trivalent oxidation state, often combined with iron and other metallic oxides, such as from chromite ores, from which it is mainly extracted [22].

Although Cr exists in several oxidation states, the zero or metallic Cr(0), trivalent Cr(III), and hexavalent Cr(VI) forms are the most relevant for commercial applications and environmental aspects.
Cr(0) is mainly used in the production of alloys, while Cr(III) and Cr(VI) are used in chrome plating, as well as in the production of pigments, dyes, and paints.
While Cr(III) is generally stable and has low toxicity, Cr(VI) is a known carcinogen. Exposure to Cr can occur through the ingestion of contaminated food and water, inhalation of polluted air in the workplace, or contact with dust, fumes, mists, or solutions containing Cr or its compounds. Occupational exposure often includes both Cr(III) and Cr(VI). It has been shown that when inhaled, Cr compounds cause irritation of the airways, and more seriously, cumulative exposure to Cr(VI) has been linked to an increased risk of lung cancer [17]. Furthermore, it has been observed that chronic exposure can lead to the accumulation of Cr in the proximal tubules, resulting in nephrotoxicity and permanent kidney damage [18].
The absorption and accumulation of Cr(VI) depends on the exposure route and the physicochemical properties of the compound. In general, Cr(VI) is more easily absorbed through the respiratory route, and once inhaled, it tends to deposit in the airways, where it can be eliminated through three main mechanisms: mucociliary transport, phagocytosis, and absorption into the blood or lymph, resulting in accumulation in organs such as the kidneys, liver, and spleen. A portion of Cr is excreted in the urine. After inhalation exposure, it is believed that Cr excretion in urine follows a triphasic process, with half-life of elimination of 7 hours, 15-30 days, and 3-5 years [6].
The concentrations of Cr in urine and blood reflect the total amount of absorbed Cr. While intraerythrocyte Cr reflects exposure to Cr(VI) over the 34 months prior to sampling, urinary Cr is an indicator of recent exposure [8] [20] .
Regarding occupational exposure to Cr, specific biological limit values are established for certain sectors, because the toxicokinetics of Cr compounds vary depending on parameters related to the type of activity, such as particle size, chemical species, and compound solubility.
ANSES sets a BLV of 2.5 μg/L (1,8 μg Cr(VI)/g Kr) for urinary Cr at the end of the shift and at the end of the week in the chrome plating sector; while for the general population, it recommends a BRV of 0,65 μg/L (0,54 μg Cr(VI)/g Kr) [4]. SUVA sets a BAT of 11 g Cr(VI)/l urine [31].

1.3 Exposure Assessment

Exposure Assessment is the process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, as well as identifying the number and characteristics of the population exposed [2], in order to assess potential health risks and the need for preventive interventions. Exposure is assessed through two main approaches:

- Bio-monitoring, involves the direct measurement of the concentration of an agent or its metabolites in biological samples in order to assess the internal dose to which individuals are exposed, thus providing direct evidence of exposure (Section 1.3.1) [32].

- Modeling, involves the use of mathematical or computational models to estimate exposure, simulating the interactions between individuals and the environment (Section 1.3.2) [37].

Additionally exposure assessment often requires the creation of "Exposure Scenarios", which are detailed combinations of facts, assumptions, and inferences that define discrete situations where potential exposures to an agent may occur. These may include the exposure source, the exposed target population, and the time frame of exposure, microenvironment, and activities. Scenarios are often created to aid exposure assessors in estimating exposure [37].

1.3.1 Bio-monitoring

Biological monitoring in humans (HBM) is widely used in the field of occupational and environmental health for exposure assessment, through the measurement of the chemical substance and/or its metabolites in a biological medium (urine, blood, nails, and hair), integrating all possible exposure pathways and sources [32]. This approach allows us to verify if and to what extent the population is exposed to harmful substances. HBM is applied in various fields such as occupational health, essential for assessing the risk of professional exposure to hazardous chemicals that may not be immediately visible but could lead to chronic or acute diseases; and in the field of environmental epidemiology, where it serves as a useful tool to monitor the effects of environmental pollution on the general population. Among the most researched and monitored substances in the occupational population are heavy metals, known for their ability to accumulate in the body and exert toxic effects [36]. These can be absorbed through inhalation, ingestion, and skin contact, depending on the element and the environmental/occupational context. Bio-monitoring of heavy metals is based on the analysis of biological samples from exposed subjects with the aim of quantifying the levels of metal present in the body. The main biological indicators include blood, to monitor recent exposure reflecting the levels of metal immediately available in the bloodstream; urine, representing the accumulation of the metal in the kidneys; and finally, hair and nails, which can provide information on long-term exposure.

1.3.2 Exposure modeling

"Exposure modeling" is defined as a conceptual or mathematical representation of one or more exposure processes [37]. The modeling of exposure to hazardous agents, through the use of specific software tools, makes it possible to predict exposure levels in a given environment even before direct measurements are taken. This approach helps in the planning of investigations and can also be used after a monitoring campaign to evaluate the effectiveness of any prevention measures introduced to reduce exposure. Moreover, it is a key feature in the regulatory process, as it is part of the marketing authorization process.

1.3.3 Exposure aggregation

Aggregate Exposure represents a fundamental concept in chemical risk assessment, defining the total sum of an individuals exposure to a specific substance from various sources (environmental, occupational, dietary, etc.) and routes (ingestion, inhalation, and dermal contact) [3]. This allows to describe more realistically the exposure model encountered by individuals in the real world, as exposures to contaminants do not occur as single, isolated events, but rather as a series of sequential or concurrent events that may overlap in time and space.

1.4 Case study: exposure to cadmium and chromium through multiple sources and routes

The case study contributes to the project P6.2.1b_Y1_ANSES "Aggregate exposure" of Activity A6.2.1 in WP6 of PARC, focusing on the analysis of exposure to Cd and Cr(VI), which are widely known for their toxic effects on human health. These metals can enter the human body through different sources and routes, from environmental or occupational exposure, making it essential to build an aggregated exposure assessment for health effect evaluation.

The analyzed data, therefore, come from two dataset: general and occupational environment. In the first case, related to environmental exposure, the data come from the pilot phase of the Swiss Health Study (SHeS-pilot), whose goal is to assess the feasibility of a national cross-sectional study for public health monitoring in Switzerland. The study was initiated by the Federal Office of Public Health and involved adults aged between 20 and 69 years who underwent human bio-monitoring (urine and venous blood analysis), health examinations (blood pressure, anthropometry, accelerometry, lung function) and questionnaires on health status, environmental exposures, attitudes towards health research, COVID-19, and quality of life [24] [32] [34].

As for the occupational exposure data, these are provided by the Swiss National Accident Insurance Found (SUVA), which is responsible for the prevention of accidents and occupational diseases, work insurance, and health protection. The institution collects data on exposure to various chemical, physical, and biological factors in the workplace, using them to monitor professional health conditions, develop guidelines and preventive measures, and support epidemiological research [30].

The analysis involves an initial processing of the selected data, followed by the creation of exposure scenarios through the identification of specific determinants which will then be used in exposure models. The results obtained will be aggregated and finally compared with real bio-monitoring data.

However, given the widespread nature of the exposure, it is crucial to understand the relative contribution of each source and route of exposure to avoid overestimating the aggregated exposure and prioritize dominant exposure source and routes for effective, targeted risk management measures. For this reason, the traditional method of aggregating exposure, as described above, has been updated with the introduction of the Decision Tree, which systematically defines the most relevant sources and routes of exposure, ensuring a more accurate and realistic assessment of the overall exposure. Figure 1, shows the contribution of the case studies to the development of harmonized method for exposure aggregation.

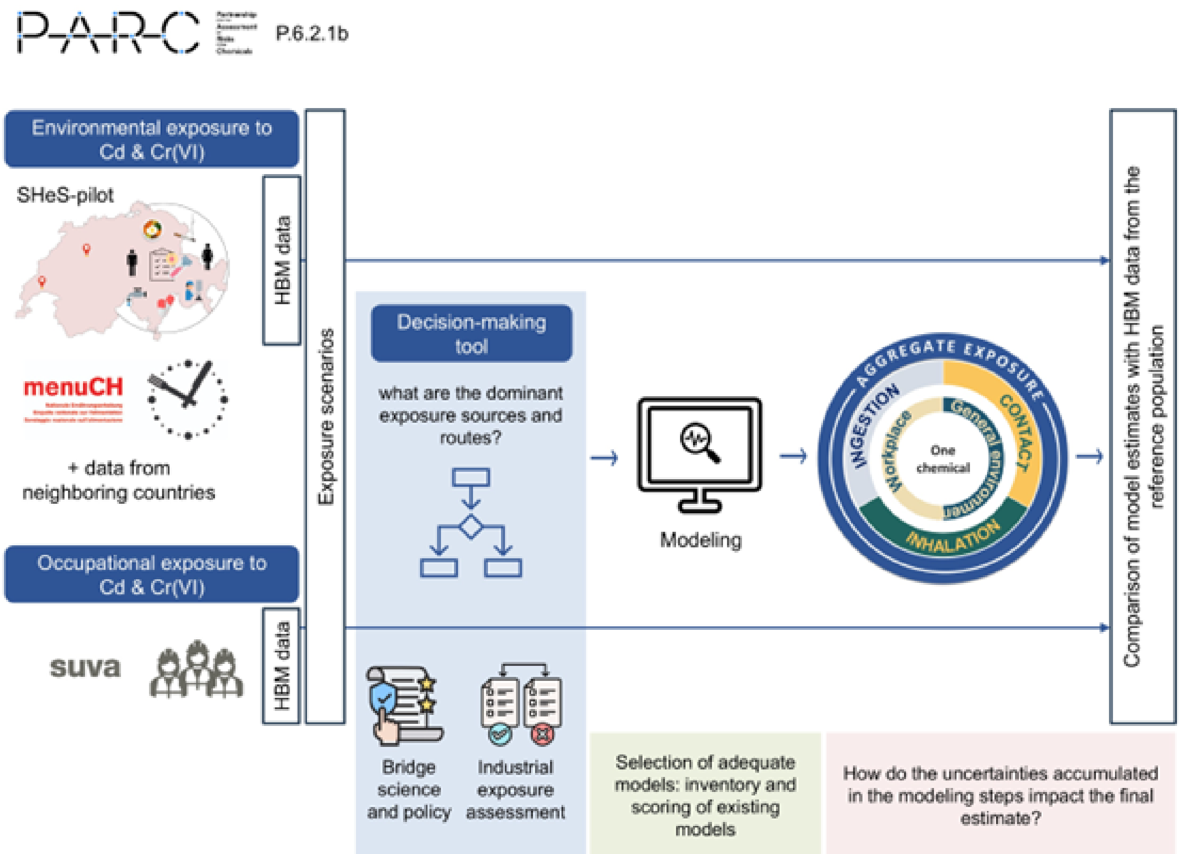


Figure 1: PARC Project. General overview of the contribution od the case studies to the project P6.2.1.b *(Chettou et al. in preparation).*

1.5 Aim

My contribution to the study involves the assessment of occupational exposure and the analysis of bio-monitoring data on Cd and Cr(VI) urinary concentrations, according to the strategy described in Section 2.

In particular, the activity carried out involved the examination and processing of the technical documentation and datasets provided by SUVA, in order to derive, through specific modeling processes, the external doses associated exclusively with the occupational component of the exposure. These doses were then converted, through the application of phisiologically-based pharmacokinetic (PBPK) models, into internal doses; thus obtaining quantitative estimates compatible with the results from other exposure routes and sources. This harmonization allows the integration of the data within the aggregated analysis, facilitating direct comparison with real bio-monitoring data.

2 Materials and Methods

The data were provided by the Swiss National Accident Insurance Fund (SUVA), the organization responsible for managing mandatory medical examinations for certain categories of workers, as outlined in the Ordinance on the Prevention of Accidents and Occupational Diseases (OPA). The study is based on the analysis of two main data sources provided by SUVA:

- Technical documentation, provided for each company, containing the history of the workplace safety, including prevention and monitoring measures.

- Dataset, consisting of 30,291 data points, collected as part of bio-monitoring programs conducted on workers from 149 different companies, over the period between 1989 and 2024, with the goal of preventing health risks in the workplace. The dataset provides information regarding the workers' age (grouped in five-year classes), gender, the company's industry sector and the levels of Cd and Cr(VI) in urine.
  In the dataset, it was necessary to pay attention to the presence of values below the limit of detection (LOD), a threshold below which the analytical instrumentation is not able to provide a reliable measurement. This step is essential to ensure the consistency and reliability of the results. Therefore, the measurements were verified based on their respective LOD values. In particular, for Cr(VI), an LOD = 4 nmol/L was adopted, while for Cd, the LOD = 1 nmol/L. In cases where the observed data were below the respective LOD (i.e., LOD < 4 nmol Cr(VI)/L and LOD < 1 nmol Cd/L), the value was replaced with LOD/2, in order to avoid distortions in future statistical analyses [14].

Considering that each company involved in the study has a variable number of workers, each with different sampling dates ranging from months to years, and that in some cases workers are not continuously monitored, we decide to consider each measurement as an independent unit, so as a unique worker. This approach allows for the preservation of the datasets integrity without losing useful information, particularly with regard to intra-individual variability. Indeed, representing each worker by a summary values, such as the median, the mean, the first or the last sampled concentration, would have resulted in a simplification leading to the loss of the internal variability that characterizes each individual over time.
For the data analysis a systematic approach was followed. Initially, data cleaning was performed following selection criteria such as available documentation, reference time, number of measurements, and completeness of technical information. A descriptive statistical analysis was performed on the cleaned dataset, followed by the development of exposure scenarios, which were used for occupational exposure modeling (Figure 2).

Figure 2: Methods scheme

2.1 Data Cleaning

Specific selection and filtering criteria were applied sequentially. Each company underwent a progressive check: only if it met the first criterion, it was evaluated against the next one, and so on (Figure 3). This approach ensured that only companies that met all the requirements were selected for the construction of exposure scenarios. The following criteria were considered:

- Availability of Technical documentation: this information is essential for understanding the activities carried out by the company and the characteristics of the production processes.
  Since data analysis and the construction of exposure scenarios require a detailed context, only data from companies for which this documentation was available were considered. In the absence of contextual information, the bio-monitoring data were excluded from the analysis.

- Reference period: only data collected from 2000 onward were included to ensure a valid representation of current exposures.

- Sufficient number of measurements: only data from companies with more than 10 measurements were considered, to ensure statistical representativeness.

- Completeness of Technical documentation: for each company, the technical documentation provided by SUVA was checked for the presence of the necessary data, that is the specific determinants required by the selected exposure models, in order to build accurate and consistent exposure scenarios (Section 2.3.2). These determinants include informations such as the type of activity carried out, the physicochemical properties of the substances, environmental conditions, duration of exposure, use of personal protective equipment, and other relevant factors.
  The availability of this data is essential to correctly define the work context and exposure conditions, thus allowing the construction of exposure scenarios and their integration into the models. For this reason, only companies with solid technical documentation were considered.

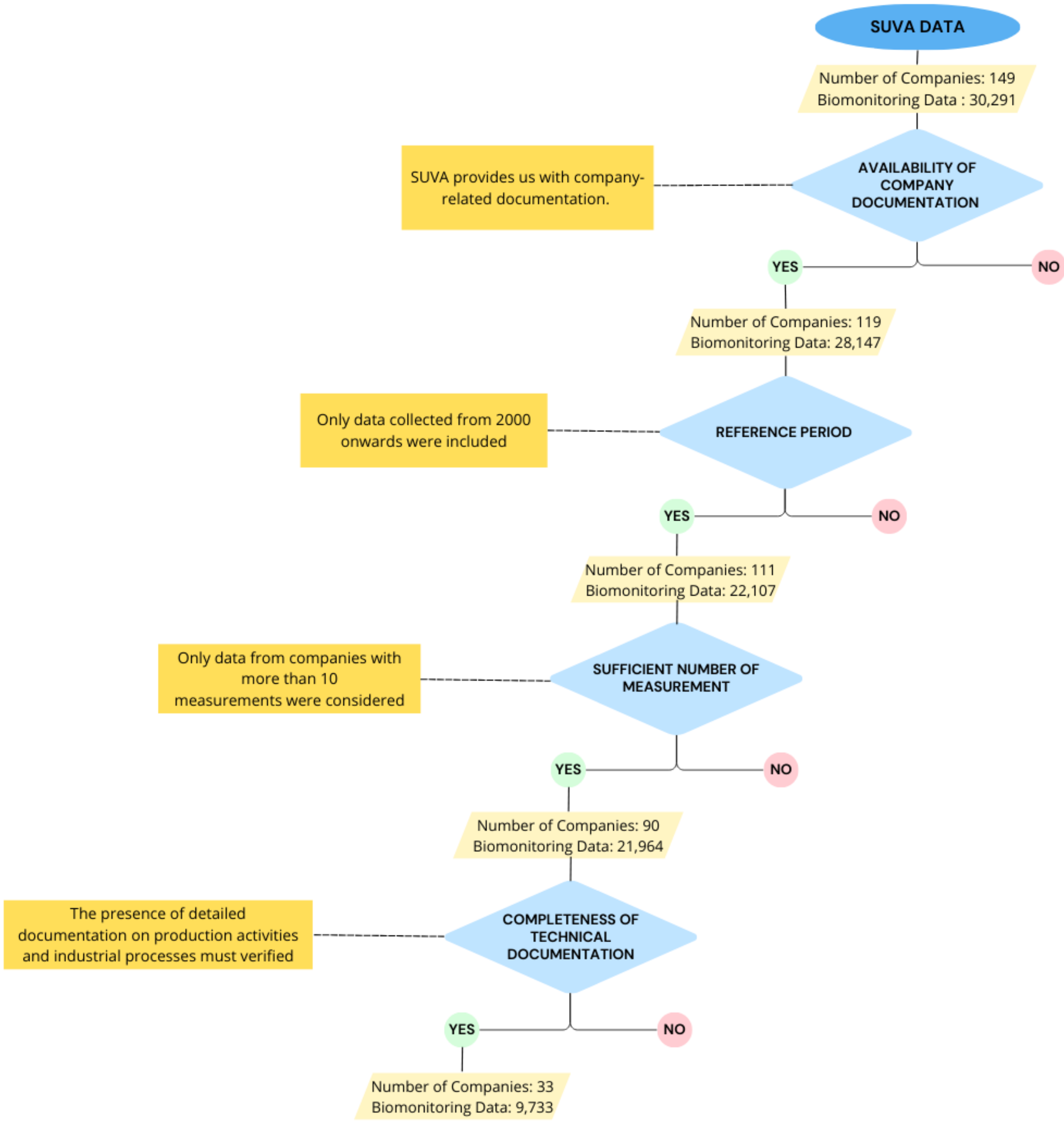


Figure 3: Flowchart data cleaning

2.2 Descriptive statistical analysis

The statistical analysis was conducted using the software STATA 17 and consists of three main phases, Figure 4. The first phase, *"Overall comparison"*, concerns the general characterization of the dataset, with a descriptive analysis of the distribution of workers based on variables such as gender, age, and sector of activity. In the second phase, called *"HEG Homogeneity assessment and comparison"*, workers from each company were grouped into homogeneous exposure groups (HEG), and through the analysis of the between-workers variance within the same HEG, their homogeneity was assessed; and then compared. The third phase *"Time trends"* studies the evolution of exposure during the differents monitoring years, in order to identify temporal trends and variations in professional exposure levels.

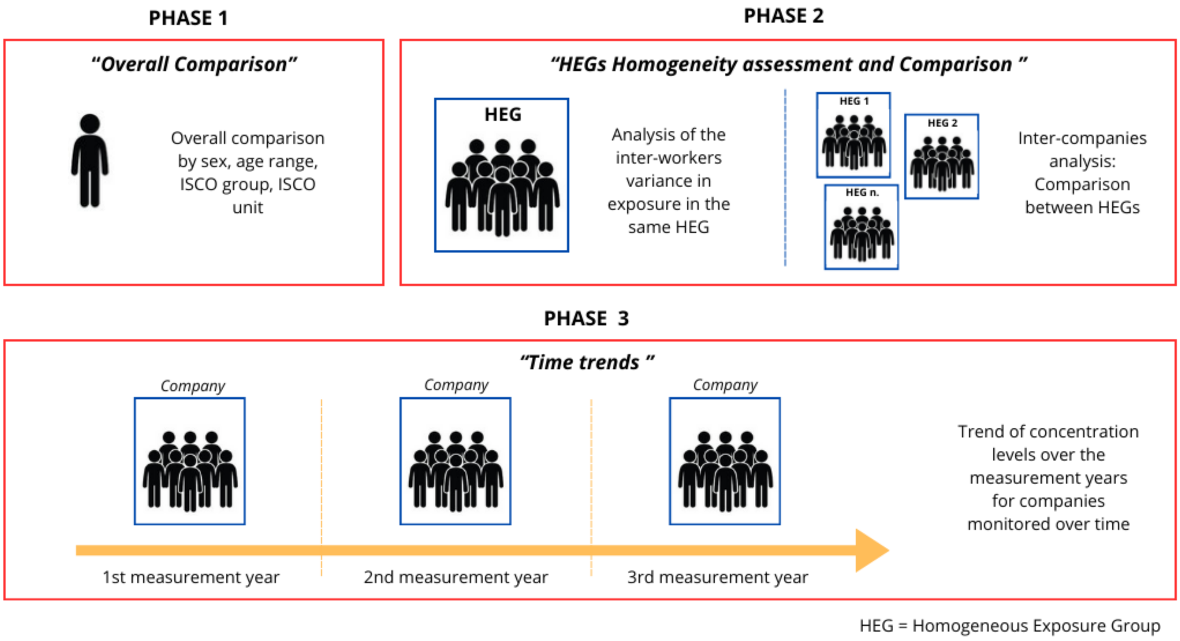


Figure 4: Descriptive statistical analysis scheme

2.2.1 Overall comparison

The statistical analysis of the dataset was conducted to characterize its structure and variability. This analysis includes the study of data distribution and the calculation of key descriptive statistics, such as arithmetic mean (AM), standard deviation (SD), median (p50), 25°percentile (p25), 75°percentile (p75), interquartile range (IQR), minimum (Min) and maximum (Max) values. The normality of the data distribution was assessed using the ShapiroWilk test in order to determine whether the urine Cd concentration [nmol Cd/mmol creatinine]) and urine Cr(VI) concentration [nmol Cr(VI)/mmol creatinine], were parametric or non-parametric. Cd and Cr(VI) were not normally distributed therefore non-parametric test were used in the analysis.
Given the large sample size, the non-normal (and non-log-normal) distribution of the data, and the presence of numerous outliers; the use of robust descriptive statistics was considered more appropriate. In particular, the p50 was preferred over the AM as a measure of central tendency because it is less affected by extreme values and better represents the typical value within the dataset. Similarly, the IQR was used to assess variability and is also persistent to the influence of outliers.
Additionally, a comprehensive analysis was carried out to provide an overview of the dataset's demographic and occupational characteristics, broken down by gender. The resulting Table 1 is structured to present data by age-range, ISCO Major group and ISCO Unit groups for both female and male workers, as well as the total counts and percent-

ages.
In particular, in terms of occupation, the workers were classified according to the International Standard Classification of Occupations (ISCO-08) [21]. This classification, developed by the International Labor Organization (ILO), provides a standardized structure for classifying jobs based on the required skills and the activities performed. The dataset includes workers from three different ISCO Major Groups, divided into nine ISCO Unit Groups.
The comparison test, Kruskal-Wallis, was conducted to compare the differences between the different ISCO group and unit, in gender and age-range. In cases where the test showed statistically significant differences, the Dunn post-hoc test was applied to perform pairwise comparisons between the groups.

2.2.2 HEG Homogeneity assessment and comparison

In this phase, workers from each company were grouped into homogeneous exposure groups (HEG). These groups are defined by the EN 689:1997 standard as *"a group of workers with the same general exposure profile for the chemical agent under examination due to the similarity and frequency of the tasks performed, the materials and processes they work with, and the similarity of the way they carry out the tasks"*.
Specifically, each company is associated with only one specific activity (ISCO), on which a homogeneous exposure group is created. Therefore, the comparison between HEGs will correspond to the comparison between activities, and thus between companies. Once the HEGs were created, their homogeneity was verified by calculating the IQR. In particular, a small IQR suggests that workers are subject to similar exposures, confirming the homogeneity of the HEG, while a large IQR indicates marked heterogeneity in exposure levels. For each HEG, the descriptive statistics were also calculated. Finally, the Kruskal-Wallis test was conducted to compare the differences between the different HEGs, and if significant ($P < 0.05$), a Dunn post-hoc test was performed.

2.2.3 Time trends

For some companies, the data provided by SUVA refer to bio-monitoring campaigns carried out periodically to monitor the concentration of Cd and Cr(VI) in urine and ensure workers' health, particularly those with high concentrations, we checked the trend of Cd and Cr(VI) concentrations over time.
For the analysis, a scatter plot of the concentration of Cd and Cr(VI) was created.
A decrease in concentration levels over time is expected, demonstrating an improvement in workplace safety, thanks to stricter processes and greater attention to health and prevention.

2.3 Exposure modeling

2.3.1 Model selection

The model selection was based on an inventory developed within the framework of the PARC project, designed as a support tool for identifying the most suitable model for the specific context. In particular, it provides, for each model: the name, a summary description of its functioning and conditions of applicability, and the list of determinants required for its correct implementation. The inventory was built using an algorithm (Figure 5) that evaluates three fundamental aspects:

- Validity refers to the consistency between the model and the exposure context.
- Matching concerns the alignment between the available data and the model's requirements.
- Performance is evaluated based on the available evidence regarding the model's effectiveness in describing the pollutant or the specific scenario.

Following a review of the PARC inventory, the selected models include: Advanced REACH Tool 1.5 (ART), MEASE, and RISKOFDERM.
ART is a tool for the assessment of inhalation exposure to chemical substances, which combines a mechanistic model, for exposure estimation, with an empirical component based on an exposure data database. MEASE is an Excel-based algorithm developed to address the specific needs of the metal industry, and finally, RISKOFDERM is an Excel-based model for the estimation of dermal exposure.

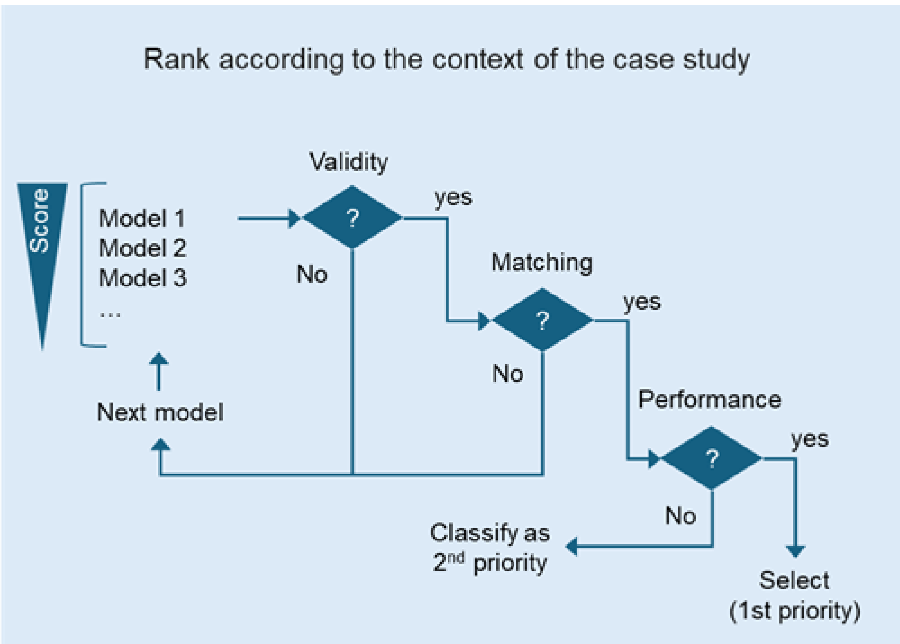


Figure 5: Algorithm model evaluation *(PARC Project)*

2.3.2 Exposure scenario creation

The development of the exposure scenario was carried out with the aim of being subsequently integrated into exposure models. The scenarios were developed for each HEG based on the technical documentation provided by SUVA. The creation was based on the specific determinants required by each selected exposure model, chosen according to the type of activity analyzed (Section 2.3.1). These determinants include consideration of the physicochemical properties of the substance analyzed, the type of activity, ventilation mechanisms, duration of exposure, use of PPE, and other relevant factors.

In cases where the documentation provided by SUVA does not include one or two determinants related to the characteristics of the production process, it is possible, knowing the type of process used, to estimate the missing data through a literature review. This is because industrial processes are generally characterized by specific and repetitive conditions, which allow a reasonable estimation.

2.3.3 Outcome estimation modeling

At this stage, the exposure scenarios developed are integrated into the selected models with the aim of predicting the exposure levels related to the analyzed activities. The results obtained from this modeling correspond to external doses, defined as the whole dose to which an organism is exposed, based on the exposure conditions.

3 Results

3.1 Data cleaning

After data cleaning, 33 different companies with a total of 9,733 valid values are available for analysis, including 3,594 Cd bio-monitoring data and 6,139 Cr(VI) bio-monitoring data.

3.2 Descriptive statistical analysis

3.2.1 Overall comparison

The dataset, described in Table 1, includes a total of 9,733 workers, of which 498 (5.12%) are female and 9,235 (94.88%) are male, indicating a higher representation of male workers.

The workers are divided into five-year age groups starting from 15 years up to 70. The group with the highest number of workers is between 46 and 50 years, with 1,670 workers (17.16%), while the lowest number is found in the 66-70 age group, with only 1 worker (0.01%).

As regard the occupation, the Table 1 shows that the majority of workers belong to the Major Group "7.Craft and related trades workers" which represents 61.30%, followed by the Group "8.Plant and machine operators and assemblers" with 35.99%. In the former group, most of workers are involved in the unit "7211.Metal moulders and coremakers" (3,939/40.47%), whereas in the latter group the majority of individuals works in the unit group "8122.Metal finishing, planting and coating machine operators" (3,474/35.69%).

In general, workers are engaged in metalworking, particularly in foundry, welding, and electroplating. While others are employed in activities involving the management of electrical components containing Cd and Cr(VI).

Figure 6a and 6b show Cd (nmol/mmol Kr) and Cr(VI) (nmol/mmol Kr) distribution. Cd and Cr(VI) were log-transformed when relevant.

Table 2 and 3 present the descriptive statistics for Cd and Cr(VI) concentration across the three ISCO Major Groups considered.

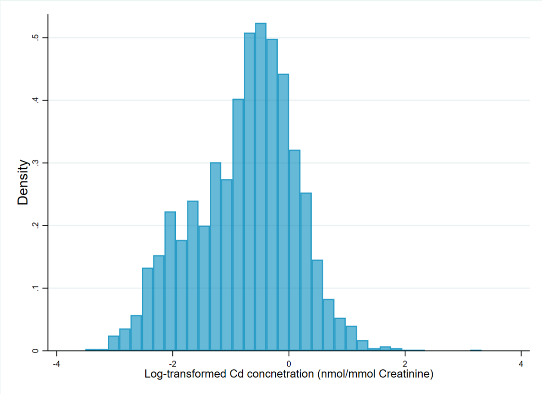
The results obtained show generally higher exposure levels among workers exposed to Cr(VI) compared to those exposed to Cd. In particular, for Cd, low variability is observed between the different groups, with relatively constant values. The highest p50 value is recorded in group 9, equal to 0.70 nmol/mmol Kr. They are followed by group 7 (0.51 nmol/mmol Kr) and group 8 (0.48 nmol/mmol Kr), with slightly lower concentrations of p50 value. Furthermore, within the groups, exposure appears fairly homogeneous, as indicated by the reduced IQRs.

Table 1: Dataset Characteristics Distribution by Gender: Age-Range, ISCO Major Group, and ISCO Unit Group

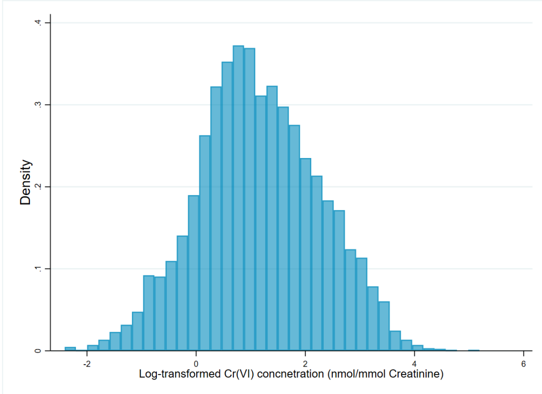
Dataset	Female (N=498)	Male (N=9,235)	Total (N=9,733)
Age-Range (frequency)			
15–20	20 (4.02%)	163 (1.77%)	183 (1.88%)
21–25	31 (6.22%)	350 (3.79%)	381 (3.91%)
26–30	46 (9.24%)	508 (5.50%)	554 (5.69%)
31–35	73 (14.66%)	894 (9.68%)	967 (9.94%)
36–40	107 (21.49%)	1,092 (11.82%)	1,199 (12.32%)
41–45	76 (15.26%)	1,427 (15.45%)	1,503 (15.44%)
46–50	52 (10.44%)	1,618 (17.52%)	1,670 (17.16%)
51–55	46 (9.24%)	1,528 (16.55%)	1,574 (16.17%)
56–60	33 (6.63%)	1,160 (12.56%)	1,193 (12.26%)
61–65	14 (2.81%)	494 (5.35%)	508 (5.22%)
66–70	0 (0.00%)	1 (0.01%)	1 (0.01%)
ISCO Major Group (frequency)			
7 Craft and Related Trades Workers	342 (68.67%)	5,624 (60.90%)	5,966 (61.30%)
8 Plant and Machine Operators, and Assemblers	156 (31.33%)	3,347 (36.24%)	3,503 (35.99%)
9 Elementary Occupations	0 (0.00%)	264 (2.86%)	264 (2.71%)
ISCO Unit Group (frequency)			
7211 Metal Moulders and Coremakers	290 (58.23%)	3,649 (39.51%)	3,939 (40.47%)
7212 Welders and Flamecutters	52 (10.44%)	1,717 (18.59%)	1,769 (18.18%)
7213 Sheet-Metal Workers	0 (0.00%)	58 (0.63%)	58 (0.60%)
7222 Toolmakers and Related Workers	0 (0.00%)	200 (2.17%)	200 (2.05%)
8121 Metal Processing Plant Operators	0 (0.00%)	29 (0.31%)	29 (0.30%)
8122 Metal Finishing, Plating and Coating Machine Operators	156 (31.33%)	3,318 (35.93%)	3,474 (35.69%)
9329 Manufacturing Labourers Not Elsewhere Classified	0 (0.00%)	33 (0.36%)	33 (0.34%)
9612 Refuse Sorters	0 (0.00%)	231 (2.50%)	231 (2.37%)

For Cr(VI), on the other hand, more marked differences between groups are observed. The highest p50 value is recorded in group 8 (p50 = 3.81 nmol/mmol Kr), while the lowest is found in group 9 (p50 = 0.38 nmol/mmol Kr). In addition, groups 7 and 8 show wide IQRs, indicating greater internal variability.
Figure 7 shows concentration variations by ISCO Major Group for Cd and Cr(VI).

The analysis at the ISCO Unit Group level, shown in Table 4 and 5, allows for a more



(a) Density of the Cd distribution



(b) Density of the Cr(VI) distribution

Figure 6: Density of distributions

Table 2: Cd [nmol Cd/mmol Kr] descriptive statistics by ISCO Major Group

ISCO Major Group	AM	SD	p50	p25	p75	IQR	Min	Max
7.Craft and Related Trades Workers	0.66	0.78	0.51	0.26	0.84	0.58	0.03	27.57
8.Plant and Machine Operators and Assemblers	0.68	0.65	0.48	0.20	0.90	0.70	0.06	3.13
9.Elementary Occupations	0.82	0.63	0.70	0.40	1.05	0.65	0.03	3.56

Table 3: Cr(VI) [nmol Cr(VI)/mmol Kr] descriptive statistics by ISCO Major Group

ISCO Major Group	AM	SD	p50	p25	p75	IQR	Min	Max
7.Craft and Related Trades Workers	4.02	4.70	2.30	1.33	4.74	3.41	0.09	38.94
8.Plant and Machine Operators and Assemblers	7.26	9.60	3.81	1.75	8.98	7.23	0.16	179.06
9.Elementary Occupations	0.56	0.56	0.38	0.23	0.53	0.30	0.14	2.50

in-depth understanding of the exposure dynamics already observed in the major groups, offering a more detailed analysis. For Cd, the data confirm the trend of stability across the different Units, with the highest p50 value recorded in Unit 8121 (0.92 nmol/mmol Kr), and low internal variability as indicated by the narrow IQRs. In the case of Cr(VI), marked differences are observed between the different Units, even when belonging to the same Major Group, in fact most of the Units showed high IQRs, as in Unit 8122 equal to 7.23 nmol/mmol Kr.
Figure 8 shows concentration variations by ISCO Unit Group for Cd and Cr(VI).

The Kruskal-Wallis test showed significant differences between the ISCO Major Group for both metals (p-value = 0.0001), further details are provided in Table 13 in Annex. Dunns pairwise comparison revealed differences in Cd between "7 vs 9" groups and "8 vs

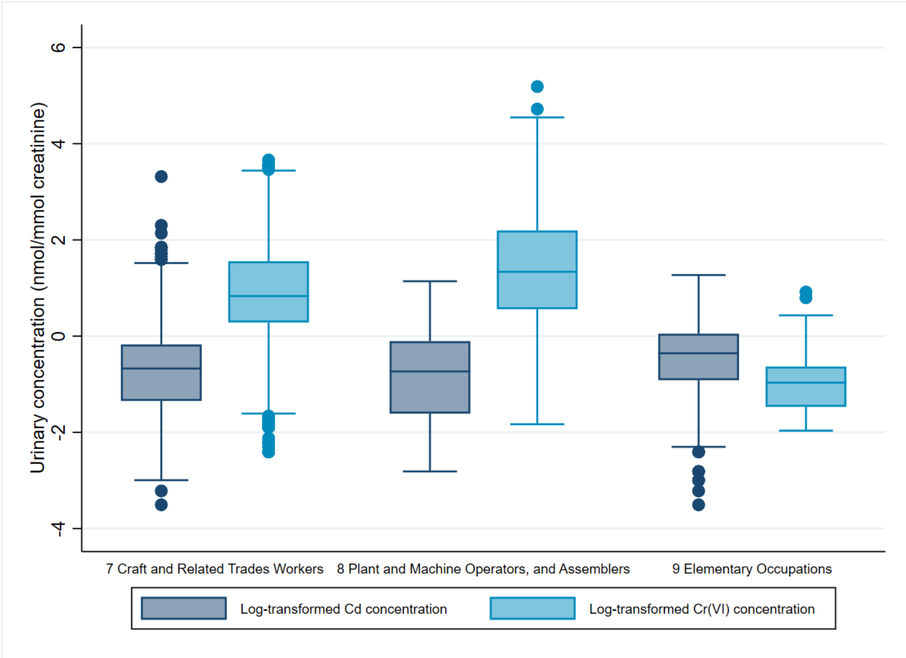


Figure 7: Cd and Cr(VI) Boxplots by ISCO Major Groups

Table 4: Cd [nmol Cd/mmol Kr] descriptive statistics by ISCO Unit Group

ISCO Major Group	AM	SD	p50	p25	p75	IQR	Min	Max
7211 Metal Moulders and Coremakers	0.65	0.77	0.51	0.25	0.85	0.60	0.03	27.57
7212 Welders and Flamecutters	.	.	.	.	.	.	.	.
7213 Sheet-Metal Workers	.	.	.	.	.	.	.	.
7222 Toolmakers and Related Workers	0.82	0.95	0.56	0.44	0.82	0.38	0.21	8.5
8121 Metal Processing Plant Operators	1.08	0.64	0.92	0.67	1.46	0.79	0.07	3.13
8122 Metal Finishing, Plating and Coating Machine Operators	0.54	0.60	0.41	0.17	0.56	0.38	0.06	2.87
9329 Manufacturing Labourers Not Elsewhere Classified	.	.	.	.	.	.	.	.
9612 Refuse Sorters	0.82	0.63	0.70	0.40	1.05	0.65	0.03	3.56

9" groups as shown in Table 14 in Annex; while for Cr(VI) significant differences were found between all groups (p-value <0.0001) (Table 15 in Annex).

The Kruskal-Wallis test conducted on the ISCO Unit Groups also shows a significant difference for both metals (p-value = 0.0001). The post-hoc test confirms the presence of numerous significant differences between the different units, for both Cd and Cr(VI), as reported in the Tables 16 and 17 in Annex.

Regarding to the comparison test between genders and different age groups, in the first case a significant difference emerged with a p-value of 0.0001, for both Cd and Cr(VI),

Table 5: Cr (VI) [nmol Cr(VI)/mmol Kr] descriptive statistics by ISCO Unit Group

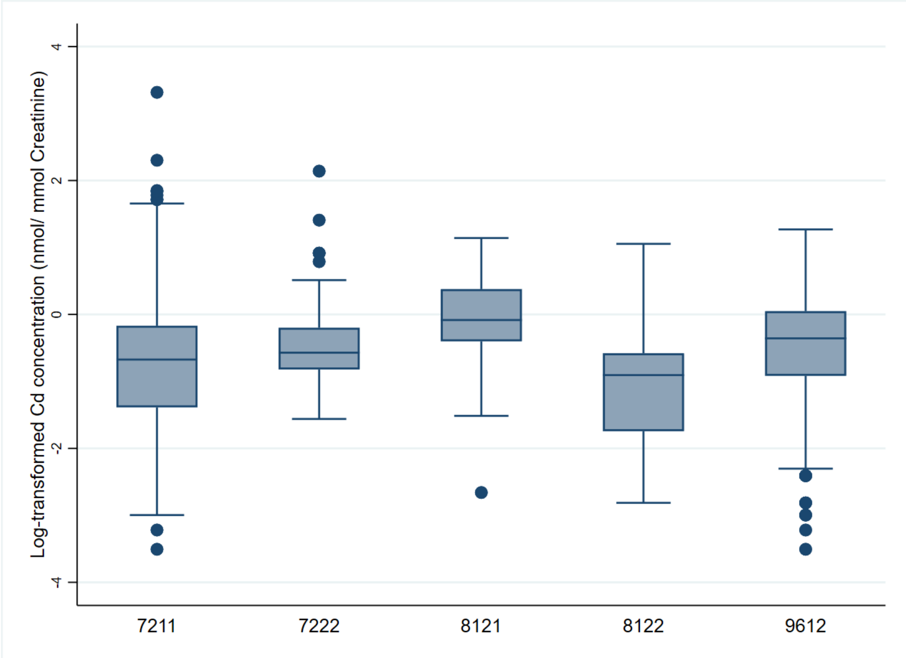
ISCO Major Group	AM	SD	p50	p25	p75	IQR	Min	Max
7211 Metal Moulders and Core-makers	1.93	2.01	1.41	0.88	2.29	1.41	0.09	31.11
7212 Welders and Flamecutters	5.09	5.34	3.2	1.71	6.26	4.55	0.09	38.94
7213 Sheet-Metal Workers	2.78	2.67	1.77	1.38	3.92	2.54	0.86	17.45
7222 Toolmakers and Related Workers	2.16	1.20	1.89	1.45	2.5	1.05	0.64	8.35
8121 Metal Processing Plant Operators	.	.	.	.	.	.	.	.
8122 Metal Finishing, Plating and Coating Machine Operators	7.26	9.6	3.81	1.75	8.98	7.23	0.16	179.06
9329 Manufacturing Labourers Not Elsewhere Classified	0.56	0.56	0.38	0.23	0.53	0.30	0.14	2.5
9612 Refuse Sorters	.	.	.	.	.	.	.	.

indicating a disparity in exposure levels between males and females (Table 13 in Annex). For Cd, the median exposure was 0.68 nmol Cd/mmol Kr for females (IQR = 0.94 nmol Cd/mmol Kr) and 0.51 nmol Cd/mmol Kr for males (IQR = 0.595 nmol Cd/mmol Kr), showing that women had higher levels. Conversely, for Cr(VI) the median was 2 nmol Cr(VI)/mmol Kr for females (IQR = 2.56 Cr(VI)/mmol Kr) and 3.05 nmol Cr(VI)/mmol Kr for men (IQR = 5.42 Cr(VI)/mmol Kr) as shown in Table 6.

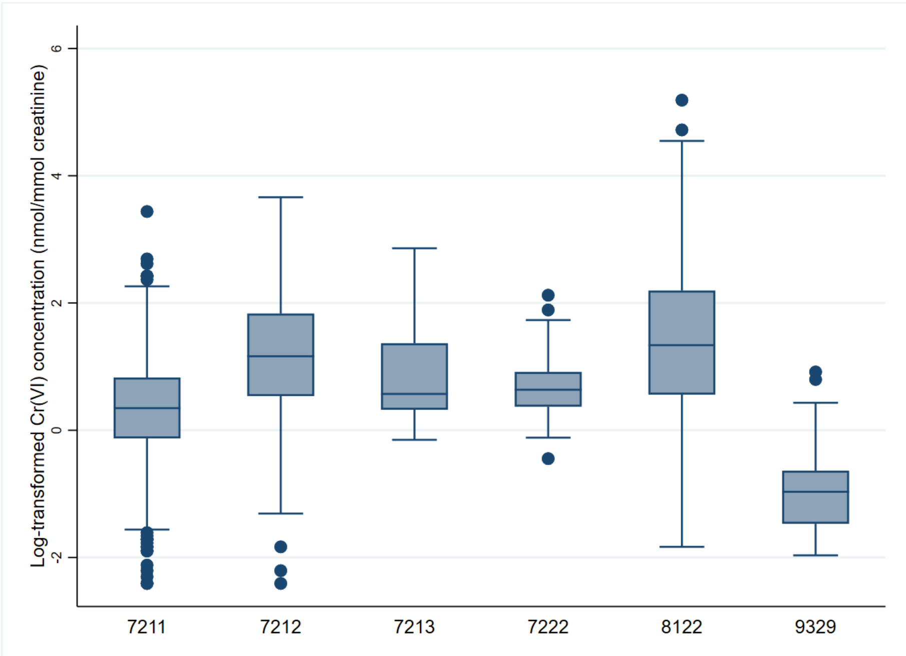
Table 6: Female and Male: Cd and Cr(VI) [nmol/mmol Kr] concentration

Cd	p50	IQR
Female	0.68	0.94
Male	0.51	0.595
Cr(VI)	**p50**	**IQR**
Female	2.00	2.56
Male	3.05	5.42

For the Kruskal-Wallis tests across age ranges, both metals show a p-value of 0.0001 (Table 13 in Annex). The Dunns post-hoc test revealed multiple significant differences between specific age groups. For a detailed list of all pairwise comparisons and their significance levels, see Table 18 and 19 in Annex. To assess the differences between the age groups, four groups of workers were created, balanced in terms of number and consistent with the age distribution, as reported in Table 7. The Kruskal-Wallis test highlighted a significant difference between the groups (p-value = 0.0001), also confirmed by the post-hoc tests for both metals (Table 20 in Annex). The median analysis, (Table 8), showed an increase in the Cd median concentration with age: the 15-30 years group has a median of 0.36



(a) Cd boxplot by ISCO Unit Groups



(b) Cr(VI) boxplot by ISCO Unit Groups

Figure 8: Concentration variation by ISCO Unit Group

nmol/mmol Kr (IQR=0.5 nmol/mmol Kr), the 31-45 years group of 0.48 nmol/mmol Kr (IQR=0.55 nmol/mmol Kr), the 46-60 years group of 0.57 nmol/mmol Kr (IQR=0.63 nmol/mmol Kr), and the 61-70 years group of 0.69 nmol/mmol Kr (IQR=0.84 nmol/ mmol Kr).

For Cr(VI), the following median levels were observed across different age groups: 2.65 nmol/mmol creatinine (IQR=4.49 mmol/nmol Kr) for the 15-30 group, 2.63 nmol/mmol Kr (IQR=4.40 mmol/nmol Kr) for the 31–45 group, 3.3 nmol/mmol Kr (IQR=6.46

mmol/nmol Kr) for the 46–60 group, and 4.6 nmol/mmol Kr (IQR=7.72mmol/nmol Kr) for the 61–70.

Table 7: New Age-range Group for Comparison test

Age-range	N. Workers
15–30	1,118
31–45	3,669
46–60	4,437
61–70	509

Table 8: New Age Range Cd and Cr(VI) [nmol/mmol Kr] concentration

Cd		
Age Range	p50	IQR
15–30	0.36	0.50
31–45	0.48	0.55
46–60	0.57	0.63
61–70	0.69	0.84
Cr(VI)		
Age Range	p50	IQR
15–30	2.65	4.49
31–45	2.63	4.40
46–60	3.30	6.46
61–70	4.60	7.72

3.2.2 HEG Homogeneity assessment and comparison

Based on construction of HEG, shown in Table 9, a total of 33 groups were identified, each corresponding to a specific activity carried out in the company; in particular, we associated one unique activity with each company, so the number of HEGs corresponds to the number of companies under study. Of these 33 HEGs, 7 are related to exposure to Cd, while the remaining 26 are associated with exposure to Cr(VI). The analysis reveals a high variability in the number of workers in each group, ranging from as many as 2,288 workers in some groups to as few as 17 in others.

The assessment of the homogeneity of each group showed that the HEGs exposed to Cd have a small IQR, indicating a substantial uniformity of exposure levels among workers within the same HEG (Table 10). On the contrary, for the HEGs exposed to Cr(VI) (Table 11), the variability is quite mixed: 14 groups display small IQR, confirming homogeneity,

while 12 groups show large IQR, indicating significant differences in exposure levels. The variations in data across the differents HEGs are observed in Figures 9 and 10.
A significant difference in Cd and Cr(VI) levels through HEGs was indicated by the Kruskal-Wallis test (p-value = 0.0001). Dunn's pairwise comparison revealed significant differences between several Unit Groups shown in Table 21 and from Tables 22 to 31 in Annex.

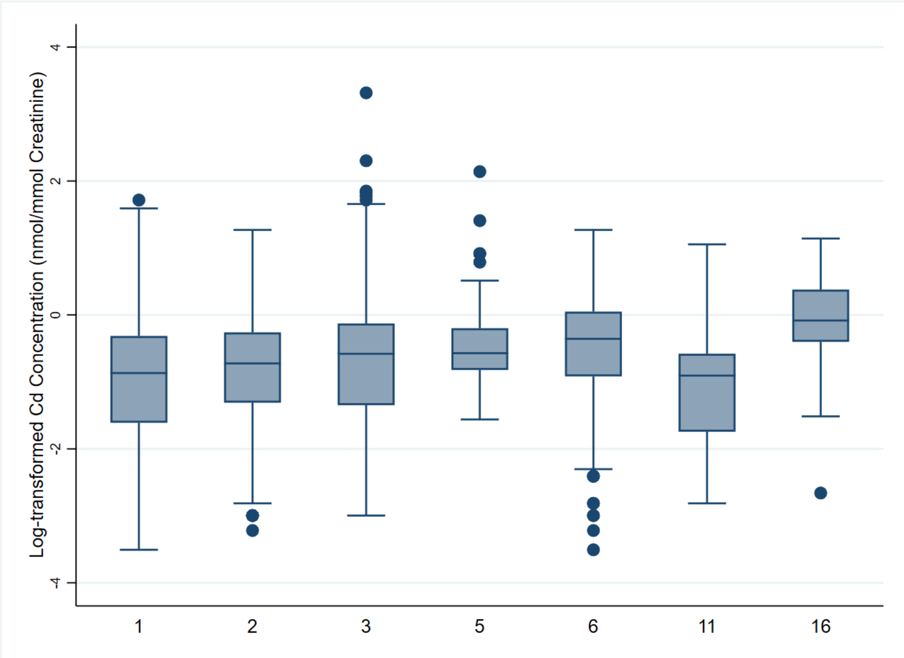


Figure 9: Cd concentration variation by HEGs

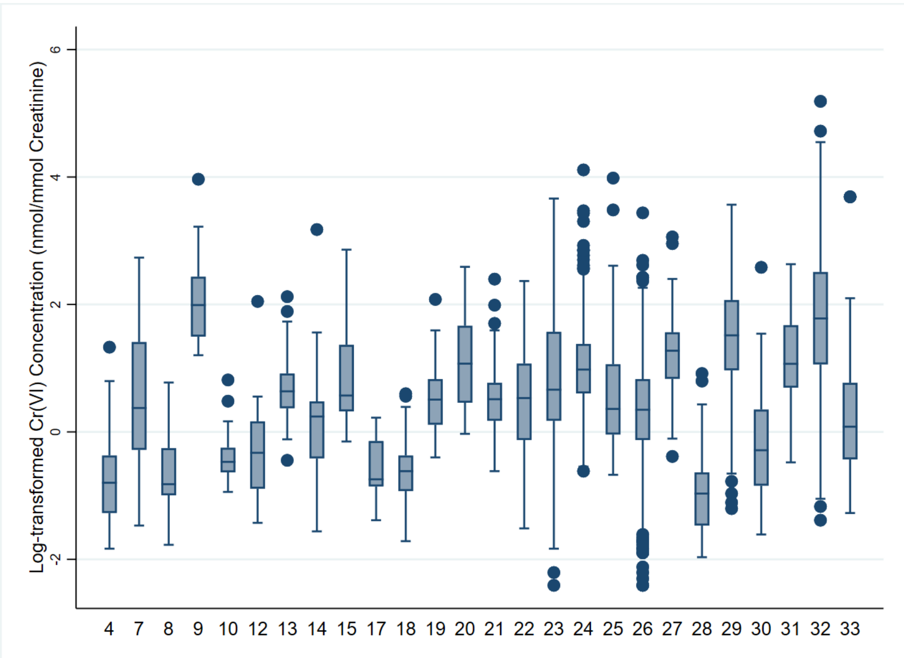


Figure 10: Cr(VI) concentration variation by HEGs

HEG	Freq_HEG	Exposure	ISCO Major Group
1	582	Cd	7 Craft and Related Trades Workers
2	800	Cd	7 Craft and Related Trades Workers
3	1771	Cd	7 Craft and Related Trades Workers
4	69	Cr(VI)	8 Plant and Machine Operators, Assemblers
5	102	Cd	7 Craft and Related Trades Workers
6	231	Cd	9 Elementary Occupations
7	44	Cr(VI)	8 Plant and Machine Operators, Assemblers
8	28	Cr(VI)	8 Plant and Machine Operators, Assemblers
9	31	Cr(VI)	8 Plant and Machine Operators, Assemblers
10	22	Cr(VI)	8 Plant and Machine Operators, Assemblers
11	84	Cd	8 Plant and Machine Operators, Assemblers
12	27	Cr(VI)	8 Plant and Machine Operators, Assemblers
13	98	Cr(VI)	7 Craft and Related Trades Workers
14	36	Cr(VI)	8 Plant and Machine Operators, Assemblers
15	58	Cr(VI)	7 Craft and Related Trades Workers
16	29	Cd	8 Plant and Machine Operators, Assemblers
17	24	Cr(VI)	8 Plant and Machine Operators, Assemblers
18	72	Cr(VI)	8 Plant and Machine Operators, Assemblers
19	17	Cr(VI)	8 Plant and Machine Operators, Assemblers
20	18	Cr(VI)	8 Plant and Machine Operators, Assemblers
21	169	Cr(VI)	7 Craft and Related Trades Workers
22	98	Cr(VI)	8 Plant and Machine Operators, Assemblers
23	479	Cr(VI)	7 Craft and Related Trades Workers
24	417	Cr(VI)	8 Plant and Machine Operators, Assemblers
25	18	Cr(VI)	8 Plant and Machine Operators, Assemblers
26	786	Cr(VI)	7 Craft and Related Trades Workers
27	132	Cr(VI)	7 Craft and Related Trades Workers
28	33	Cr(VI)	9 Elementary Occupations
29	884	Cr(VI)	7 Craft and Related Trades Workers
30	69	Cr(VI)	8 Plant and Machine Operators, Assemblers
31	105	Cr(VI)	7 Craft and Related Trades Workers
32	2288	Cr(VI)	8 Plant and Machine Operators, Assemblers
33	112	Cr(VI)	8 Plant and Machine Operators, Assemblers

Table 9: Homogeneous exposure group (HEG) creation

Table 10: Cd [nmol Cd/mmol Kr] - HEG Homogeneity assessment

HEG	AM	SD	p50	p25	p75	IQR	Min	Max
1	0.57	0.58	0.42	0.20	0.73	0.53	0.03	5.56
2	0.62	0.53	0.49	0.27	0.77	0.50	0.04	3.56
3	0.69	0.91	0.56	0.26	0.88	0.62	0.05	27.57
4	.	.	.	.	.	.	.	.
5	0.82	0.95	0.56	0.44	0.82	0.38	0.21	8.5
6	0.82	0.63	0.70	0.40	1.05	0.65	0.03	3.56
7	.	.	.	.	.	.	.	.
8	.	.	.	.	.	.	.	.
9	.	.	.	.	.	.	.	.
10	.	.	.	.	.	.	.	.
11	0.54	0.60	0.41	0.17	0.56	0.38	0.06	2.87
12	.	.	.	.	.	.	.	.
13	.	.	.	.	.	.	.	.
14	.	.	.	.	.	.	.	.
15	.	.	.	.	.	.	.	.
16	1.08	0.64	0.92	0.67	1.46	0.79	0.07	3.13
17	.	.	.	.	.	.	.	.
18	.	.	.	.	.	.	.	.
19	.	.	.	.	.	.	.	.
20	.	.	.	.	.	.	.	.
21	.	.	.	.	.	.	.	.
22	.	.	.	.	.	.	.	.
23	.	.	.	.	.	.	.	.
24	.	.	.	.	.	.	.	.
25	.	.	.	.	.	.	.	.
26	.	.	.	.	.	.	.	.
27	.	.	.	.	.	.	.	.
28	.	.	.	.	.	.	.	.
29	.	.	.	.	.	.	.	.
30	.	.	.	.	.	.	.	.
31	.	.	.	.	.	.	.	.
32	.	.	.	.	.	.	.	.
33	.	.	.	.	.	.	.	.

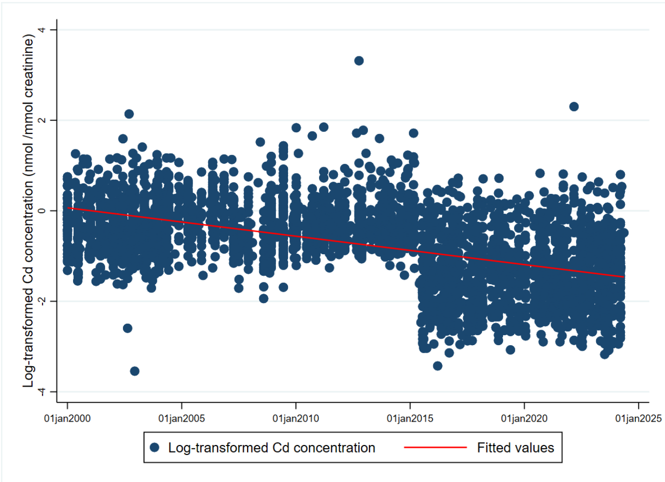
Table 11: Cr(VI) [nmol Cr(VI)/mmol Kr] - HEG Homogeneity assessment

HEG	AM	SD	p50	p25	p75	IQR	Min	Max
1	.	.	.	.	.	.	.	.
2	.	.	.	.	.	.	.	.
3	.	.	.	.	.	.	.	.
4	0.61	0.55	0.45	0.28	0.69	0.41	0.16	3.78
5	.	.	.	.	.	.	.	.
6	.	.	.	.	.	.	.	.
7	3.12	3.79	1.46	0.75	4.15	3.39	0.23	15.41
8	0.59	0.41	0.44	0.37	0.77	0.40	0.17	2.17
9	10.19	9.59	7.32	4.46	11.42	6.96	3.33	52.73
10	0.76	0.43	0.63	0.53	0.78	0.25	0.39	2.26
11	.	.	.	.	.	.	.	.
12	1.03	1.41	0.72	0.41	1.18	0.77	0.24	7.75
13	2.16	1.20	1.89	1.45	2.50	1.05	0.64	8.35
14	1.98	3.88	1.27	0.66	1.62	0.95	0.21	23.94
15	2.78	2.67	1.77	1.38	3.92	2.54	0.86	17.45
16	.	.	.	.	.	.	.	.
17	0.61	0.29	0.47	0.43	0.87	0.44	0.25	1.25
18	0.60	0.31	0.54	0.40	0.69	0.29	0.18	1.82
19	2.15	1.79	1.66	1.12	2.29	1.17	0.67	8.00
20	4.22	3.55	2.95	1.58	5.29	3.71	0.97	13.34
21	1.87	1.17	1.67	1.19	2.16	0.97	0.54	11.00
22	2.24	1.87	1.70	0.88	2.92	2.04	0.22	10.67
23	4.01	4.57	1.94	1.19	4.81	3.62	0.09	38.94
24	3.79	4.51	2.66	1.83	3.98	2.15	0.54	61.05
25	6.96	14.00	1.43	0.96	2.89	1.93	0.51	53.69
26	1.93	2.01	1.41	0.88	2.29	1.41	0.09	31.11
27	3.99	2.85	3.58	2.30	4.78	2.48	0.68	21.33
28	0.56	0.56	0.38	0.23	0.53	0.30	0.14	2.50
29	6.58	6.17	4.55	2.63	7.92	5.29	0.30	35.37
30	1.21	1.71	0.75	0.43	1.42	0.99	0.20	13.23
31	4.02	3.02	2.91	2.00	5.34	3.34	0.62	13.90
32	9.42	10.59	5.93	2.88	12.30	9.41	0.25	179.06
33	2.32	5.31	1.09	0.65	2.16	1.51	0.28	40.00

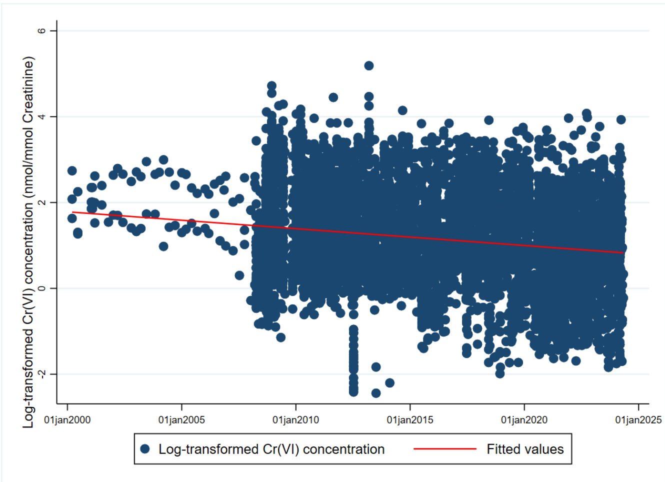
3.2.3 Time trends

From the analysis of the temporal trend of concentrations, represented by the scatter plot in Figure 11, a clear decreasing trend emerges for both metals. This trend confirms expectations and suggests an overall improvement in workplace health conditions, attributable to stricter regulations and an increasing focus on prevention and the protection of workers health. It is observed that Cd presents a clear decrease in the period between 2014 and 2015, characterized by a sudden reduction in concentrations.

As for Cr(VI), no major variations are observed in the trend, although an increase in data availability is noted starting from 2008. This increase is attributable to the expansion of the sample of monitored companies for which SUVA has data. Finally, a series of low concentrations is observed in 2012, recorded for the company identified as the HEG 26, active in the foundry sector. As illustrated in the Figure 12 in Annex, this reduction appears to be localized to the month of July 2012 only.



(a) Correlation between time and Cd



(b) Correlation between time and Cr(VI)

Figure 11: Correlation between time and Concentration

3.3 Exposure modeling

3.3.1 Exposure scenario creation

The developed exposure scenarios are presented, for each HEG, in Section 3.3.3. For each scenario, the reference company, the ISCO codes, and the various specific determinants, according to the selected model, are reported.

3.3.2 Outcome estimation modeling

The results are reported in the same section previously used for the description of the exposure scenarios, Section 3.3.3. This choice was made to ensure consistency and to facilitate the immediate association between each exposure value and the specific scenario to which it refers.
It is important to note that all the results obtained refer to the 75th percentile.

3.3.3 Exposure scenario

Exposure scenario n.1
HEG : 1
ISCO Major Group : 7. Craft and Related Trades Workers
ISCO Unit Group : 7211 Metal Moulders and Coremakers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cd (Cadmium)*
Molecular weight (g/mol)	*112.41*
Melting Point (°C)	*321.07*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC22)*
Content in preparation	*<1%*
Process category	*Open processing and transfer operations with minerals/metals at elevated temperature*
Process temperature (°C)	*800*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.099*
Inhalation exposure estimate [mg/m^3]	*0.05*

Exposure scenario n.2
HEG : 2
ISCO Major Group : 7. Craft and Related Trades Workers
ISCO Unit Group : 7211 Metal Moulders and Coremakers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cd (Cadmium)*
Molecular weight (g/mol)	*112.41*
Melting Point (°C)	*321.07*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC22)*
Content in preparation	*<1%*
Process category	*Open processing and transfer operations with minerals/metals at elevated temperature*
Process temperature (°C)	*800*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=20*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.099*
Inhalation exposure estimate [mg/m^3]	*0.003*

Exposure scenario n.3
HEG : 3
ISCO Major Group : 7. Craft and Related Trades Workers
ISCO Unit Group : 7211 Metal Moulders and Coremakers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cd (Cadmium)*
Molecular weight (g/mol)	*112.41*
Melting Point (°C)	*321.07*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC22)*
Content in preparation	*1%-5%*
Process category	*Open processing and transfer operations with minerals/metals at elevated temperature*
Process temperature (°C)	*800*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.198*
Inhalation exposure estimate [mg/m^3]	*0.332*

Exposure scenario n.4
HEG : 4
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*No RMMs*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.006*

Exposure scenario n.5
HEG : 5
ISCO Major Group : 7. Craft and Related Trades Workers
ISCO Unit Group : 7211 Metal Moulders and Coremakers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cd (Cadmium)*
Molecular weight (g/mol)	*112.41*
Melting Point (°C)	*321.07*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*1%-5%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*300*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=!0*
Use of gloves	*No gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.98*
Inhalation exposure estimate [mg/m^3]	*0.008*

Exposure scenario n.6
HEG : 6
ISCO Major Group : 9. Elementary Occupations
ISCO Unit Group : 9612. Refuse Sorters
ART: Inhalation

Determinants	
Product type of the substance/preparation	*Powders, granules or pelletized material*
Dustiness	*Extremely fine and light powder*
Weight fraction (0-1)	*0.085* [*PARC WG Metals - Occupational environment in elaboration*]
Moisture content	*Dry product (<5% moisture content)*
Source distance from the workers breathing zone (mouth and nose)	*Less than 1 metre (near-field zone)*
Secondary sources present at workplace	*No*
Surface contamination/Fugitive emission sources	*General good housekeeping practices*
Activity class	*Handling of contaminated solid objects or paste*
Situation which best represents activity	*Handling of apparently clean objects*
Type of handling	*Normal handling, involves regular work procedures*
Task duration (min)	*60 minutes*
Localized controls - primary	*No localized controls*
Exposure site	*Indoors*
Ventilation rate	*Only good natural ventilation*
Workplace volume	*1000* m^3
Modeling results	
Exposure prediction (p75) [mg/m^3]	*0.00039*

RISKOFDERM: Dermal contact

Determinants	
Activity type	*Mechanical treatment*
What is the physical state of the product or substance assessed?	*Solid*
What is the distance of the worker to the source	*Less than or about arms length*
What is the frequency of contacts between worker and the contamination during the task?	*Frequent or constant contact*
Percentile for the exposure rate distribution to be assessed	*75*
What is the cumulative duration of the scenario during a shift (min)?	*60*
Modeling Results	
Resulting exposure rate body [mg/min]	*10*
Exposure loading per shift body [mg]	*601*

Exposure scenario n.7
HEG : 7
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*>25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*53*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*2.4*
Inhalation exposure estimate [mg/m^3]	*0.008*

Exposure scenario n.8

HEG : 8

ISCO Major Group : 8.Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*1%-5%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*20*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.48*
Inhalation exposure estimate [mg/m^3]	*0.001*

Exposure scenario n.9
HEG : 9
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=4*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.001*

Exposure scenario n.10

HEG : 10

ISCO Major Group : 8.Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*88*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.11
HEG : 11
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*<1%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*70*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=20*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.24*
Inhalation exposure estimate [mg/m^3]	*<0.001*

Exposure scenario n.12
HEG : 12
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*No gloves*
Modeling Results	
Total dermal loading [mg/day]	*14.4*
Inhalation exposure estimate [mg/m^3]	*0.005*

Exposure scenario n.13
HEG : 13
ISCO Major Group : 7 Craft and Related Trades Workers
ISCO Unit Group : 7222 Toolmakers and Related workers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other work operations with metals*
Process temperature (°C)	*300*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*No gloves*
Modeling Results	
Total dermal loading [mg/day]	*5.94*
Inhalation exposure estimate [mg/m^3]	*0.249*

Exposure scenario n.14
HEG : 14
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*1%-5%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*35*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*No gloves*
Modeling Results	
Total dermal loading [mg/day]	*14.4*
Inhalation exposure estimate [mg/m^3]	*0.005*

Exposure scenario n.15
HEG : 15
ISCO Major Group : 7.Craft and Related Trades Workers
ISCO Unit Group :7213 Sheet Metal Workers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*3000*
Scale of operation	*Industrial use*
Duration exposure	*60-240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=20*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.356*
Inhalation exposure estimate [mg/m^3]	*0.03*

Exposure scenario n.16
HEG : 16
ISCO Major Group : 8. Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal Finishing, Plating and Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cd (Cadmium)*
Molecular weight (g/mol)	*112.41*
Melting Point (°C)	*321.07*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC22)*
Content in preparation	*5%-25%*
Process category	*Open processing and transfer operations with minerals/metals at elevated temperature*
Process temperature (°C)	*1000*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.594*
Inhalation exposure estimate [mg/m^3]	*0.3*

Exposure scenario n.17
HEG : 17
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=10*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*<0.001*

Exposure scenario n.18

HEG : 18

ISCO Major Group : 8.Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*42*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.19
HEG : 19
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*60*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.20
HEG : 20
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.21
HEG : 21
ISCO Major Group : 7. Craft and Related Trades Workers
ISCO Unit Group : 7212. Welders and Flame Cutters

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not Relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*300*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.594*
Inhalation exposure estimate [mg/m^3]	*0.249*

Exposure scenario n.22

HEG : 22

ISCO Major Group : 8.Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*60*
Scale of operation	*Industrial use*
Duration exposure	*60-240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.864*
Inhalation exposure estimate [mg/m^3]	*0.001*

Exposure scenario n.23
HEG : 23
ISCO Major Group :7.Craft and Rekated Trades Workers
ISCO Unit Group : 7212 Welders and Flame Cutters

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other work operations with metals*
Process temperature (°C)	*3000*
Scale of operation	*Industrial use*
Duration exposure	*60-240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Non-Direct handling*
Contact level	*Incidental*
Implemented RMMs	*general ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.036*
Inhalation exposure estimate [mg/m^3]	*0.598*

Exposure scenario n.24
HEG : 24
ISCO Major Group : 8.Plant and Machine Operators, and Assemblers
ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.144*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.25

HEG : 25

ISCO Major Group : 8.Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal finishing, Plating adn Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Acqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*40*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.144*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.26
HEG : 26
ISCO Major Group :7. Craft and Related Trades Workers
ISCO Unit Group : 7211.Metal Moulders and Coremakers

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC22)*
Content in preparation	*<1%*
Process category	*Open processing and transfer operations with minerals/metals elevated temperatures*
Process temperature (°C)	*800*
Scale of operation	*Industrial use*
Duration exposure	*15-60 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Non-Direct handling*
Contact level	*Incidental*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=20*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.002*
Inhalation exposure estimate [mg/m^3]	*<0.001*

Exposure scenario n.27
HEG : 27
ISCO Major Group : 7 Craft and Related Trades Workers
ISCO Unit Group : 7212 Welders and Flame Cutters

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*300*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.594*
Inhalation exposure estimate [mg/m^3]	*0.075*

Exposure scenario n.28
HEG : 28
ISCO Major Group : 9. Elementary occupations
ISCO Unit Group : 9329 Manufacturing Laboures Not Elsewhere Classified
ART: Inhalation

Determinants	
Product type of the substance/preparation	*Powders, granules or pelletized material*
Dustiness	*Extremely fine and light powder*
Weight fraction (0-1)	*0.25* [13]
Moisture content	*Dry product (<5% moisture content)*
Source distance from the workers breathing zone (mouth and nose)	*Less than 1 m (Near-Field zone)*
Secondary sources present at workplace	*No*
Surface contamination/Fugitive emission sources	*Demostrable and effective housekeeping*
Activity class	*Transfer of powder, granules or pelletized*
Activity sub-class	*Falling powder*
Situation which best represents activity	*Transferring <10 gram/minute*
Type of handling	*Careful transfer involves workers showing attention to potential danger, error or harm and carrying out the activity in a very exact thorough manner*
Drop height	*Drop height > 0.5 m*
Containment of source	*Open process*
Task duration (min)	*60*
Localized controls - primary	*Local exhaust ventilation*
Technique of applied primary localized controls Localized controls - secondary	*Canopy hood* *No localized controls*
Exposure site	*Indoors*
Ventilation rate	*No restrictions on general ventilation*
Workplace volume	*1000* m^3
Modeling Results	
Exposure prediction (p75) [mg/m^3]	*0.0015*

RISKOFDERM: Dermal contact

Determinants	
Activity type	*Mechanical treatment*
What is the physical state of the product or substance assessed?	*Solid*
What is the distance of the worker to the source	*Less than or about arms length*
What is the frequency of contacts between worker and the contamination during the task?	*Rare od irregular contact*
Percentile for the exposure rate distribution to be assessed	*75*
What is the cumulative duration of the scenario during a shift (min)?	*60*
Modeling results	
Resulting exposure rate body [mg/min]	*3.21*
Exposure loading per shift body [mg]	*193*

Exposure scenario n.29
HEG : 29
ISCO Major Group : 7 Craft and Related Trades Workers
ISCO Unit Group : 7212 Welders and Flame Cutters

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*300*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Intermittent*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=10*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.594*
Inhalation exposure estimate [mg/m^3]	*0.025*

Exposure scenario n.30

HEG : 30

ISCO Major Group : 8 Plant and Machine Operators, and Assemblers

ISCO Unit Group : 8122 Metal Finishing, Plating and Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Aqueous solution*
Content in preparation	*5%-25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*40*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*Exterior LEV*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*1.44*
Inhalation exposure estimate [mg/m^3]	*0.002*

Exposure scenario n.31
HEG : 31
ISCO Major Group : 7 Craft and Related Trades Workers
ISCO Unit Group : 7212 Welders and Flame Cutters

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Not relevant (PROC25)*
Content in preparation	*5%-25%*
Process category	*Other hot work operations with metals*
Process temperature (°C)	*1500*
Scale of operation	*Industrial use*
Duration exposure	*60-240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Incidental*
Implemented RMMs	*General ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=40*
Use of gloves	*No gloves*
Modeling Results	
Total dermal loading [mg/day]	*3.564*
Inhalation exposure estimate [mg/m^3]	*0.004*

Exposure scenario n.32

HEG : 32

ISCO Major Group : 8.Plant and Machine Operators and Assemblers

ISCO Unit Group : 8122 Metal Finishing, Plating and Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Aqueous solution*
Content in preparation	*>25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*52*
Scale of operation	*Industrial use*
Duration exposure	*>240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Direct handling*
Contact level	*Extensive*
Implemented RMMs	*No RMMs*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*No RPE*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*204*
Inhalation exposure estimate [mg/m^3]	*0.01*

Exposure scenario n.33

HEG : 33

ISCO Major Group : 8.Plant and Machine Operators and Assemblers

ISCO Unit Group : 8122 Metal Finishing, Plating and Coating Machine Operators

MEASE: Inhalation + Dermal contact

Determinants	
Substance	*Cr(VI) (ChromiumVI)*
Molecular weight (g/mol)	*51.966*
Melting Point (°C)	*1907*
Vapour Pressure (Pa)	*Not specified*
Physical Form	*Aqueous solution*
Content in preparation	*>25%*
Process category	*Treatment of articles by dipping and pouring*
Process temperature (°C)	*50*
Scale of operation	*Industrial use*
Duration exposure	*60-240 min*
Pattern of use	*Non-dispersive use*
Pattern of exposure control	*Non-Direct handling*
Contact level	*incidental*
Implemented RMMs	*General Ventilation*
RMM efficiency based on type of enclosure ventilation	*Lower confidence limit*
Respiratory protective equipment (RPE)	*APF=4*
Use of gloves	*Properly designed/selected gloves*
Modeling Results	
Total dermal loading [mg/day]	*0.014*
Inhalation exposure estimate [mg/m^3]	*0.001*

4 Discussion

The results obtained indicate a higher concentration of Cd in women compared to men, as well as a progressive increase in the levels of this metal with advancing age. These data are consistent with what is reported in the literature and can be explained by considering a series of biological and non-biological factors that influence the kinetics and toxicity of chemical substances in the body.

The non-biological factors that influence toxicity include exposure situations in the workplace or general environment and lifestyle factors such as smoking, diet, physical activity, cosmetics, and various stress factors. In particular, the main source of Cd is tobacco smoke; smokers show kidney Cd concentrations 4–5 times higher than non-smokers [28].

Regarding the aspect of occupational exposure to Cd, the literature does not show clear references describing the various differences in exposure among these specific work activities. However, we can hypothesize that the recorded median levels are attributable to several factors: firstly, to the nature of the activities carried out, which involve different degrees of Cd release into the work environment and potential contact with workers; secondly, to the actual concentration of the metal in the materials processed. It should also be noted that exposure can be significantly influenced by the effectiveness of the preventive measures adopted, such as the use of personal protective equipment and the presence of adequate ventilation systems. These factors can introduce elements of uncertainty, contributing to intra-group and inter-group variability that may explain the differences observed in the median concentrations.

From a biological point of view, women are subject to important physiological changes that can modulate the absorption, distribution, and accumulation of Cd; such as processes related to menstruation, pregnancy, breastfeeding, and menopause, which represent critical periods during which iron (Fe) metabolism and, consequently, that of Cd can undergo significant variations [35] [27] [15]. In fact, these studies confirm that Cd absorption increases substantially in the presence of reduced Fe stores. This is because Fe deficiency stimulates the increased expression of intestinal transporters involved in the absorption of divalent metals, such as DMT1 (Divalent Metal Transporter 1), which do not selectively distinguish between Fe and Cd. As a result, when Fe stores are low, the intestine may absorb greater amounts of Cd, increasing the risk of accumulation in the body. This phenomenon is mainly observed in women of childbearing age due to menstrual blood loss, and during pregnancy, when intestinal Fe absorption physiologically increases to meet the high maternal and fetal demand. Moreover, it is observed that the differences in Cd levels between men and women tend to decrease when women enter menopause, a period in which blood loss ceases and iron stores tend to stabilize.[10].

The increase of Cd with age is instead due to the accumulation of Cd in the renal cortex [10], caused by its long half-life: from 4 to 19 years in the liver and from 10 to 20 years in the kidneys [5].

Regarding chromium exposure, Cr(VI) levels tend to be higher in men compared to women, and similar concentrations are observed in the age groups 15-30 and 31-45, after which they increase. However, there is no scientific explanation for Cr(VI) in the literature.

We can say that exposure to Cr(VI) depends solely on exposure to contaminated diet and air, and occupational exposure. From the study of exposure concentrations for Cr(VI), a significant difference emerges between the various ISCO professional groups. Marked differences are also reflected in the analysis at the Unit Group level. This variation can be attributed to the fact that each Unit Group represents different activities, and thus different levels of exposure, justifying the discrepancies in concentration levels between the various Unit Groups. When analyzing each of these in detail, two situations emerge: when the IQR is low, companies within the same Unit Group have similar exposure levels. On the other hand, when the IQR is high, it is possible that within the same Unit Group, companies with different exposure scenarios coexist, due to differences in industrial processes, safety measures, or operating conditions. Another explanation is that exposure may be influenced by additional external sources outside the occupational context. Workers may be subject to environmental exposures related to the geographical area in which they live, or to factors related to their individual lifestyle, such as diet or tobacco use.

The creation of HEGs for Cr(VI) and the homogeneity assessment showed high intra-HEG variability, which may be due to various factors. Firstly, it may result from the presence of different workstations or tasks within the same company, exposing workers to varying levels of contaminant. Additionally the variability may come from the duration of exposure during the working day and week; differences in exposure time among individual workers can contribute to greater heterogeneity in the exposure levels observed. Lastly, another cause of heterogeneity could lie in the presence of exposure sources outside the working environment, such as general environmental exposure or lifestyle-related factors, like dietary habits and tobacco use.

The time trends confirm expectations and suggests an overall improvement in workplace health conditions, attributable to stricter regulations and an increasing focus on prevention and the protection of workers health.

In particular, the marked decrease in Cd levels recorded between 2014 and 2015 deserves thorough analysis. The companies involved operate in heterogeneous industrial sectors (foundry, disassembly of electronic devices, chemical deposition), making it unlikely that this variation is attributable to the simultaneous adoption of technological or operational changes in production processes by the companies. A more plausible explanation could

instead lie in a regulatory revision that occurred during that period, or in a change in the protocols governing the execution of bio-monitoring or laboratory analyses.
From a regulatory point of view, it is important to underline that possible legislative changes during the period considered are unlikely to justify such a marked variation in exposure levels. Cd, in fact, is a metal with a long biological half-life, which can exceed 20 years. This means that any reductions in internal levels appear in the long term, and that the decrease in 2014 could be linked to a legislative change in the early 2000s. From the analysis of the legislation, no significant changes were found in the years considered.
Regarding the technical aspects, SUVA informed us of the introduction, in April 2015, of a new ICP-MS device for the analyses. However, according to the monthly quality checks, the values obtained with the new instrument are comparable to the previous ones, excluding, at first analysis, the influence of the device as the cause of the observed variation.
A further hypothesis takes into account sources of general exposure, in particular that of dietary origin. It is known that diet represents one of the main routes of exposure to Cd. Several studies have highlighted that the concentration of Cd in the soil is influenced by multiple factors, including atmospheric deposition, the use of phosphate fertilizers, and the input of sludge containing heavy metals [29] [7]. The variations in these inputs over time are directly reflected in the amount of Cd absorbed by plants, and therefore in the crops intended for human consumption. From the analysis of the available data, the study [29] observed a progressive decrease in Cd concentrations in crops over the years. This trend seems to be mainly attributable to better control of contamination sources, such as the reduction in the use of fertilizers with high Cd content and a decrease in atmospheric pollution, resulting in less accumulation of the metal in agricultural soils. Therefore, the reduction of Cd in crops could also be reflected, in the long term, in a decrease in body levels of Cd. However, while representing a possible contribution to the general decreasing trend, this phenomenon does not seem sufficient to explain the sudden and marked drop recorded in a single year, such as in 2015.
All the hypotheses examined so far have been considered in order to justify the sudden drop in Cd levels, without reaching a definitive explanation. There is currently an active discussion ongoing with SUVA, in order to clarify the origin of the decrease.
As for the time trend of Cr(VI) concentrations, we can state that the series of low concentrations recorded in 2012 for the Company-HEG 26 could be caused by a temporary contraction in production due to a decrease in demand or to possible periods of plant shutdown.

By analyzing the different model's results for each scenario, it is possible to observe how even a minimal variation in the determinants can significantly influence the estimates.
A clear example can be seen in the comparison between scenarios HEG 1 and HEG 2, in which the activity performed is the same, foundry, as also confirmed by the ISCO code,

and so are all the determinants. The only variable that differs between the two scenarios is the use of respiratory protective equipment (RPE): in scenario HEG 1, no device is used, whereas in scenario HEG 2, the use of an RPE with an Assigned Protection Factor (APF) of 20 is foreseen. This variation allows the isolation and quantification of the impact of protective equipment effectiveness on the estimated exposure level. The comparison highlights how the adoption of an RPE results in a significant reduction in the exposure estimated by the model, confirming the importance of proper selection and use of personal protective equipment in the management of chemical risk. This observation also underlines the sensitivity of the model MEASE to parameters related to personal protection and highlights its usefulness as a tool to support decision-making in the field of prevention and occupational safety.

5 Study Limitations

Despite efforts to ensure the validity and reliability of the results, it is important to acknowledge that this study has certain limitations that must be considered.
A first limitation concerns the variable number of participants in the different groups analyzed, limiting the possibility of making homogeneous comparisons between groups. Another important source of uncertainty comes from external factors that influence the measured concentrations. Among these, smoking is particularly relevant in the analysis of Cd, as it can cause a significant increase in body levels while also dietary habits represent variables that are difficult to control. Furthermore, the lack of information about the geographical location of companies or workplaces limits the ability to correctly assess the general environmental exposure of workers.
A second category of limitations concerns the construction of exposure scenarios, as complete and accurate data regarding the determinants necessary for modeling were not provided for all companies. To fill these gaps, some assumptions were made, which may have generated errors, compromising the accuracy and reliability of the estimates.
Finally, limitations arise from the models used for the analysis. In particular, the ART and RISKOFDERM models do not consider the use of personal protective equipment (PPE), unlike the MEASE model, which could lead to an underestimation or overestimation of the workers actual exposure.
Such limitations must be taken into consideration in the interpretation of the results.

6 Conclusion

In a European context where the protection of health from chemical risks is an increasing priority, having solid tools to assess human exposure becomes essential. This work is part of the PARC project, with the aim of contributing to the development of integrated and innovative approaches for the assessment of aggregate exposure to heavy metals such as Cd and Cr(VI).
The activity was structured in an initial phase, where bio-monitoring data provided by SUVA were analyzed, revealing significant differences in exposure levels among occupational groups, age ranges, and genders. These results allowed for an initial overview of the distribution of exposure in the analyzed work environments. Subsequently, homogeneous exposure groups (HEG) were constructed, and specific exposure scenarios were defined, developed based on company technical documentation. These scenarios were used to estimate external exposure doses through selected models (ART, MEASE, RISKOFDERM). The resulting exposure estimates represent the starting point for the next phases of the case study: they will be transformed into internal doses through the use of PBPK models and aggregated with other sources of exposure, to be finally compared with bio-monitoring data. This comparison will be crucial for realistically assessing the individual's overall exposure, thus enabling a more solid interpretation of chemical risk.
The work, therefore, not only provides a concrete contribution to the understanding of occupational exposure to Cd and Cr(VI), but also represents an important step in building a harmonized, transparent, and scientifically grounded approach to chemical risk management at the European level.

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Annex

Table 12: Legend

Abbreviation	Description
AM	Arithmetic Mean
SD	Standard Deviation
P_{50}	Median
P_{25}	25°Percentile
P_{75}	75°Percentile
IQR	Interquartile Range
Min	Minimum
Max	Maximum

Table 13: Kruskal-Wallis Test Results by ISCO Group

ISCO Major Group	**p-value**
Cd	0.0001
Cr(VI)	0.0001
ISCO Unit Group	
Cd	0.0001
Cr(VI)	0.0001
Gender (Female - Male)	
Cd	0.0001
Cr(VI)	0.0001
Age Range	
Cd	0.0001
Cr(VI)	0.0001
HEG	
Cd	0.0001
Cr(VI)	0.0001

Table 14: Cd - Dunn's test ISCO Major Group

	7	8
8	0.453263	
	(0.3252)	
9	-5.260273	-3.498004
	(<0.0001)	(0.0002)

Table 15: Cr(VI) - Dunn's test ISCO Major Group

	7	8
8	-1.54e+01	
	(<0.0001)	
9	7.372743	9.646849
	(<0.0001)	(<0.0001)

Table 16: Cd - Dunn's test ISCO Unit Group

	7211	7222	8121	8122
7222	-3.045599			
	(0.0012)			
8121	-4.443731	-2.483161		
	(<0.0001)	(0.0065)		
8122	2.999457	4.330234	5.388570	
	(0.0014)	(<0.0001)	(<0.0001)	
9612	-5.395700	-0.516478	2.340863	-5.489373
	(<0.0001)	(0.3028)	(0.0096)	(<0.0001)

Table 17: Cr(VI) - Dunn's Test ISCO Unit Groups

7211	7212	7213	7222	7224	8122
7212	-1.92e+01				
	(<0.0001)				
7213	-2.499088	3.612225			
	(0.0062)	(0.0002)			
7222	-2.199212	5.651258	0.630431		
	(0.0139)	(<0.0001)	(0.2642)		
8122	-2.40e+01	-4.308997	-4.594347	-6.956989	
	(<0.0001)	(0.2231)	(<0.0001)	(<0.0001)	
9329	4.158885	8.885171	4.948701	4.842436	9.646849
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)

Table 18: Cd - Dunn's Test Age ranges

	15-20	21-25	26-30	31-35	36-40	41-45
21-25	-0.0799 (0.4682)					
26-30	-0.022448 (0.4910)	0.143336 (0.4430)				
31-35	-1.037771 (0.1497)	-2.453109 (0.0071)	-3.547849 (<0.0001)			
36-40	-1.388124 (0.0825)	-3.447699 (0.0003)	-5.053715 (<0.0001)	-1.668008 (0.0477)		
41-45	-1.264957 (0.1029)	-3.137237 (0.0009)	-4.646137 (<0.0001)	-1.089052 (0.1381)	0.698880 (0.2423)	
46-50	-1.606163 (0.0541)	-4.060759 (<0.0001)	-5.976422 (<0.0001)	-2.809860 (0.0025)	-1.240746 (0.1073)	-2.010411 (0.0222)
51-55	-2.124606 (0.0168)	-5.436610 (<0.0001)	-7.909693 (<0.0001)	-5.374720 (<0.0001)	-4.190978 (<0.0001)	-5.036039 (<0.0001)
56-60	-2.195412 (0.0141)	-5.547619 (<0.0001)	-7.936898 (<0.0001)	-5.446056 (<0.0001)	-4.308042 (<0.0001)	-5.087690 (<0.0001)
61-65	-2.607726 (0.0046)	-5.944024 (<0.0001)	-7.673605 (<0.0001)	-5.455907 (<0.0001)	-4.550814 (<0.0001)	-5.045229 (<0.0001)
66-70	0.852388 (0.1970)	0.920240 (0.1787)	0.903317 (0.1832)	1.247159 (0.1062)	1.363815 (0.0863)	1.322228 (0.0930)

Table 19: Cr(VI) - Dunn's Test Results for Age Ranges

	15–20	21–25	26–30	31–35	36–40	41–45
21–25	-1.945281 (0.0259)					
26–30	0.959123 (0.1687)	3.583510 (0.0002)				
31–35	1.519777 (0.0643)	4.535483 (<0.0001)	0.670330 (0.2513)			
36–40	0.003276 (0.4987)	2.683574 (0.0036)	-1.369712 (0.0854)	-2.334310 (0.0098)		
41–45	-1.022888 (0.1532)	1.515572 (0.0648)	-2.857228 (0.0021)	-4.145027 (<0.0001)	-1.663230 (0.0481)	
46–50	-1.198416 (0.1154)	1.325071 (0.0926)	-3.135168 (0.0009)	-4.506987 (<0.0001)	-1.975492 (0.0241)	-0.300017 (0.3821)
51–55	-3.217629 (0.0006)	-1.243421 (0.1069)	-5.895523 (<0.0001)	-7.689984 (<0.0001)	-5.244298 (<0.0001)	-3.893558 (<0.0001)
56–60	-3.576064 (0.0002)	-1.737913 (0.0411)	-6.227403 (<0.0001)	-7.923152 (<0.0001)	-5.617539 (<0.0001)	-4.360932 (<0.0001)
61–65	-4.239579 (<0.0001)	-2.674154 (0.0037)	-6.590745 (<0.0001)	-7.920349 (<0.0001)	-5.999353 (<0.0001)	-4.940792 (<0.0001)

Table 20: Cd and Cr(VI) - Dunn's Test New Age Ranges

Cd	15-40	41-50
41-50	-3.632375 (0.0001)	
51-70	-9874701 (<0.0001)	-6.428828 (<0.0001)
Cr(VI)	15-40	41-50
41-50	-3.811803 (0.0001)	
51-70	-1.06e+01 (<0.0001)	-6.577074 (<0.0001)

Table 21: Cd - Dunn's Test for HEGs

	1	2	3	5	6	11
2	-2.716030 (0.0033)					
3	-5.342338 (<0.0001)	-2.521335 (0.0058)				
5	-4.540429 (<0.0001)	-3.228065 (0.0006)	-2.277737 (0.0114)			
6	-7.056022 (<0.0001)	-5.365864 (<0.0001)	-4.192846 (<0.0001)	-0.516478 (0.3028)		
11	1.289926 (0.0985)	2.603618 (0.0046)	3.636207 (0.0001)	4.330234 (<0.0001)	5.489373 (<0.0001)	
16	-5.308175 (<0.0001)	-4.559871 (<0.0001)	-4.030244 (<0.0001)	-2.483161 (0.0065)	-2.340863 (0.0096)	-5.388570 (<0.0001)

Table 22: Cr(VI) - Dunn's Test Results HEGs (Parte A)

	4	7	8	9	10	12
7	-4.760962					
	(<0.0001)					
8	0.043562	3.839840				
	(0.4826)	(0.0001)				
9	-11.000000	-6.215923	-9.151132			
	(<0.0001)	(<0.0001)	(<0.0001)			
10	-0.398675	3.143793	-0.376878	8.173284		
	(0.3451)	(0.0008)	(0.3531)	(<0.0001)		
12	-0.870687	2.948700	-0.768964	8.275462	-0.348296	
	(0.1920)	(0.0016)	(0.2210)	(<0.0001)	(0.3638)	
13	-6.058633	-0.185263	-4.488815	6.910246	-3.622045	-3.471267
	(<0.0001)	(0.4265)	(<0.0001)	(<0.0001)	(0.0001)	(0.0003)
14	-2.639824	1.672052	-2.192680	7.482322	-1.644886	-1.355507
	(0.0041)	(0.0473)	(0.0142)	(<0.0001)	(0.0500)	(0.0876)

Table 23: Cr(VI) - Dunn's Test Results HEGs (Parte B)

	4	7	8	9	10	12
15	-5.931093	-0.690576	-4.633782	5.930779	-3.829831	-3.686720
	(<0.0001)	(0.2449)	(<0.0001)	(<0.0001)	(0.0001)	(0.0001)
17	0.002985	3.622388	-0.032546	8.741680	0.333103	0.707042
	(0.4988)	(0.0001)	(0.4870)	(<0.0001)	(0.3695)	(0.2398)
18	0.031387	4.827693	-0.020085	11.085477	0.422405	0.899265
	(0.4875)	(<0.0001)	(0.4920)	(<0.0001)	(0.3364)	(0.1843)
19	-3.149001	0.230604	-2.804876	5.047834	-2.338163	-2.115563
	(0.0008)	(0.4088)	(0.0025)	(<0.0001)	(0.0097)	(0.0172)
20	-5.474563	-1.895791	-4.828369	3.128717	-4.251831	-4.112144
	(<0.0001)	(0.0290)	(<0.0001)	(0.0009)	(<0.0001)	(<0.0001)
21	-5.525454	0.762933	-3.916653	8.120860	-3.052117	-2.855130
	(<0.0001)	(0.2228)	(<0.0001)	(<0.0001)	(0.0011)	(0.0022)

Table 24: Cr(VI) - Dunn's Test Results HEGs (Parte C)

	4	7	8	9	10	12
22	-5.641262	0.176179	-4.182725	7.228549	-3.344025	-3.169492
	(<0.0001)	(0.4301)	(<0.0001)	(<0.0001)	(0.0004)	(0.0008)
23	-9.320191	-1.787664	-6.222767	6.345369	-5.056382	-5.068094
	(<0.0001)	(0.0369)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
24	-10.600000	-2.893550	-7.104281	5.365836	-5.849316	-5.939674
	(<0.0001)	(0.0019)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
25	-3.857352	-0.366000	-3.411592	4.573107	-2.905094	-2.705522
	(0.0001)	(0.3572)	(0.0003)	(<0.0001)	(0.0018)	(0.0034)
26	-5.706739	1.303768	-3.776501	9.062965	-2.863195	-2.651052
	(<0.0001)	(0.0962)	(0.0001)	(<0.0001)	(0.0021)	(0.0040)
27	-10.500000	-3.697519	-7.555056	4.078047	-6.359787	-6.460245
	(<0.0001)	(0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)

Table 25: Cr(VI) - Dunn's Test Results HEGs (Parte D)

	4	7	8	9	10	12
28	0.106209	4.086220	0.049499	9.589539	0.436313	0.848273
	(0.4577)	(<0.0001)	(0.4803)	(<0.0001)	(0.3313)	(0.1981)
29	-14.900000	-6.144817	-9.780629	2.782442	-8.200788	-8.548022
	(<0.0001)	(<0.0001)	(<0.0001)	(0.0027)	(<0.0001)	(<0.0001)
30	-1.799566	3.172892	-1.410900	9.572216	-0.852659	-0.478988
	(0.0360)	(0.0008)	(0.0791)	(<0.0001)	(0.1969)	(0.3160)
31	-9.605299	-3.174257	-7.044541	4.341930	-5.932188	-5.982551
	(<0.0001)	(0.0008)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
32	-16.800000	-7.439381	-10.800000	1.799087	-9.117392	-9.572789
	(<0.0001)	(<0.0001)	(<0.0001)	(0.0360)	(<0.0001)	(<0.0001)
33	-4.109022	1.628041	-3.022439	8.609387	-2.277999	-2.011225
	(<0.0001)	(0.0518)	(0.0013)	(<0.0001)	(0.0114)	(0.0222)

Table 26: Cr(VI) - Dunn's Test Results HEGs (Parte E)

	13	14	15	17	18	19
14	2.100604					
	(0.0178)					
15	-0.630431	-2.421688				
	(0.2642)	(0.0077)				
17	4.183662	2.062247	4.356136			
	(<0.0001)	(0.0196)	(<0.0001)			
18	6.168156	2.684789	6.018311	0.019432		
	(<0.0001)	(0.0036)	(<0.0001)	(0.4922)		
19	0.378613	-1.053116	0.739362	-2.691977	-3.181659	
	(0.3525)	(0.1461)	(0.2298)	(0.0036)	(0.0007)	
20	-1.937341	-3.139135	-1.454226	-4.649192	-5.518379	-1.763095
	(0.0264)	(0.0008)	(0.0729)	(<0.0001)	(<0.0001)	(0.0389)
21	1.281754	-1.343645	1.755725	-3.621995	-5.646626	0.248662
	(0.1000)	(0.0895)	(0.0396)	(0.0001)	(<0.0001)	(0.4018)
22	0.459135	-1.764051	1.026351	-3.895669	-5.745587	-0.128964
	(0.3231)	(0.0389)	(0.1524)	(<0.0001)	(<0.0001)	(0.4487)
23	-2.236771	-3.803880	-1.032485	-5.740743	-9.536528	-1.407851
	(0.0127)	(0.0001)	(0.1509)	(<0.0001)	(<0.0001)	(0.0796)
24	-3.786200	-4.803478	-2.287662	-6.563918	-10.800000	-2.119831
	(0.0001)	(<0.0001)	(0.0111)	(<0.0001)	(<0.0001)	(0.0170)

Table 27: Cr(VI) - Dunn's Test Results HEGs (Parte F)

	13	14	15	17	18	19
25	-0.268229	-1.656426	0.132160	-3.276470	-3.894152	-0.497508
	(0.3943)	(0.0488)	(0.4474)	(0.0005)	(<0.0001)	(0.3094)
26	2.199212	-1.019644	2.499088	-3.461291	-5.862222	0.555277
	(0.0139)	(0.1539)	(0.0062)	(0.0003)	(<0.0001)	(0.2894)
27	-4.575003	-5.421722	-3.209418	-7.042931	-10.700000	-2.753445
	(<0.0001)	(<0.0001)	(0.0007)	(<0.0001)	(<0.0001)	(0.0029)
28	4.842436	2.345322	4.948701	0.081155	0.081779	2.931371
	(<0.0001)	(0.0095)	(<0.0001)	(0.4677)	(0.4674)	(0.0017)
29	-8.599073	-7.792353	-5.983813	-9.031263	-15.300000	-4.145260
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
30	4.109069	1.149642	4.211226	-1.295831	-1.849996	2.017492
	(<0.0001)	(0.1251)	(<0.0001)	(0.0975)	(0.0322)	(0.0218)
31	-3.819217	-4.897153	-2.640517	-6.582306	-9.762939	-2.432382
	(0.0001)	(<0.0001)	(0.0041)	(<0.0001)	(<0.0001)	(0.0075)
32	-10.700000	-8.977810	-7.477422	-9.997845	-17.200000	-4.921706
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
33	2.337191	-0.449417	2.644002	-2.798837	-4.198044	0.859836
	(0.0097)	(0.3266)	(0.0041)	(0.0026)	(<0.0001)	(0.1949)

Table 28: Cr(VI) - Dunn's Test Results HEGs (Parte G)

	20	21	22	23	24	25
21	2.660146					
	(0.0039)					
22	2.193119	-0.765167				
	(0.0141)	(0.2221)				
23	1.036353	-4.590716	-2.828381			
	(0.1500)	(<0.0001)	(0.0023)			
24	0.298122	-6.445807	-4.370479	-2.643483		
	(0.3828)	(<0.0001)	(<0.0001)	(0.0041)		
25	1.284064	-0.933815	-0.524007	0.746400	1.479850	
	(0.0996)	(0.1752)	(0.3001)	(0.2277)	(0.0695)	
26	3.072336	0.859212	1.586945	8.342671	10.904523	1.276838
	(0.0011)	(0.1951)	(0.0563)	(<0.0001)	(<0.0001)	(0.1008)
27	-0.450653	-6.652770	-5.066905	-3.682997	-1.852418	-2.154156
	(0.3261)	(<0.0001)	(<0.0001)	(0.0001)	(0.0320)	(0.0156)

Table 29: Cr(VI) - Dunn's Test Results HEGs (Parte H)

	20	21	22	23	24	25
28	5.021603	4.265870	4.516542	6.793162	7.739914	3.560862
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0002)
29	-1.758646	-1.28e+01	-9.215137	-1.18e+01	-8.256210	-3.556376
	(0.0393)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0002)
30	4.316960	3.380897	3.691698	6.940831	8.239049	2.699750
	(<0.0001)	(0.0004)	(0.0001)	(<0.0001)	(<0.0001)	(0.0035)
31	-0.155335	-5.626637	-4.286201	-2.676820	-1.020224	-1.833149
	(0.4383)	(<0.0001)	(<0.0001)	(0.0037)	(0.1538)	(0.0334)
32	-2.543393	-1.58e+01	-1.13e+01	-1.69e+01	-1.27e+01	-4.352232
	(0.0055)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
33	3.229487	1.317585	1.862998	5.442816	7.031301	1.543948
	(0.0006)	(0.0938)	(0.0312)	(<0.0001)	(<0.0001)	(0.0613)

Table 30: Cr(VI) - Dunn's Test Results HEGs (Parte I)

	26	27	28	29	30	31
27	-8.989974					
	(<0.0001)					
28	4.158885	8.142042				
	(<0.0001)	(<0.0001)				
29	-2.35E+01	-3.273830	-1.07E+01			
	(<0.0001)	(0.0005)	(<0.0001)			
30	3.266620	8.453350	-1.553779	12.490572		
	(0.0005)	(<0.0001)	(0.0601)	(<0.0001)		
31	-7.430198	0.562869	-7.571602	3.672515	-7.628317	
	(<0.0001)	(0.2868)	(<0.0001)	(0.0001)	(<0.0001)	
32	-3.23+e01	-5.458410	-11.8	-4.624086	-14.3	-5.633130
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
33	0.868182	7.264917	-3.288362	12.351159	-2.107075	6.328895
	(0.1926)	(<0.0001)	(0.0005)	(<0.0001)	(0.0176)	(<0.0001)

Table 31: Cr(VI) - Dunn's Test Results HEGs (Parte L)

	32
33	14.692909
	(<0.0001)

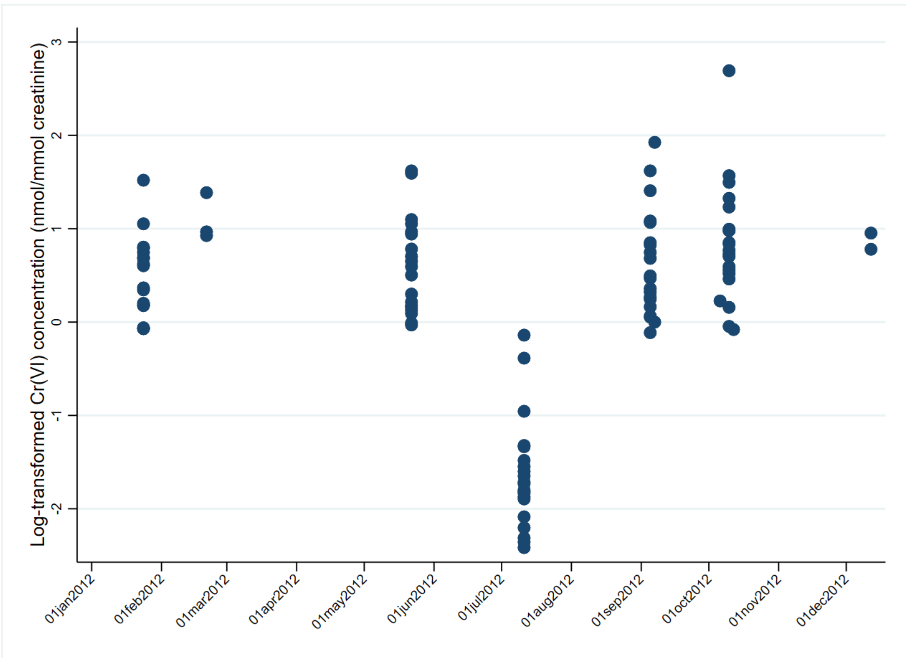

Figure 12: Company- HEG 26, Cr(VI) 2012 Trend

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