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par

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Human health risk assessment of occupational exposure to trace metallic elements mixtures in metalworking industries in the Sfax metropolis (Tunisia)

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Dedication

Praise to GOD the most merciful and compassionate for giving me the strength and patience to accomplish this work.

This work is dedicated to:

My parents; mom and dad, no words can describe the love, respect and gratitude for your endless support all along my studying journey. This support is the key of all achievements. I'm thankful for everything; from tiny details to big sacrifices.

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LIST OF ABBREVIATIONS

ABS: Acrylonitrile butadiene styrene
ACGIH: American Conference of Governmental Industrial Hygienists
ACH: air changes per hour
AIHA: American Industrial Hygiene Association
ANSES*: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*
ATSDR: Agency for Toxic Substances and Disease Registry
Cal/ OSHA: Division of Occupational Safety and Health in California
Chronic ReV: Chronic Reference Value
EF: emission factor
FCF: fume correction factor
FF: Far Field
FSA : free surface area
G: generation rate
GMAW: Gas Metal Arc Welding
HHRA: Human Health Risk Assessment
HI: hazard index method
HIint: Interaction-based hazard index
HM: heavy metal
HQ: hazard quotients
IAE (or Rm): *Indice d'exposition des effets Additionnels*
IHMOD: Industrial Hygiene Modeling
INRS: Institut National de Recherche et de Sécurité
IPCS: International Programme on Chemical Safety
IRIS: Integrated Risk Information System
LEV: local exhaust ventilation
LM: *location measures*
MAG: metal active gas
MAK: *Maximum Permissible Concentration*
MMA: Manual Metal Arc welding
MOA: mode of action
MRL: Minimal Risk Levels
NF: Near Field
NIOSH: National Institute for Occupational Safety and Health
NM: Not Mentioned,
NRC: National Research Council
OEHHA: California Office of Environmental Health Hazard Assessment
OSHA: Occupational Safety and Health Administration
PBPK: Physiologically Based PharmacoKinetic
PEL: Permissible Exposure Limit

Q: ventilation rate
REL: Chronic Reference Exposure Level
RfC: Reference concentration
RIVM: Netherlands National Institute for Public Health and the Environment
RPF: relative potency factors methods
RSW: resistance spot welding
SMAW: Shielded Metal Arc Welding
SS: steady state
TC or TCA: Tolerable Concentration in Air
TCEQ: Texas Commission on Environmental Quality
TEF: Toxic Equivalency Factor
TEQ: total equivalent quantity
TLV: Threshold Limit Value
TRV: Toxicological Reference Value
TTC: target-organ toxicity concentration
TTD: target-organ toxicity dose
TWA: time –weighted average
UPMI: *Union des Petites et Moyennes Industries*
URF or UR: inhalation Unit Risk or Unit Risk Factor: increased cancer risk from inhalation exposure to a of 1 µg.m-3 for a lifetime
US EPA: US Environmental Protection Agency
V: air volume
VLEP: Valeurs Limites d'Expositions Professionnelles
VTR: *Valeur Toxicologique de Référence*
WHO: World Health Organization
WMB: Well Mixed Box
WOE: weight of evidence

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(GMAW and system control of the tube welding machine) during four-hour shift

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GENERAL INTRODUCTION

GENERAL INTRODUCTION

I.   Context and general objectives

I.1. State of the art

Some trace metallic elements are considered as among the most threatening toxic elements for human health especially for exposed workers and residents nearby industrial units and polluted sites [1]. They were identified by ATSDR (Agency for Toxic Substances and Disease Registry) in a list that prioritizes substances based on their frequency, toxicity, and potential for human exposure. On the top of the list stands arsenic (As), then lead (Pb) in the second place and cadmium (Cd) in the seventh place [2]. Even in trace amounts, TMEs are considered as pollutants of great concern because of their toxicity, in particular due to their carcinogenic and mutagenic potencies [3–5] and their accumulation and non biodegradation in the living environments [6–8].

Acute exposure causes harmful effects such as respiratory irritations and lung inflammation [3,4], hepatic cell destruction, kidney and neurological damages and sometimes even death [9]. However, chronic exposure to TMEs is more of concern due to their cumulative property [10].

On the other hand, combined exposure to various chemical products is unavoidable in everyday life, and humans are exposed to mixtures simultaneously and /or consecutively [11]. It must be emphasized that the majority of polluted sites contain several TMEs at the same time [12–15].

Nonetheless, considering the complexity of studying chemical mixtures and the lack of toxicological studies, the greater part of chemical risk assessment studies of TMEs deal with exposures and associated effects to single substances [16–18]. Response prediction of biological organisms exposed to more than one toxic chemical is one of the hardest tasks in environmental toxicology and risk assessment [16]. Thus, it is necessary to study the combined effects of mixtures reflecting more realistically the real exposure [11]. That is why, in this study, we will assess the joint effects of exposure to trace metallic elements mixtures. Among the reasons of the increasing interest about mixtures is that some unresolved questions arise [11]. For example, joint exposure to Cd and Pb showed synergistic effects on kidney, neurological and reproduction impairments [10].

I.2. Study site

Sfax is Tunisian's second largest city, and is considered the economic capital due to the presence of many industrial zones [19] and its significant role in exports. Figure 1 shows the location map of industrial areas and the main sources of pollution in the Sfax metropolis. In this region, residents living close to industrial zones for years are constantly exposed to harmful metallic pollutants [1]. In fact, Sfax is suffering from a serious ecological situation caused primarily by many industrial units [20]. It is important to note that effluents from some industrial activities exceed the trace metallic element levels fixed by the current standards [20]. These metals are generally derived from many anthropogenic sources like industrial sewage and fumes [1,6,14,20–22].

II. Literature review

II.1. Metallic pollution in Sfax:

Several studies conducted in the Sfax region have shown that industrial activities are generating multiple metallic pollutants affecting all three compartments of the environment (air, water and soil) [18–21] and pollutants are found in soils [15,23], surface and sub-surface sediments [12,14,24] as well as in sea water along the Sfax coastline [25]. Moreover, several living beings have been proven to be affected, including marine organisms (fish, mollusks, cuttlefish, tuna, etc.) living near the industrialized coastline [6–8,13,21,26–28]and the fishing harbor of Sfax [14,22,29–31]. Epidemiological studies among populations from Sfax metropolis have investigated the relationship between metallic pollution and certain illnesses [18,20,32,33].
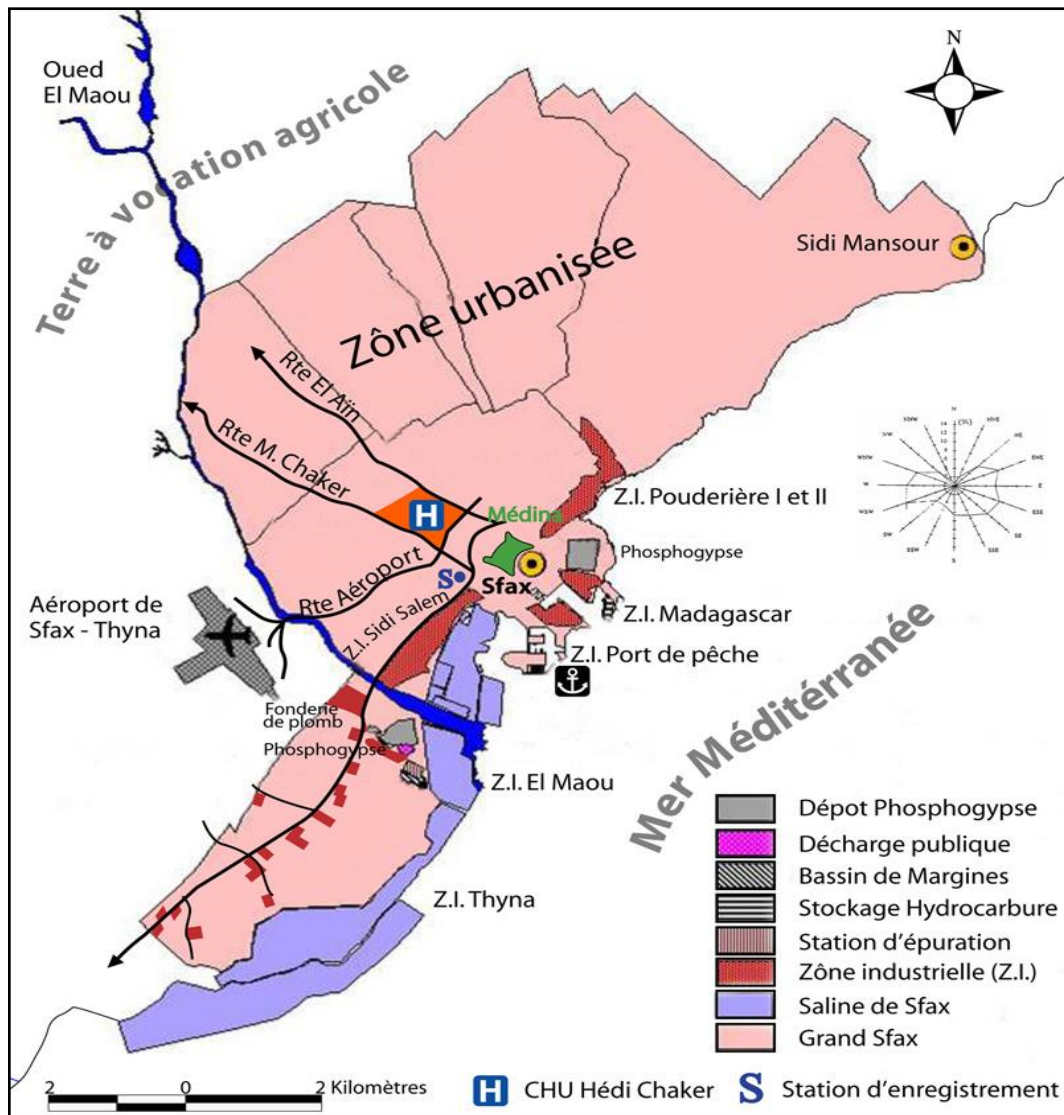
Figure i. Location map showing industrial areas and the main sources of pollution in the Sfax metropolis [19]**.**

These studies focused on coastal zone residents and the downtown population, and mention that occupational exposure to TMEs may be a probable factor in explaining the high risk of various cancers identified in the region. The metals most frequently found are Cd, followed by Zn, Pb, Ni, Cr, As, Cu, and Hg [6–8,12–15,18,20–23,25–37].

In this context, assessment of occupational exposure to such metals calls for thorough investigation both for the scientific communities and decision makers. To our knowledge, there is no study that has assessed the occupational exposure to TMEs, qualitatively nor quantitatively in this region. And the combined effects of mixtures have never been explored. Thus, in this study, we are interested in occupational exposure to trace metallic elements in the Sfax metropolis and its quantitative human health risk assessment.

II.2. Human health risk assessment

II.2.1. Presentation of the approach

Human Health Risk Assessment (HHRA) was introduced in 1983 by the National Research Council (NRC) in the United States [38–40]. This scientific approach strives to use the available knowledge in a systematic manner through a standardized, transparent and coherent methodology [39]. It encompasses four steps: (i) hazard identification, (ii) dose-response assessment, (iii) exposure assessment, and (iv) risk characterization.

II.2.2. Hazard identification

Hazard identification is also referred to as "Hazard characterization" [40]. In the hazard identification step, one should define the potential adverse effects on biological endpoints/ target organs due to exposure to the considered trace metallic elements, based on the available toxicological data [41]. Toxicological data are principally explored in the Toxicological Profiles documents from ATSDR [42], the IRIS (Integrated Risk Information System) from USEPA [43] and the Toxicological Sheets from INRS (*French National Research and Safety Institute for the Prevention of Occupational Accidents and Diseases)*. There are also some newer Development Support Documents established by TCEQ (Texas Commission on Environmental Quality) [44].

Hazard identification was initially introduced as the first step in HHRA. Still, according to a newer framework of risk assessment presented by IPCS (the International Programme on Chemical Safety) and WHO (World Health Organization) [45], it could be achieved in parallel with its closely linked second step of dose-response assessment and exposure assessment [40].

Accordingly, in the first and the second parts of our study manuscript, we will first deal with the exposure assessment step, introduce our methodology and expose the results. Then, in the third part, we will tackle the choice of the reference values and the risk characterization.

II.2.2.1. Trace metallic elements

Trace metallic elements are special inorganic pollutants. They attracted a particular attention of USEPA so as to develop a framework for metals risk assessment [46]. Some TMEs such as iron, copper and zinc are essential elements to human body since they are consumed as

nutrients [47]. Furthermore, unlike other pollutants, some TMEs are naturally occurring elements in the environment and their concentrations may differ across geographic sites [40].

Additionally, in contrast to organic compounds, metals cannot be produced or deteriorated by either chemical or biological reactions. But these reactions could change the valence state of the metal, or turn inorganic forms into organic ones, consequently altering their toxicity [46].

II.2.2.2.   Identification of potential hazards of the selected trace metallic elements

Potential adverse effects of the selected metals on biological endpoints/ target organs for the inhalation exposure are explored according to the identified exposure route.

The selection of the metals is detailed in the following part.

a.   Health effects of chronic exposure to Al by the inhalation route

Workers exposed to Al dust showed respiratory effects [48]. Lung problems vary from coughing and occupational asthma to alteration in chest X-rays and pulmonary fibrosis. Animal studies have also revealed adverse respiratory effects, such as the increases in alveolar macrophages and increase in lung weight [48].

TRVs were not constructed for Al because there are doubts on whether the respiratory effects are due to general dust or specifically to the Al in it. Moreover, exposure assessment in occupational studies did not allow calculating an inhalation TRV [48].

On the other hand, occupational studies about workers exposed to Al dusts and fumes reported neuro-toxic symptoms [49,50].

Actual data do not show evidence of carcinogenicity [48].

b.   Health effects of chronic exposure to Cr by the inhalation route

Occupational and especially animal studies have thoroughly assessed the chronic effects of inhalation of Cr and its compounds Cr(III) and Cr(VI). The respiratory system and the skin were confirmed to be the main affected organs [51].

In some specific industries like electroplating, Cr(VI) compounds are used. It was reported that chronic exposure to this particular form of Cr may increase death risk due to non-cancer respiratory illnesses [51]. In our study, we are not considering chromium speciation, but merely the total and/or metallic Cr.

Eye inflammation was also reported from occupational studies where workers were exposed to mists and aerosols of Cr compounds [51].

Metallic Cr and Cr III are not classified as a human carcinogen according to WHO [52]. However, Health Canada [53] has considered total Cr as a carcinogen and established a Tumorigenic Concentration 05 $TC_{05} = 4.6$ µg/m^3. This value refers to a concentration in the air that is associated with a 5% increase in incidence or mortality due to tumors. It is not a carcinogenic TRV, but a Unit risk can be derived based on this value.

c.   Health effects of chronic exposure to Ni by the inhalation route

Soluble and insoluble nickel compounds showed adverse respiratory effects in rodents. Lung problems include active lung inflammation, alveolar proteinosis and fibrosis [54]. Several occupational and more animal studies confirm the damages in the respiratory tract [4].

Epidemiological studies demonstrated that Ni is a carcinogenic element [55,56]. In 2012, Ni was classified by the WHO as carcinogenic to humans (group 1) [52].

d.   Health effects of chronic exposure to Cu by the inhalation route

Occupational studies have reported that Cu is a respiratory irritant [3] with, among other consequences, pulmonary fibrosis.

Other adverse effects were also reported: gastrointestinal, hematological, hepatic and neurological [3].

Cu is not classified as to human carcinogenicity [57]

e.   Health effects of chronic exposure to Pb by the inhalation route

Many studies on Pb chronic exposure have reported several adverse effects such as hematological, digestive, neurological, renal, cardiovascular, bone and reproductive toxic effect [5,58].

Some studies has indicated probable increases in lung and stomach cancer [5,59].

In 2006, inorganic compounds of Pb were classified by WHO as Probably carcinogenic to humans (stomach cancer) (group 2A) [52].

Moreover, OEHHA [60] has established an Inhalation Unit Risk = $1.2 \times 10^{-5} (\mu g/m3)^{-1}$ for kidney tumors based on animal data.

<p style="text-align:center">f.   Health effects of chronic exposure to Zn by the inhalation route</p>

Acute exposure studies have shown respiratory adverse effects. However, there is little information about chronic exposure to zinc dust or fumes and their effects [61]. No TRV was established because of lack of exposure quantification.

The US EPA declared that there was no adequate data to assess Zn's carcinogenicity [62]

II.2.2.3. Mixture and interactions of metals

Metals are frequently occurring as components of a mixture, especially in occupational settings. That is why it is necessary to take into account the interactions between metals in the hazard characterization analysis [46,47].

TMEs' joint effects could be distinct from simply additive; they can be synergistic, antagonistic or potentiating [40]. There is another kind of interaction between metals which is named "*molecular or ionic mimicry*". It is a competitive interaction when two metals/metalloids are chemically similar; in most cases, a toxic metal replaces an essential metal [40]. Moreover, many MHs form complexes with several proteins in the human body, which could affect their toxicity [40].

The ATSDR has focused on some trace metallic elements and established two interaction profiles about lead, manganese, zinc, and copper, and arsenic, cadmium, chromium and lead [10,63]. Interaction data reports and guidance are limited [40] and relatively old. Thus, we will also explore new published studies.

II.2.2.4. Toxicokinetics: Physiologically Based PharmacoKinetic models

At the beginning of the study design for this project, in order to explore internal doses in target organs/tissues, we intended to use a PBPK (Physiologically Based PharmacoKinetic) model [64]. Though PBPK models have been used extensively for mixtures such as organic solvents, this is not, to the best of our knowledge, the case for TME mixtures [65]. In spite of the critical need for such a model, particular complexities regarding TMEs prevented their implementation due to the extreme variability of biological half-lives of the main toxic TMEs

[66], which range from days (for As) to decades (for Pb). Hence, PBPK models will not be elaborated upon hereafter.

II.2.3.   Exposure assessment

II.2.3.1.   Occupational exposure to trace metallic elements

In the general population, the most likely exposure route of TMEs such as Pb, Cu, Zn and Al is the oral pathway. By contrast, in occupational settings, workers are predominantly exposed by inhalation [5]. Thus, we are especially interested in the inhalation pathway and the airborne amount of trace metallic elements in the workplace.

For the inhalation route, metals are generally in solid phase under regular environmental conditions of the atmosphere, so they normally exist in particle phase [40]. However, in occupational circumstances using combustion process (e.g. for melting), metals and metal compounds may also exist as vapors.

II.2.3.2.   Mathematical modeling of occupational exposure to chemicals

Recent developments in modeling allow prediction of exposure to chemicals by using descriptive environmental characteristics and/or the human physiological factors. Since we are dealing with occupational exposures and according to the selection criteria for the study companies (detailed in the first part), inhalation is the main exposure route. We have chosen mathematical models to estimate occupational exposure to airborne pollutants [67,68]. In this framework, a variety of models have been used to predict indoor air pollutants' concentrations. The models differ in their hypotheses as to (i) pollutant transport mechanisms and (ii) uniformity of the air mixture in the workplace. In our study, these models were executed using the IHMOD "Industrial Hygiene Modeling" software [69,70], which is a model compilation for the calculation of inhalation concentration. It is available from the American Industrial Hygiene Association (AIHA) website [69]. IHMOD currently offers 11 models. The three most commonly-used categories are: (i) the Well Mixed Box, (ii) the Near Field and Far Field model and (iii) the Eddy Diffusion Turbulent model [67].

These predictive models of indoor air concentrations are based on environmental working conditions as well as certain other specific information about the manufacturing process [67]. These models were initially developed for solvents and other volatile compounds, in relation to their physicochemical proprieties. With regards to metals, to the best of our knowledge,

similar models were applied only to arc welding processes, in a study in which Boelter et al. calculated field-derived emission rates of total particulate encompassing only iron and manganese [71]. Another newer study [72] have used the well mixed box and Near Field and Far Field model to predict cobalt exposure levels in two job tasks involving powder weighing and mixing. The authors also calculated the emission rates using source air sampling. In the preset study, we aim to broaden the application of these mathematical models to TMEs, as well as to several types of emissions in various production processes.

a. Well mixed box model

This model suggests a simplified representation of chemicals dispersion. It estimates the air concentration of a completely well mixed room. It means that the pollutant is equally distributed over the room [73].

The input main parameters are the emission or generation rate "G", ventilation rate "Q" and the volume of the air in the workplace "V".

The predicted indoor air concentrations in the WMB are computed using the IHMOD software [69,70], using the following formula;

$$C_{WMB}(t) = \frac{G + C_{in}Q}{Q + K_L V}\left[1 - e^{-(\frac{Q+K_L V}{V}t)}\right] + C_0 e^{-(\frac{Q+K_L V}{V}t)}$$

Where;
G: generation rate or emission rate, expressed in mg/min

Q: ventilation rate, expressed in m^3/min

V: volume of the air in the workplace, expressed in m^3

C_{in}: pollutant concentration in supply air, expressed in mg/ m^3 (generally assumed to be zero)

K_L: loss value due to "non-ventilatory" losses (sorption or chemical degradation of the pollutant) [73], expressed in fraction/time. Values ranges from 0 (default: no loss except via ventilation) up to 1.

C_0: pollutant concentration in the room at t_0, expressed in mg/m^3. It is used when there is already a known concentration of the pollutant before the beginning of the emission [73].

After a certain time, the pollutant concentration becomes almost constant as much as the parameters remain the same [73]. It is called the steady state where the predicted concentration reaches a maximum value, and the formula turns into, as below;

$$C_{WMB,SS} = \frac{G}{Q}$$

The input parameters are going to be detailed later.
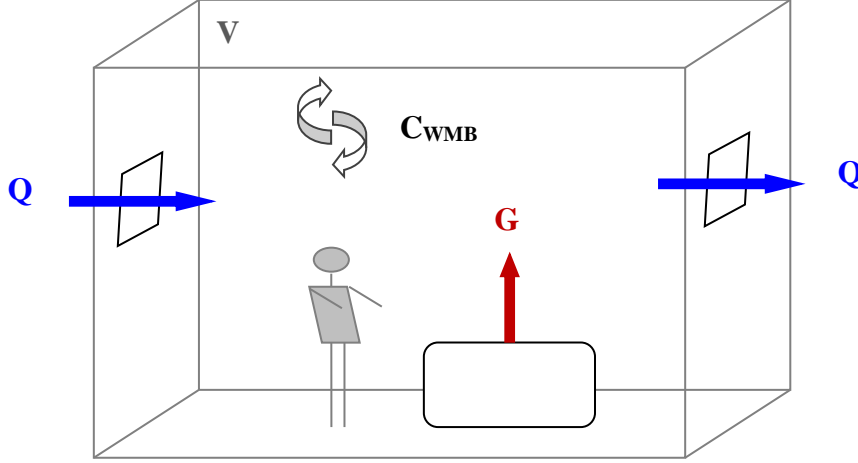
Figure ii: Well mixed box model presentation; G: generation rate, Q: ventilation rate, V: air volume, C_WMB: predicted concentration of the pollutant

      b.   Near field –far field model

It is a two-zone model that tries to provide more accurate pollutant estimation for employees working near the emission source. It divides the workplace conceptually into two zones. The Near Field (NF) box includes, by definition, the emission source of the pollutant and the breathing zone of the worker whose exposure is to be estimated [74]. It is conceptualized depending on the exposure situation as a parallelepiped or hemisphere on the floor, on the machine or on work surface. The Far field (FF) is the remaining volume of the workplace, where pollutant concentration is assumed to be lower, and homogeneous over the FF [74].

The NF-FF model is recognized in the scientific community as an occupational exposure assessment tool [75].

The indoor air concentrations of TME in the NF and FF box are computed using the following formulas [74];

$$C_{NF}(t) = \frac{G}{Q} + \frac{G}{\beta} + G\left(\frac{\beta.Q + \lambda_2.V_{NF}(\beta + Q)}{\beta.Q.V_{NF}(\lambda_1 - \lambda_2)}\right)e^{\lambda_1 t} - G\left(\frac{\beta.Q + \lambda_1.V_{NF}(\beta + Q)}{\beta.Q.V_{NF}(\lambda_1 - \lambda_2)}\right)e^{\lambda_2 t}$$

$$C_{FF}(t) = \frac{G}{Q} + G\left(\frac{\lambda_1.V_{NF} + \beta}{\beta}\right)\left(\frac{\beta.Q + \lambda_2.V_{NF}(\beta + Q)}{\beta.Q.V_{NF}(\lambda_1 - \lambda_2)}\right)e^{\lambda_1 t}$$

$$- G\left(\frac{\lambda_2.V_{NF} + \beta}{\beta}\right)\left(\frac{\beta.Q + \lambda_1.V_{NF}(\beta + Q)}{\beta.Q.V_{NF}(\lambda_1 - \lambda_2)}\right)e^{\lambda_2 t}$$

Where;

G and Q: the same as in WMB model.

V_{NF}: the NF volume, expressed in (m^3).

β: the inter-box air flow rate between the NF and the FF, expressed by (m^3/min).

λ_1 and λ_2: the air turnover rates in the FF and NF, respectively (expressed by min^{-1}).

At the steady state, the formulas become as the following;

$$C_{NF,SS} = \frac{G}{Q} + \frac{G}{\beta} \qquad \text{and} \qquad C_{FF,SS} = \frac{G}{Q}$$
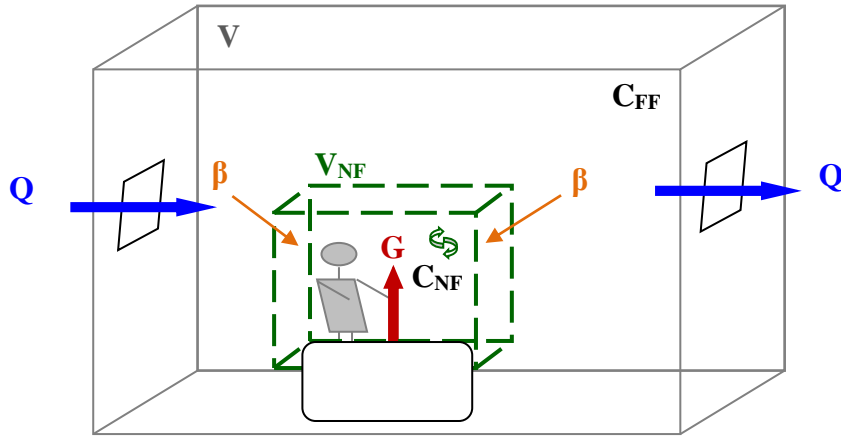
Figure iii: Near-Field, Far-Field model presentation; G: generation rate, Q: ventilation rate, β: inter-box air flow rate, V: air volume, V_{NF}: NF air volume, $C_{NF/FF}$: predicted concentration of the pollutant in the NF and FF, respectively

    c.   Parameters calculations

        i.   *Ventilation rate "Q"*

Prior to Q determination, mass conservation of the quantity of matter in the air needs to be verified, so as to prove that there is no backpressure effect in the workplace. Confirmation of the basic assumption allowing calculation of the ventilation rate for the whole workplace is a necessary pre-step. This assumption considers air in the workplace room to be an ideal gas, and that the air flow rate entering the room is equal to that leaving it [76].

Mass conservation is calculated following the basic formulas of the ideal gas law:

$$P_{in/out} \times V = n_{in/out} \times R \times T_{in/out}$$

Where:

$P_{in/out}$: the air pressure entering or leaving the workplace room in Pascal (Pa)

V: the air volume (m^3);

n: the quantity of matter (mol);

R: the ideal gas constant (unit $J.K^{-1}.mol^{-1}$);

T: the temperature inside or outside the workplace in Kelvin (K)

So, it is necessary to demonstrate that the quantity of matter entering and leaving the room is approximately the same [76].

$$n_{in} \approx n_{out}$$

We therefore calculate that n_{in} / n_{out} should be approximately equal to 1.

Then, we assume air direction to be constant; therefore the volumetric air flow rate is conserved:

$$Q_{in} = Q_{out}$$

When the workplace is naturally ventilated by doors and windows, the Q_{in} entering from the main door is calculated by measuring the average air face velocity "V_{face}" through the door over the time range of interest, and recording the dimensions of the doors. The average "Q" within the volume of interest is calculated using the following formula [76]:

$$Q_{average} = V_{face_{average}} \times S$$

Where:

$V_{face average}$: mean of air face velocity values ($m.s^{-1}$)

S: the cross-sectional surface of the main door or air inlet opening (m^2)

Some authors also use the air changes per hour ACH as an indicator of the ventilation rate [67]. It is calculated using the effective air volumes in workplaces V and the air flow rates Q by the following formula:

$$ACH = \frac{60 \times Q}{V}$$

ii.   The air volume "V"

In order to calculate the air volume inside of the room, all volumes within the room have to be subtracted, so to have a more accurate value. These volumes include the machines, material stocks, etc.

iii.   Generation rate "G"

The generation rate or the emission rate, noted G, is the amount of pollutant released over a period of time. It is generally expressed per mg. min^{-1}.

The available studies uses sample concentration measurements to calculate G. This is majorly used with volatile organic compounds [72,77–81]. As for metal compounds, both identified studies [71,72] have used prior sample concentration measurements conducted in the vicinity of the emission source to determine the G for Fe, Mn and Co.

In fact, to demonstrate the usefulness and validity of these models as an alternative and cost-effective method of indoor air concentration determination [82], we looked for other alternative methods in literature in order to avoid relying on concentration measurements to determine G.

There are also other methods in literature, where the G could be calculated without using air sampling. However, the utility of these methods need to be evaluated.

The main two methods are: (i) mass balance and (ii) Emission Factor (EF).

1)   The mass balance method

During the manufacturing process, masses of the materials are maintained. The quantity of pollutant emitted into the workplace can thus be calculated using the equation [83]:

$$\text{mass}_{\text{into process}} - \text{mass}_{\text{incorporated into product}} - \text{mass}_{\text{collected as waste}}$$
$$= \text{mass}_{\text{released in room}}$$

One should take into account the division of the mass per time (production per year or per day for example). The result is an average G.

To use the mass balance method, all forms of metal transformation during the processes are evaluated: mass of end-products, mass collected as waste (often sold to other companies for

other usages) and even dust deposited on the workplace floor. The difference between the sum of the latter and the raw metal quantity will be the suspended aerosol. Concentrations of the various TMEs within this aerosol will be assessed.

2) The emission factor method

An EF is calculated for a specific process, and sometimes for specific parameters and conditions. It relates the quantity of pollutants to a particular activity. It facilitates estimation of the generation rate, especially where there is a lack of information or difficulty in calculating it [83]. US-EPA (US-Environmental Protection Agency) has used EFs extensively to assess air pollution related to industrial emissions, compiling this data in the AP-42 *Compilation of Air Pollutant Emission Factors* [84,85]. The common equation for emissions estimation is the following [86]:

$$G = \ Emission = A \times EF \times (\frac{1 - ER}{100})$$

Where:

G is expressed in mass per time; in our case (mg. min^{-1})

A = activity rate;

ER = overall emission reduction efficiency, in %

Generally, the EFs in AP-42 are calculated from all acceptable quality studies. Identification of true emission factors at a specific plant is difficult. For this reason, AP-42 is recommended, which provides tools for the estimation of emission factors applicable to the situation of interest [84,85]. In this investigation, since we were unable to find EFs for each process, we attempted to retrieve the information from external studies. In order to cope with these uncertainties, a Monte Carlo simulation could be considered [83].

- *Emission factors for electric arc welding*

US EPA specifically treated some specific job processes in AP 42: Compilation of Air Pollutant Emission Factors [85]. Among those we are interested in, we can find the Electric arc welding and electroplating processes.

In the section dedicated to electric arc welding [87], US EPA provides EFs for some trace metallic elements (Cr, Ni, Pb) depending on the welding process and the electrode type.

Furthermore, in the chapter dedicated to metallurgical Industry in AP 42 [85], the US EPA treated also the electroplating process [88]. In this section, we can find emission factors for uncontrolled emissions or controlled emissions from electroplating baths.

The EFs proposed by AP-42 for the electrodes were only established for Cr and Ni. However, the electrodes can also contain other TMEs. So, to calculate the emission rate G for the rest of the existing TMEs, AP 42 provides also the EFs of the total fumes.

Furthermore, the SAN DIEGO Air Pollution Control District established a fume correction factors FCF for SMAW and GMAW processes [89] in order to calculate the emission rate G for the TMEs which are not established in AP 42. In fact, factor calculations were fully based on an earlier report established by the Department of the Navy Carderock Division [90].

The new proposed formula is:

$$G = A \times EF \times FCF \times C_i \times (\frac{1 - ER}{100})$$

Where;

C_i :the concentration of the metal (i) in the welding wire

FCF: fume correction factor per NASSCO –Richard bell (metal mass/fume mass)

=0.5464 for GMAW

=0.2865 for SMAW.

- *Emission factors for electroplating*

A special focus was also given to chromium electroplating and chromic Acid anodizing where many EFs were established depending on the control system devices. Several control systems were considered such as moisture extractors chemical fume suppressants and polypropylene balls. In addition, only particular cases of Ni, Cu and Cd emissions were developed. Finally, for other metals or if we have another control system, US EPA provides equations to calculated our own EFs using specific technical information about the electroplating baths.

To estimate an EF for a metal "m" from non-chromium the following formulas are used [88]:

i. For uncontrolled electroplating tanks:

$$EF_m = 3.3 \times 10^{-7} \left(\frac{EE_m}{e_m}\right) C_m D_m$$

ii. For controlled electroplating tanks:

$$EF_m = 0.028 \times EF_{Cr} \times C_m$$

Where:

EE_m: electrochemical equivalence for the considered metal; expressed in A-hr/mil-ft^2

e_m: cathode efficiency for the metal; expressed in %

C_m: the metal concentration; expressed in oz/gal

D_m: current density for the metal; expressed in A/ft^2

The EF values are expressed either in grains/ A-hr or in grains/ dscf (dry standard cubic foot). Possible conversions are allowed from grains/ A-hr to grains/ dscf and from grains/ dscf to mg/ dscm (dry standard cubic meter) by multiplying with 0.01 and 2290, respectively [88,91].

Finally, the concentrations have to be converted into mg/m^3. In fact, US EPA is considering the plating emissions on dry basis. Thus, we have to take into account moisture in the emitted gas using the following formula [92]:

$$C_{Dry} = C_{Wet} \times \frac{100}{(100 - H_2O\%)}$$

In chromic acid anodizing, the EFs are converted from grains/hr-ft^2 to mg/hr-m^2 by multiplying with 697 [88]. So, in order to calculate the G, the surface of the bath is required.

- *Emission factors for Resistance sport welding*

Elsewhere, the city of Toronto has illustrated a method to calculate the emission rate in the context of a Public Health program named Chemical Tracking in Industry "ChemTRAC" [93]. An emission factor is specially established for RSW and presented only Ni and Cr.

The used formula is the following:

$$\text{Metal Released}_{Ni/Cr} = L_W \times EF$$

Where;

Metal released: is equivalent to G and expressed by kg/ time

EF: is estimated as 0.000033 kg/m per weld length

$$L_w = d_w \times N_{piece} \times N_w^{piece}$$

L_w: weld length; expressed by m

d_w: weld diameter; expressed by m

N_{piece}: number of workpieces (or metal sheets)

N_w^{piece}: number of welds per workpiece(or per metal sheet)

This method doesn't consider the percentage of the metal in the materials which is variable for each material. In addition, it doesn't allow us to calculate the G of other metals. That's why we looked for an alternative method to calculate the G. In fact, this method is available for industrial use and has not been documented in a research references.

So, we tried to find an alternative way. Therefore, research studies that are interested in calculating the fume emission rate released from RSW were explored. Then, the TMEs generation rates could be calculated using the percentage of each metal in the materials.

3) Other model-specific parameters:

We formerly mentioned the key essential parameters for all models. Since we actually have 11 subtypes of models in IH-Mod modeling software tool [69,94], there are other model specific parameters. As examples, we mention the concentration of a pollutant in room air at time t_0, noted C_0 and the emission rate constant, noted α. These two parameters are usually used with volatile organic compounds like toluene and acetone [67].

In our case, we are interested in identifying the specific parameters of NF-FF model. In order to calculate the indoor air concentration of TME in the NF box, the formulas previously presented are used;

The first parameter is β ($m^3.min^{-1}$); the inter-box air flow rate. It is calculated using the following formula[74];

$$\beta = {}^1\!/_2 . FSA . S$$

Where:

FSA (m^2): is the free surface area of the NF box which means the value of the geometrical surface of the NF box where air is free to flow through.

S(m/min): is the average random air speed close to the NF boundary.

The second ones are λ_1 and λ_2 (min^{-1}); corresponding to the air turnover rates in the FF and NF, respectively. We don't have to determine them because they are directly calculated from the other parameters by means of the following equations [74]:

$$\lambda_1 = 0.5 \left[-\left(\frac{\beta.V_{FF} + V_{NF}(\beta + Q)}{V_{NF}.V_{FF}} \right) + \sqrt{\left(\frac{\beta.V_{FF} + V_{NF}(\beta + Q)}{V_{NF}.V_{FF}} \right)^2 - 4\left(\frac{\beta.Q}{V_{NF}.V_{FF}} \right)} \right]$$

$$\lambda_2 = 0.5 \left[-\left(\frac{\beta.V_{FF} + V_{NF}(\beta + Q)}{V_{NF}.V_{FF}} \right) - \sqrt{\left(\frac{\beta.V_{FF} + V_{NF}(\beta + Q)}{V_{NF}.V_{FF}} \right)^2 - 4\left(\frac{\beta.Q}{V_{NF}.V_{FF}} \right)} \right]$$

II.2.4.   Risk characterization methods for chemical mixtures

Regarding mixture risk assessment, two main methods are proposed in the literature: (i) methods for "whole-mixture data" where the mixture is studied as a whole component, such as fuels, diesel, coke oven emissions, etc. [41,47]; and (ii) methods for component data where the components are considered as a particular combination of specific chemicals [41].

There are several methods to calculate the combined or cumulative effect of exposure to multiple chemicals. The majority of these methods are either dose-addition methods (e.g. the hazard index method-HI), relative potency factors methods (RPF)) or response-addition methods. They all ignore interactions between the mixture components by considering them as toxicologically similar or as "toxicologically independent", respectively [41]. Here are more details about these methods.

(i) Addition hazard index : US EPA developed the Hazard index method in the Guidelines for the Health Risk Assessment of Chemical Mixtures [95]. Ideally, HI is recommended for chemical mixtures whose components have the same mode of action (MOA); in a practical

manner, a similar target organ is deemed sufficient to apply the method [41]. The HI should be considered for a specific route of exposure and exposure period [41].

HI is the sum of individual hazard quotients (HQ) of the mixture components. By definition, a HQ is dimensionless and calculated by dividing the exposure measures by an acceptable level [41]. The acceptable level is the threshold Toxicological Reference Value (TRV, termed as *VTR* in French, *Valeur Toxicologique de Référence*) which is mostly replaced by RfC (Reference concentration, for inhalation exposure) as the TRV illustrated by US EPA [43].

(ii) The Relative potency factors method: it is a widely used method nowadays. This method is rather a Dose-Response Assessment method [41]. It is used for mixtures of chemicals with a common mode of action. An index compound (usually the most studied chemical) is used as a reference. Then, RPFs are calculated for each component, relative to this index compound, and a total equivalent quantity TEQ is computed for the whole mixture. Finally, a ratio between TEQ and the TRV of the index compound is calculated [96]. A more particulate version of RPF is the Toxic Equivalency Factor TEF method, widely used for dioxins or Poly Hydrocarbon Aromatic compounds. It is considered as a more specific method when the components share the same mechanism of action [41].

RPF is an excellent method for specific groups of mixtures. However, it stills a dose additive method. Hence, when synergistic or antagonistic interactions are suspected or demonstrated in literature, alternative methods should be considered. Actually, the US EPA recommends a new modified version of HI that takes into account mixture interactions [41], the Interaction-based hazard index.

(iii) Interaction-based hazard index: In fact, for many years, studies relied on "no-interaction" concept by justifying the similarity or the independence of toxic effects in their mixtures. However, more recent work confirmed that these methods cannot be generalized for chemical mixtures when there is not enough or comprehensive evidence [41]. That is why new approaches have to be implemented to consider toxicological interactions.

To address some of these issues, the dose-additive HI was modified taking into account binary interactions between the pollutants in a mixture. It is called the Interaction-based hazard index HI_{int}. While toxicological interactions are insufficiently quantified and generally studied using simple methods that include two chemicals, HI_{int} includes qualitative methods aimed at appraising the "weight of evidence" (WOE) of the available information on

interactions [41]. It is basically founded on a WOE approach formerly introduced by Mumtaz and Durkin [97]. Then, the final following formula was introduced by US EPA in the mixture guidelines [41]. More details are discussed and presented later in the third part of this thesis.

III.   Specific scientific objectives

In this risk assessment study of metal mixtures, we will develop3parts:

(i)   Estimation of pollutants concentrations using mathematical models for assessing occupational exposure [67,68];

(ii)   Performance of direct measurements of indoor air TMEs concentrations [98], comparing them with the theoretical results derived from models so as to "validate" the models, and biological monitoring of TMEs in the urine of workers volunteering to participate, to evaluate how well they correlate with model estimations.

(iii)   Finally, the risk characterization step of the trace metallic element mixtures in the metalworking industry, using a decision support' tool to investigate effects of interactions, based the hazard index.

IV. Bibliography

1. Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Hammami B, Rebai A, et al. Biomonitoring of cadmium, chromium, nickel and arsenic in general population living near mining and active industrial areas in Southern Tunisia. Environ Monit Assess. 2014;186:761–79.

2. ATSDR. Detailed data table for the 2011 priority list of hazardous substances that will be the subject of toxicological profiles [Internet]. 2011 [cited 2014 Feb 7]. Available from: http://www.atsdr.cdc.gov/spl/resources/ATSDR_2011_SPL_Detailed_Data_Table.pdf

3. ATSDR. Toxicological Profile: Copper [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=206&tid=37

4. ATSDR. Toxicological Profile: Nickel [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=245&tid=44

5. ATSDR. Toxicological Profile: Lead [Internet]. 2007. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22

6. Barhoumi S, Messaoudi I, Deli T, Saïd K, Kerkeni A. Cadmium bioaccumulation in three benthic fish species, Salaria basilisca, Zosterisessor ophiocephalus and Solea vulgaris collected from the Gulf of Gabes in Tunisia. J Environ Sci. 2009;21:980–4.

7. Kessabi K, Kerkeni A, Saïd K, Messaoudi I. Involvement of Cd Bioaccumulation in Spinal Deformities Occurrence in Natural Populations of Mediterranean Killifish. Biol Trace Elem Res. 2008;128:72–81.

8. Banni M, Jebali J, Daubeze M, Clerandau C, Guerbej H, Narbonne JF, et al. Monitoring pollution in Tunisian coasts: application of a classification scale based on biochemical markers. Biomarkers. 2005;10:105–16.

9. Garnier R. Toxicité du plomb et de ses dérivés. Pathol Prof Environ EMC. 2006;1:1–15.

10. ATSDR. Interaction Profile: Arsenic, Cadmium, Chromium and Lead [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/interactionprofiles/ip04.html

11. Løkke H, Ragas AMJ, Holmstrup M. Tools and perspectives for assessing chemical mixtures and multiple stressors. Toxicology. 2013;313:73–82.

12. Serbaji MM, Azri C, Medhioub K. Anthropogenic Contributions to Heavy Metal Distributions in the Surface and Sub-surface Sediments of the Northern Coast of Sfax, Tunisia. Int J Environ Res. 2012;6:613–26.

13. Kessabi K, Annabi A, Hassine AIH, Bazin I, Mnif W, Said K, et al. Possible chemical causes of skeletal deformities in natural populations of Aphanius fasciatus collected from the Tunisian coast. Chemosphere. 2013;90:2683–9.

14. Gargouri D, Azri C, Serbaji MM, Jedoui Y, Montacer M. Heavy metal concentrations in the surface marine sediments of Sfax Coast, Tunisia. Environ Monit Assess. 2010;175:519–30.

15. Hentati O, Chaker S, Wali A, Ayoub T, Ksibi M. Effects of long-term irrigation with treated wastewater on soil quality, soil-borne pathogens, and living organisms: case study of

the vicinity of El Hajeb (Tunisia). Environ Monit Assess [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s10661-013-3570-z

16. Kong IC. Joint effects of heavy metal binary mixtures on seed germination, root and shoot growth, bacterial bioluminescence, and gene mutation. J Environ Sci. 2013;25:889–94.

17. Martínez-Pacheco M, Hidalgo-Miranda A, Romero-Córdoba S, Valverde M, Rojas E. mRNA and miRNA expression patterns associated to pathways linked to metal mixture health effects. Gene. 2014;533:508–14.

18. Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Hammami B, Rebai A, et al. Risk of laryngeal and nasopharyngeal cancer associated with arsenic and cadmium in the Tunisian population. Environ Sci Pollut Res. 2013;21:2032–42.

19. Gargouri I, Rebaï A, Khadhraoui M, Kallel M, Jmal-Hammami K, Medhioub K, et al. Impact sanitaire des variations quotidiennes de la pollution atmosphérique urbaine: étude de faisabilité dans la ville de Sfax (Tunisie). Environ Risques Santé. 2006;5:467–75.

20. Feki-Tounsi M, Olmedo P, Gil F, Khlifi R, Mhiri M-N, Rebai A, et al. Cadmium in blood of Tunisian men and risk of bladder cancer: interactions with arsenic exposure and smoking. Environ Sci Pollut Res. 2013;20:7204–13.

21. Annabi A, Said K, Messaoudi I. Heavy metal levels in gonad and liver tissues—effects on the reproductive parameters of natural populations of Aphanius facsiatus. Environ Sci Pollut Res. 2013;20:7309–19.

22. Smaoui-Damak W, Berthet B, Rebai T, Hamza-Chaffai A. Effets de la pollution par les metaux sur le potentiel reproducteur de la palourde Ruditapes decussatus (L.) issue du Golfe de Gabes (Tunisie). Bull Société Zool Fr. 2008;133:131–139.

23. Ben Fredj F, Wali A, Khadhraoui M, Han J, Funamizu N, Ksibi M, et al. Risk assessment of heavy metal toxicity of soil irrigated with treated wastewater using heat shock proteins stress responses: case of El Hajeb, Sfax, Tunisia. Environ Sci Pollut Res [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s11356-013-2411-5

24. Banni M, Bouraoui Z, Ghedira J, Clearandeau C, Jebali J, Boussetta H. Seasonal variation of oxidative stress biomarkers in clams Ruditapes decussatus sampled from Tunisian coastal areas. Environ Monit Assess. 2008;155:119–28.

25. El Ati-Hellal M, Hedhili A, Hellal F, Boujlel K, Dachraoui M, Bousnina M, et al. Lead and cadmium concentrations in seawater and algae of the Tunisian coast. Arch Inst Pasteur Tunis. 2005;82:75–82.

26. Hamza-Chaffai A, Cosson RP, Amiard-Triquet C, El Abed A. Physico-chemical forms of storage of metals (Cd, Cu and Zn) and metallothionein-like proteins in gills and liver of marine fish from the Tunisian coast: ecotoxicological consequences. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol. 1995;111:329–41.

27. Kessabi K, Navarro A, Casado M, Saïd K, Messaoudi I, Piña B. Evaluation of environmental impact on natural populations of the Mediterranean killifish Aphanius fasciatus by quantitative RNA biomarkers. Mar Environ Res. 2010;70:327–33.

28. Hamza-Chaffai A, Roméo M, el Abed A. Heavy metals in different fishes from the middle eastern coast of Tunisia. Bull Environ Contam Toxicol. 1996;56:766–73.

29. Smaoui-Damak W, Berthet B, Hamza-Chaffai A. In situ potential use of metallothionein as a biomarker of cadmium contamination in Ruditapes decussatus. Ecotoxicol Environ Saf. 2009;72:1489–98.

30. Ketata I, Smaoui-Damak W, Guermazi F, Rebai T, Hamza-Chaffai A. In situ endocrine disrupting effects of cadmium on the reproduction of Ruditapes decussatus. Comp Biochem Physiol Part C Toxicol Pharmacol. 2007;146:415–30.

31. Lahbib Y, Mleiki A, Marigomez I, Trigui El Menif N. Copper, zinc, and cadmium body concentrations in Hexaplex trunculus collected from the Tunisian coast. Environ Monit Assess. 2013;185:8967–75.

32. Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Chakroun A, Rebai A, et al. Blood nickel and chromium levels in association with smoking and occupational exposure among head and neck cancer patients in Tunisia. Environ Sci Pollut Res. 2013;20:8282–94.

33. Khlifi R, Olmedo P, Gil F, Hammami B, Chakroun A, Rebai A, et al. Arsenic, cadmium, chromium and nickel in cancerous and healthy tissues from patients with head and neck cancer. Sci Total Environ. 2013;452–453:58–67.

34. Smaoui-Damak W, Rebai T, Berthet B, Hamza-Chaffai A. Does cadmium pollution affect reproduction in the clam Ruditapes decussatus? A one-year case study. Comp Biochem Physiol Part C Toxicol Pharmacol. 2006;143:252–61.

35. Khlifi R, Hamza-Chaffai A. Head and neck cancer due to heavy metal exposure via tobacco smoking and professional exposure: A review. Toxicol Appl Pharmacol. 2010;248:71–88.

36. Saïdi SA, Azaza MS, Windmolders P, van Pelt J, El-Feki A. Cytotoxicity evaluation and antioxidant enzyme expression related to heavy metals found in tuna by-products meal: An in vitro study in human and rat liver cell lines. Exp Toxicol Pathol. 2013;65:1025–33.

37. Mezghani-Chaari S, Hamza A, Hamza-Chaffai A. Mercury contamination in human hair and some marine species from Sfax coasts of Tunisia: levels and risk assessment. Environ Monit Assess. 2011;180:477–87.

38. Committee on the Institutional Means for Assessment of Risks to Public Health, National Research Council, Division on Earth and Life Studies, Commission on Life Sciences. Risk Assessment in the Federal Government:: Managing the Process. National Academies Press; 1983.

39. InVS, Afsset. Estimation de l'impact sanitaire d'une pollution environnementale et évaluation quantitative des risques sanitaires [Internet]. 2007. Available from: http://www.invs.sante.fr/publications/2008/pollution_invs_afsset/rap_pollution_invs_afsset_nov_2007.pdf

40. Fairbrother A, Wenstel R, Sappington K, Wood W. Framework for Metals Risk Assessment. Ecotoxicol Environ Saf. 2007;68:145–227.

41. US EPA. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures [Internet]. 2000 [cited 2015 Dec 24]. Available from: http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486

42. ATSDR. Toxicological Profiles. Agency for Toxic Substances and Disease Registry (US); 2009.

43. US EPA. IRIS Assessments; Integrated Risk Information System [Internet]. [cited 2016 May 25]. Available from: https://cfpub.epa.gov/ncea/iris2/atoz.cfm

44. TCEQ. Final Development Support Documents (DSDs) [Internet]. TCEQ. [cited 2017 Dec 8]. Available from: https://www.tceq.texas.gov/toxicology/dsd/final.html

45. MacIntosh DL, International Programme on Chemical Safety, editors. Human exposure assessment. Geneva: World Health Organization; 2000.

46. US EPA, Office of the Science Advisor. Framework for Metals Risk Assessment [Internet]. 2007 Mar. Available from: https://www.epa.gov/risk/framework-metals-risk-assessment

47. Nordberg GF, Gerhardsson L, Mumtaz MM, Ruiz P, Fowler BA. Chapter 11: Interactions and Mixtures in Metal Toxicology. Handb Toxicol Met [Internet]. Elsevier; 2015 [cited 2017 Dec 22]. p. 213–38. Available from: http://linkinghub.elsevier.com/retrieve/pii/B9780444594532000111

48. ATSDR. Toxicological Profile for Aluminum - tp22.pdf [Internet]. 2008 [cited 2016 May 24]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp22.pdf

49. ATSDR. Toxicological Profile: Aluminum [Internet]. 2008. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=191&tid=34

50. INRS. Aluminium et ses composés minéraux (FT 306) - Fiche toxicologique [Internet]. 2014 [cited 2016 May 25]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_306

51. ATSDR. TOXICOLOGICAL PROFILE FOR CHROMIUM [Internet]. 2012. Available from: https://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=17

52. WHO World Health Organization. IARC Monographs- Classifications [Internet]. [cited 2018 Jan 16]. Available from: http://monographs.iarc.fr/ENG/Classification/latest_classif.php

53. Health Canada. ARCHIVED - Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/Concentrations for Priority Substances [Internet]. 2013 [cited 2016 May 25]. Available from: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/hbct-jact/index-eng.php#TC

54. OEHHA. Air Chemicals | Nickel and Nickel Compounds | OEHHA [Internet]. 2012 [cited 2016 Jun 2]. Available from: http://oehha.ca.gov/air/chemicals/nickel-and-nickel-compounds

55. Regional Office for Europe Copenhagen, Frank Theakston, editors. Air quality guidelines for Europe. 2nd edition. Copenhagen: World Health Organization, Regional Office for Europe; 2000.

56. US EPA. Nickel refinery dust CASRN NA | IRIS | US EPA, ORD [Internet]. 1987 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=272

57. US EPA. Copper (CASRN 7440-50-8) | IRIS | US EPA - 0368_summary.pdf [Internet]. 1988 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0368_summary.pdf

58. INRS. Plomb et composés minéraux - Fiche toxicologique [Internet]. 2006 [cited 2016 Jun 8]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_59

59. US EPA. Lead and compounds (inorganic) CASRN 7439-92-1 | IRIS | US EPA, ORD [Internet]. 2004 [cited 2016 Jun 17]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=277

60. OEHHA. Air Chemicals | Lead and Lead Compounds [Internet]. OEHHA. 2016 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/air/chemicals/lead-and-lead-compounds

61. INRS. Zinc et composés minéraux (FT 75) - Fiche toxicologique [Internet]. 2012 [cited 2016 Jun 1]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_75

62. US EPA. Zinc and Compounds CASRN 7440-66-6 | IRIS | US EPA, ORD [Internet]. 2005 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=426

63. U.S. Department of Health and Human Services Public Health Service, ATSDR. INTERACTION PROFILE FOR: LEAD, MANGANESE, ZINC, AND COPPER [Internet]. 2004 May. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip-metals2/ip06.pdf

64. Mumtaz M, Fisher J, Blount B, Ruiz P. Application of Physiologically Based Pharmacokinetic Models in Chemical Risk Assessment. J Toxicol. 2012;2012:1–11.

65. von Stackelberg K, Guzy E, Chu T, Henn BC. Mixtures, Metals, Genes and Pathways: A Systematic Review. 2013 [cited 2014 Feb 10]; Available from: http://www.hsph.harvard.edu/hcra/files/2013/09/von-Stackelberg-et-al.-Sept-2013.pdf

66. Sasso AF, Isukapalli SS, Georgopoulos PG. A generalized physiologically-based toxicokinetic modeling system for chemical mixtures containing metals. Theor Biol Med Model. 2010;7:17.

67. AIHA, Charles B. Keil, Cathrine E. Simmons, T. Renée Anthony. Mathematical Models for Estimating Occupational Exposure to Chemicals. 2nd edition. AIHA press; 2009.

68. Bertrand N, Vincent R. Modélisation des expositions professionnelles aux agents chimiques. Bilan et perspectives. Hygiène Sécurité Trav ND [Internet]. 2010 [cited 2014 Feb 9];2333. Available from: http://www.hst.fr/inrs-pub/inrs01.nsf/IntranetObject-accesParIntranetID/OM:Document:6DD39CCF247C5DBDC12577B5002C6497/$FILE/Visu.html

69. AIHA. Exposure Assessment Strategies Committee [Internet]. [cited 2016 Nov 14]. Available from: https://www.aiha.org/get-involved/VolunteerGroups/Pages/Exposure-Assessment-Strategies-Committee.aspx

70. IHMod - Outil - INRS [Internet]. [cited 2016 Nov 14]. Available from: http://www.inrs.fr/media.html?refINRS=outil27

71. Boelter FW, Simmons CE, Berman L, Scheff P. Two-Zone Model Application to Breathing Zone and Area Welding Fume Concentration Data. J Occup Environ Hyg. 2009;6:298–306.

72. Arnold SF, Shao Y, Ramachandran G. Evaluation of the well mixed room and near-field far-field models in occupational settings. J Occup Environ Hyg. 2017;14:694–702.

73. Patricia H. Reinke, Charles B. Keil. Chapter 4: Well-Mixed Box Model. Math Models Estim Occup Expo Chem. USA; 2009.

74. Mark Nicas. Chapter 6: The Near Field/ Far Field (two box) Model with a constant contaminant emission rate. Math Models Estim Occup Expo Chem. USA: AIHA press; 2009. p. 47–52.

75. Jayjock MA, Armstrong T, Taylor M. The Daubert Standard as Applied to Exposure Assessment Modeling Using the Two-Zone (NF/FF) Model Estimation of Indoor Air Breathing Zone Concentration as an Example. J Occup Environ Hyg. 2011;8:D114–22.

76. Charles B. Keil. chapter 2: General principals of physical-chemical models. Math Models Estim Occup Expo Chem. USA; 2009.

77. Keil CB, Nicas M. Predicting Room Vapor Concentrations Due to Spills of Organic Solvents. AIHA J. 2003;64:445–54.

78. Nicas M, Neuhaus J. Predicting Benzene Vapor Concentrations with a Near Field/Far Field Model. J Occup Environ Hyg. 2008;5:599–608.

79. Nicas M. The near field/far field model with constant application of chemical mass and exponentially decreasing emission of the mass applied. J Occup Environ Hyg. 2016;13:519–28.

80. Nicas M, Plisko MJ, Spencer JW. Estimating Benzene Exposure at a Solvent Parts Washer. J Occup Environ Hyg. 2006;3:284–91.

81. Spencer JW, Plisko MJ. A Comparison Study Using a Mathematical Model and Actual Exposure Monitoring for Estimating Solvent Exposures During the Disassembly of Metal Parts. J Occup Environ Hyg. 2007;4:253–9.

82. Jayjock MA, Chaisson CF, Arnold S, Dederick EJ. Modeling framework for human exposure assessment. J Expo Sci Environ Epidemiol. 2007;17:S81–9.

83. Charles B. Keil. Chapter 3: Modeling Pollutant Generation Rates. Math Models Estim Occup Expo Chem. USA; 2009.

84. US EPA. AP-42: Compilation of Air Emissions Factors [Internet]. US EPA. 2016 [cited 2018 Mar 26]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emissions-factors

85. US EPA O. AP-42: Compilation of Air Emission Factors [Internet]. 1995 [cited 2018 Jan 12]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

86. US EPA Office of Air Quality Planning and Standards. Intoduction. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

87. US EPA Office of Air Quality Planning and Standards, US EPA. Chapter 12: Metallurgical Industry, section 19: Electric Arc Welding. AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1995. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

88. US EPA Office of Air Quality Planning and Standards. Chapter 12: Metallurgical Industry, section 20: Electroplating. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1996. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

89. SAN DIEGO Air Pollution Control District, editor. WELDING OPERATIONS [Internet]. 1998 [cited 2018 Jan 9]. Available from: http://www.sdapcd.org/content/dam/sdc/apcd/PDF/Toxics_Program/APCD_welding1.pdf

90. U.S. DEPARTMENT OF THE NAVY CARDEROCK DIVISION. Characterizing Shipyard Welding Emissions and Associated Control Options. NSRP 0457 [Internet]. 1995. Available from: http://www.dtic.mil/dtic/tr/fulltext/u2/a455525.pdf

91. US EPA. Emission Factor Documentation for AP-42 Section 12.20 Electroplating Final Report [Internet]. 1996 Jul. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/bgdocs/b12s20.pdf

92. Environmental Protection Agency Johnstown Castle Estate Wexford, Ireland. Emissions Monitoring Guidance Note (AG2) [Internet]. 2017 Sep. Available from: http://www.epa.ie/pubs/advice/air/emissions/AG2%20Air%20Emissions%20Monitoring%20Guidance%20Note_rev3.pdf

93. ChemTRAC - Environmental Health - Toronto Public Health | [Internet]. [cited 2016 May 11]. Available from: http://www1.toronto.ca/wps/portal/contentonly?vgnextoid=8e00ebfc2bb31410VgnVCM10000071d60f89RCRD

94. Armstrong T. IH Mod "Mathematical Modeling to Estimate Exposures" User's Blog [Internet]. Welcome IH Mod Math. Model. Estim. Expo. Users Blog. [cited 2018 Jan 3]. Available from: http://ihmod.org/about-this-site-and-ih-mod.html

95. US EPA O. Guidelines for the Health Risk Assessment of Chemical Mixtures [Internet]. 1986 [cited 2018 Jan 22]. Available from: https://www.epa.gov/risk/guidelines-health-risk-assessment-chemical-mixtures

96. Fournier K, Glorennec P, Bonvallot N. Derivation of toxicological reference values for taking mixtures into account in health risk assessment: Existing methods and recent applications. Environ Risques Santé. 2014;203–221.

97. Mumtaz MM, Durkin PR. A weight-of-evidence approach for assessing interactions in chemical mixtures. Toxicol Ind Health. 1992;8:377–406.

98. INRS. Métaux et métalloïdes M-122 - MétroPol [Internet]. 2016 [cited 2016 Jun 13]. Available from: http://www.inrs.fr/publications/bdd/metropol/fiche.html?refINRS=METROPOL_122

1st PART:

Indoor Air Concentrations Modeling of Occupational Exposure to Trace Metallic Elements in Metalworking Industries

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I. Introduction

Over the last decade, mathematical models for estimating indoor air concentrations of chemicals in occupational settings were developed for exposure assessment as a possible alternative to air monitoring. Occupational hygienists are interested in such models because monitoring is not always available, so they could be used as a quantitative and scientifically explicit method to support expert judgment [1].

Several studies have used such models for volatile organic compounds exposures [2–4] and compared them with actual exposure monitoring. Predicted concentrations were considered as "reasonable estimations" as they were within a factor of 0.5 to 2 to measurements [5]. Regarding metals' exposure, to the best of our knowledge, similar models were applied only to the arc welding process [6] where the authors have calculated models' parameters based on air monitoring measurements. Contrarily to the latter approach, we seek to calculate all models parameters independently of air monitoring data.

In our study, the trace metallic elements are present in the air either as particulates during job tasks where dusts are generated from metallic materials, or in the vapor form as aerosols coming from processes that incur heating of metallic materials or substances containing TMEs.

The objective of this part is to apply the mathematical models for estimating indoor air occupational exposure to trace metallic element TMEs in metalworking industries. Unlike other studies that used simulation designs for jobs and workplaces, this study aims also to explore the model's prediction ability in real and more complex exposure scenarios.

II. Materials and Methods

II.1. Population sampling

The study involves workers directly exposed to TMEs at their workplaces and manipulating some of the abovementioned chemicals in manufacturing processes. For purposes of comparison, we also included administrative staff as non occupationally-exposed employees.

II.1.1. Selection of metalworking industrial sectors and companies

In order to localize companies handling TMEs, and to define the main pollutants of interest, we conducted a thorough review of earlier studies addressing metallic pollution in the Sfax metropolis [7–31].

In addition, with the help of the chamber of commerce [32], and following investigation of the local industrial sectors and recommendations from the union of small and medium-scale industries ("*Union des Petites et Moyennes Industries*": UPMI), we identified industries and companies that are recognized to be likely sources of TMEs emissions according to literature [33]. A wide range of industrial activities was covered, including the steel and metal machining and processing, welding, electrical and wiring, electroplating, phosphate fertilizers, plastic, paint and glass industries. Lastly, we randomly selected one company from each industrial sector, and contacted company executives to request their cooperation. Where participation was declined, we selected another company in the same sector and sought cooperation. To solicit approval, we explained to the entrepreneurs, by a written letter (in appendix), the aim of the study regarding possible risks to workers in industries manipulating TMEs.

II.1.2. Inclusion and exclusion criteria

Inclusion criteria: The selected companies were industries manipulating TMEs in their production processes likely to incur occupational exposure to a mixture of such chemicals. Metal manipulation had to be identified where small particles emission was found in the air as small particles aerosol (cold: dust; or hot: vapor).

Exclusion criteria: (i) Companies not manipulating TMEs; (ii) and employees exposed to a single metal.

II.2. Description of companies and of the study materials

Two questionnaires were established and used to identify the TMEs that were processed and to collect information for the modeling scenarios in view to choose the proper model types or to calculate their parameters (in appendices section).

The first questionnaire was an identification/descriptive questionnaire aimed at identifying and defining:

- The specific activity of each job task and the emission source,
- All substances and materials manipulated in the processes, to ensure that our qualitative and quantitative inventory was as accurate as possible,
- The exposed and indirectly-exposed employees, based on their activities and possible exposure to TMEs.

The second questionnaire was related to the job-task of the exposed workers:

- Description of the overall atmosphere of the workplaces and the nature and quality of ventilation; it was also used to register measurements of the relative humidity and the inside and outside temperature and pressure.
- Collection of the dimensions of the workplaces, machines, stocks, etc.
- Identification of workers' position in relation to the emission configuration, in space and time

II.3. Mathematical modeling of occupational exposure

II.3.1. Model's choice

The main criteria for selection of the appropriate model are (i) the worker's position and location in relation to the emission source, and (ii) the configuration of workplace ventilation [5]. Indeed, variability or steadiness of the job process in time and space is an important factor in choosing a model subtype, which is why a study of each job process is necessary to model selection. In order to calculate model parameters, it was necessary to fill a second questionnaire about job and workplace specifications, as well as to perform certain direct measurements. These are specified in the next section.

II.3.2. Parameters calculations

II.3.2.1. Ventilation rate "Q"

First of all, we need to verify mass conservation of the quantity of matter in the air [34].

Mass conservation was verified for every workplace following the basic formulas of the ideal gas law mentioned previously. Then, the ratio between the quantities of matters entering and leaving the workplace n_{in} / n_{out} should be approximately equal to 1.

To this end, direct measurements of pressure and temperature inside and outside each workplace should be performed prior to using the method described below to calculate Q.Q is also commonly called as the total room air flow rate [5].

In our case, open doors and windows are the only or major source of ventilation; air comes in and out of these two openings, generally located at opposite ends of the rooms [34]. We assume air direction to be constant; therefore the volumetric air flow rate is conserved:

$$Q_{in} = Q_{out}$$

To calculate Q_{in} entering from the main door, we measured average "V_{face}", and recorded the dimensions of the doors. Air face velocity measurements were conducted using fixed anemometers, every 15 minutes along the four-hour shifts. This was performed through 3 days in the middle of the week; Tuesday, Wednesday and Thursday, to get an idea of the variability of Q in the workplace.

In some cases, the workplace is separated into two or three compartments that are connected with communicating doors (e.g. figure 1.1 and 26 of A1 and A8, respectively). So, ideally, every compartment should be considered as an independent workplace. However, based on the available information, only the total quantity used into process for all compartments is provided which means only a total generation rate (defined later) could be calculated. Therefore, to rectify this, we decided to calculate the individual ventilation rates for every compartment, and then calculate a volume-weighted average of Q for the whole workplace.

The ACH [5] was also calculated The air volume "V"

II.3.2.2. The air volume "V"

Workplace dimensions are used to calculate the volume of the rooms. Specific volumes within the room are also considered, such as an upstairs floor inside the room, or stocks of raw materials or manufactured products. Machine volumes are also accounted for, either by gathering information from managers, or measured by the authors.

II.3.2.3. Generation rate "G"

Several studies uses sample concentration measurements to calculate G [6]. However, to demonstrate the usefulness and validity of these models as an alternative and cost-effective method of indoor air concentration determination [1], we preferred not to rely on

concentration measurements to determine G. Therefore, G is only calculated based on information from the companies' managers and literature. According to the collected information and the variability in steels composition, we won't have an exact single value of emission rate; we will have an interval [Min – Max]. So, we are going to work with the average value of generation rate noted $G_{average}$.

The used methods are both mass balance and Emission Factor (EF) methods.

II.3.2.4. The inter-box air flow rate "β"

β is calculated using the previously mentioned formula [35].

S (m/min) is calculated as the mean of several direct measurements with anemometers that were performed next to the NF every 15 minutes for 4hour-shifs throughout 3 days in the middle of the week; Tuesday, Wednesday and Thursday.

Both FSA and *S* will be presented in results.

II.3.3. Processes & Jobs presentation

Job tasks are categorized according to their work processes. In addition, they are further subcategorized into more specific tasks. Each type is modeled individually.

All workplaces were mapped in order to show the workplace volume, the ventilation configuration and the location of the machines or the emission source. These figures highlight also the position of the workers in their job tasks.

Each worker is on a press machine for a continuous 4 hour-shifts.

II.3.3.1. Metal sheet cutting

a. Stamping

The first job task is stamping, which means metal cutting forming. The press operator is using a mechanical or hydraulic press machine to cut or form steel sheets into specific shapes by stamping.

b. Sheering & slitting

Other kinds of steel sheets cutting are sheering or slitting. The first one is cutting metal steel rolls into big rectangular sheets using a steel sheet cutting machine. The second one is cutting large steel rolls by slitting them into narrower ones using a roll slitting machine.

II.3.3.2.   Welding

Welding is a quite widespread process in several industries [36]. The welding process consists in joining two metal parts to connect them by heating up to a particular temperature either with or without a consumable filler metal [36,37].

There are many different types of welding processes (over 80 welding types) [37]. We are particularly interested in 4 different types; resistance spot welding (RSW), induction welding, Gas Metal Arc Welding (GMAW) and Shielded Metal Arc Welding (SMAW).

a.   Resistance spot welding

Spot welding or also referred to as RSW is the most common kind of resistance welding [38,39]. This type of welding consumes neither filler materials nor gases. It is used to weld thin steel sheets that are tightened by two electrodes. Then, a high electric current introduced through the two sheets, produces heat and coalesces them because of the resistance [38,39]. RSW is considered as "clean technique" compared to other welding kinds because of its low mass emission rate during process [36,39].

b.   Induction welding

The induction welding process is also called high-frequency induction welding. In our study, this method is used in longitudinal welding of steel tubes. During the process, a high-frequency current is supplied through an induction coil, which is placed nearby or around the workpiece to be welded [39]. Subsequently, the induced current heats the metal by the Joule effect [40]. Then, the workpiece is deformed and the two edges are welded together without any additional material. This process is considered to have a relatively high welding rate because of the speed of heating [39].

c.   Electric arc welding

The electric arc welding process encompasses several types. Among them, we can find GMAW (or MAG) and SMAW that are considered from the most common welding processes [36,37]. Both processes use consumable electrodes as a filler metal.

i.   Shielded Metal Arc Welding (SMAW)

SMAW is also called Manual Metal Arc welding (MMA). It is particularly considered as an old, simple and a multipurpose welding processes [36].

SMAW process produces an electric arc between the covered electrode and the basic metal. This process consumes only the electrode as filler metal. In fact, the electrode consists in the core which is a solid metal stick and a flux coating which is required to release a shielding gas for the welding process. Therefore, SMAW is a better process to use outside workplaces and even in windy weather conditions [37].

ii.   Gas metal arc welding (GMAW): Metal Active Gas (MAG)

MAG welding is a subtype of GMAW process. In GMAW, an electric arc is generated between the basic metal and the metallic wire, which is the consumable electrode. Contrary to SMAW, the GMAW process consumes also a shielding gas that is supplied externally [37]. The MAG subtype is using active gas such as carbon dioxide CO_2.

It is considered to be a faster process than the SMAW. In fact, it is a continuous process contrarily to SMAW that is consuming elemental electrodes [36].

II.3.3.3.   Electroplating

a.   Metal electroplating

The electroplating process is also known as the electrodeposition of a metallic coat onto an article. An electric current passes through an electrolyte and reduces the metal cations that are dissolved in order to form a metal coating. Therefore, the articles must have an electrically conductive surface. Thus, these articles are simply metal workpieces [41]. This electroplating type is referred to as the metal electroplating

In our study, we particularly dealt with zinc and nickel electroplating processes. Each process encompasses two plating lines. Every line can include several plating baths where the electroplating of other metals could occur. For example, in nickel-plating lines, there are nickel, copper, chromium and brass plating baths.

b.   ABS plating

Even though, plastics do not have an electrically conductive surface, electroplating could be realized over a plastic article after a special treatment such as electroless plating [41]. In our study, we are especially interested in the decorative chromium electroplating of a thermoplastic polymer named Acrylonitrile butadiene styrene (ABS). In fact, ABS is the most common plastic used in chromium electroplating [41]. The two lines include also cleaning pretreatment baths such as with chromic acid. Metal emissions from both pretreatments and plating baths are considered in our study.

II.3.3.4.   Indirect trace metallic element handling jobs

a.   Product packaging and displacement

This job task will be considered in three different workplaces, workers are collecting the final products and either wrap them with plastic films or join them with metallic strips. They also gather them in cardboard boxes or specific locations. Finally, they often have to displace the products using adequate devices. Therefore, workers are not in a steady position. They could move in the whole workplace and commonly work in a specific area.

b.   Quality control

Quality controllers are merely verifying the quality of the electrodeposition of decorative chromium onto ABS workpieces. They are using magnifying lens to check every workpiece.

c.   Plastic injection

Plastic injection molding is not among metallurgical or metalworking industries; however, this process involves the use of color additives called color masterbatches. In reality, metallic compounds such as salts, oxides and complexes are the basic substances in inorganic pigments of masterbatches [42]. Thus, color additives can contain trace metallic elements like Zn, Ni, Cu, Pb, Cr, Al, Cd [43,44] . Nevertheless, it should be noted that Pb and Cd are generally replaced [44] and that masterbatches designed to food and medication packaging are highly controlled and should not contain TMEs [42]. Consequently, we integrated the plastic injection process in our study to assess the possible indoor air exposure to TMEs of the workers.

II.3.4.   Results presentation

All modeled concentrations are calculated as time weighted averages, TWA. The IHMOD tool enables us to calculate TWAs as a time function in regards to the previous concentrations.

III.   Results

III.1.   Voluntary metalworking companies

We stress that participation in this study was voluntary, both at the level of industrial plants and for workers.

Based on the metals issued from metallic pollution in Sfax metropolis, we identified, from the literature [33], the industrial sectors most likely responsible for occupational exposure to these TMEs. Table 1.1 illustrates the identified industrial sectors and the corresponding TMEs.

Afterwards, we identified 53 companies in Sfax metropolis from the selected metals sectors; they are also listed in table 1.1 (4 of them belong to two different industrial sectors). Next, 24 randomly selected companies were contacted to seek approval. Some companies refused at the first contact; other ones took us up to 6 months of negotiations, appointments and field visits, and also eventually declined to participate. In the end, as we can see in the table, only 5 industrial plants agreed to be involved.

The corresponding industrial activities of the 5 companies are the steel cutting, welding, electroplating and plastic industries.

All company names are hidden for confidentiality reasons; hereafter, we present a translation of their names or their main activities.

Table 1.1: Industrial sectors responsible for Occupational exposure to TMEs and probable companies in Sfax metropolis [32,33]

Industrial sectors [33]	Trace metallic elements	Companies in Sfax : translation of their names	Random selection	Final approval
i. Metallic construction/ Metal processing/ Welding	Cd, As, Zn, Ni, Cu, Cr, Pb, Al	i.1. ▮▮▮▮ :Company of Brass articles production i.2. ▮▮▮ : general industry of machines and tools i.3. ▮▮▮ : industrial mechanical workshops i.4. ▮▮▮▮ : Mechanical workshops of precision i.5. ▮▮▮▮ : technical Manufactures of metals i.6. « ▮▮▮ » smelter i.7. ▮▮▮ : company of the new metallic construction i.8. ▮▮▮▮ : Industrial company of Metallic construction i.9. ▮▮ : industrial group of Metal processing i.10. "▮▮▮▮" metals: metal cutting and processing i.11. ▮▮▮▮ : company of precision machining i.12. ▮▮▮▮ : manufacturing of metallic stepladder and air-compressors i.13. ▮▮▮▮ : company of Metal processing i.14. "▮▮▮▮▮▮" founding: Metallic construction i.15. ▮▮▮▮ : company of non-ferrous alloy smelting i.16. "▮▮▮" company of smelting i.17. ▮▮ : company of zamak alloy smelting	i.1. ▮▮▮ : Company of Brass articles production - i.3. ▮▮ : industrial mechanical workshops i.6. ▮▮▮▮ smelter i.10. "▮▮▮" metals: metal cutting and processing i.14. "▮▮▮▮▮▮" founding: Metallic construction i.15. ▮▮▮ : company of non-ferrous alloy smelting i.16. "▮▮▮" company of smelting i.17. ▮▮ : company of zamak alloy	 i.14

			i.18. ⬛ : company of steel sheet slitting	i.18. ⬛ : company of steel sheet slitting	i.18
			i.19. "⬛" copper and brass smelter	i.19. "⬛" copper and brass smelter	
			i.20. ⬛ : company of metallic industry	i.20. ⬛ : company of metallic industry	
			i.21. ⬛ :Company of electromechanical manufacturing and maintenance	i.21. ⬛ :Company of electromechanical manufacturing and maintenance	i.21
ii.	Metal sheet cutting	Zn, Ni, Cu, Cr, Pb, Al	ii.1. ⬛ : company of global metallic cutting and construction	ii.1. ⬛ : company of global metallic cutting and construction	
			ii.2. = i.3. ⬛ : industrial mechanical workshops	ii.2. = i.3. ⬛ : industrial mechanical workshops	
			ii.3. ⬛ : industrial group of Metal processing		
			ii.4. =i.14. ⬛ founding: Metallic construction	ii.4. =i.14. ⬛ founding: Metallic construction	ii.4 = i.14
			ii.5. ⬛ : technical Manufactures of metals		
			ii.6. = i.18. ⬛ : company of steel sheet slitting	ii.6. = i.18. ⬛ : company of steel sheet slitting	ii.6 = i.18
			ii.7. ⬛ : company of cutting and deep drawing		
			ii.8. "⬛" metals: metal cutting and processing	ii.8. = i.10. "⬛" metals: metal cutting and processing	
iii.	Electrical and wire industry	Cu, Cd	iii. 1. ⬛ : International Company of Electricity and Automation	iii.1. ⬛ : International Company of Electricity and Automation	None
			iii. 2. ⬛ : industrial company of electronics and electricity		
			iii. 3. ⬛ : Tunisian company of electronics and electricity works		
			iii. 4. ⬛ : Company of wire and electrical cabinets industry		
			iii. 5. ⬛ : Company of cable and wire manufacturing		
			iii. 6. ⬛ : Company of electricity	iii.6. ⬛ : Company of electricity	

			systems	systems	
			iii. 7. ███████ : Company of electrical cabinets and wiring		
			iii. 8. ███████ : power cables and wiring manufacturing		
iv.	Surface finishing : electroplating	Zn, Ni, Cu, Pb, Hg, Cr, Cd	iv. 1. ██████ : Company of Brass articles production	iv.1. █████ : Company of Brass articles production	
			iv. 2. "████" company of Electroplating	iv.2. "█████" company of Electroplating	iv.2
			iv. 3. █████ : Surface finishing company in Sfax		
			iv. 4. "█████"- Steel-Galvanizing- Industries		
v.	Plastic industry	Cd, Pb, Hg, Zn	v. 1. ████████ : Tunisian company of rubber	v.1. █████ : Tunisian company of rubber	
			v. 2. ██████████ : Mediterranean company of plastic		
			v. 3. ████ : modern company of plastic		
			v. 4. █████ : Sfaxian counter of plastic		
			v. 5. █████████ : Sfaxian company of clothespin manufacturing		
			v. 6. ████ : Tunisian company of synthetic industry		
			v. 7. ███ : company of industrial progress in plastics	v.7. ████ : company of industrial progress in plastics	v.9
			v. 8. █████ company of plastics	v.8. █████ company of plastics	
			v. 9. ██████████ founding: plastic injection	v.9. ██████████ founding: plastic injection	
vi.	Glass industry	As, Hg	vi. 1. ██████ : Company of optical glass	vi.1. ██████ : Company of optical glass	None
vii.	Varnish manufacturing	Pb, Zn	vii. 1. ██████ : industrial company for glue and Varnish	vii.1. ██████ : industrial company for glue and Varnish	None
viii.	Phosphate fertilizers manufacturing	Cd, Zn, Pb, Cr, Al	viii. 1. ████ : Tunisian chemical group	viii.1. ████ : Tunisian chemical group	None

III.2.   Identified materials and metals in each company/ workplace

In order to respect the confidentiality agreement with the participating companies, we attributed an identifier number to each one. As illustrated in table 1.2, we also ordered the workplaces and the job tasks as A_i and P_i, respectively.

We identified the used materials in every workplace using the first questionnaire. Materials commercial names and references are illustrated in table 1.3.Afterwards, TMEs were identified using research studies that have used the same materials, technical or safety data sheets or the official websites of the used materials (see table 1.3). The identified TMEs are presented in table 1.2 for each workplace.

Table 1.2: Presentation of TMEs contained in the used materials in every job task

Company ID	Workplace N°	Job task ID	References of materials	Metals
I	A1	P1: Steel stamping	S355MC	Al, Cu, Ni, Cr
			S235JR	
		P3: Packaging	Inox 304	
			DX51 AS120	
	A2	P4: Resistance spot welding	S355MC	Al, Cu, Ni, Cr
			S235JR	
			DX51 AS120	
II	A3	P5: Shielded Metal Arc Welding	OK 48 00 (also known as E7018)	Al, Cu, Ni, Cr, Pb
			E6013	
III	A4	P6: Steel cutting & shearing	S235JR	Al, Cu, Ni, Cr, Zn
		P7: Packaging &displacement	DX51D+Z	

	A5	P8: Reception, packaging & displacement	DX51D+Z	Al, Cu, Ni, Cr, Zn
		P9: Induction welding machine operator		
		P16: System controller & Gas metal arc welding (GMAW)	DX51D+Z ER70S-6	Al, Cu, Ni, Cr, Pb, Zn
IV	**A6**	P 10: Zinc-plating	Professional secret	Zn, Cu, Ni, Cr
		P11: Nickel-plating: System control	Professional secret	
		P 12: Nickel-plating: Lifting hooks		
	A7	P 13: ABSplating	Professional secret	Cu, Ni, Cr
		P 14: Quality control		
V	**A8**	P 15: Plastic injection operator	Color masterbatches	Al, Cu, Ni, Cr, Pb, Zn

Table 1.3: Materials' commercial names and references

Materials' commercial names	References of materials	Sources
Hot rolled steel sheet	S355MC	[45–51]
	S235JR	
Inox sheet metal	Inox 304	[46,52,53]
Aluminized steel sheet	DX51 AS120	[54]
Galvanized steel sheet	DX51D+Z	[46,54,55]
Basic coated electrode	OK 48 00 (also known as E7018)	[56]
Ordinary welding rod	E6013	[57]
Coppered welding wire	ER70S-6	[58–61]
Masterbatches	Color masterbatches	[33,42,46]

III.3. Occupational exposure modeling

III.3.1. Metal sheet cutting modeling

- The first considered job task is steel sheets stamping (P1).

Press operators are working in the workplace named **A1** and mapped in figure 1.1. It is relatively crowded with workers, with about 23 press operators. The room is only ventilated thought three large main doors and windows that are located on the opposite side.
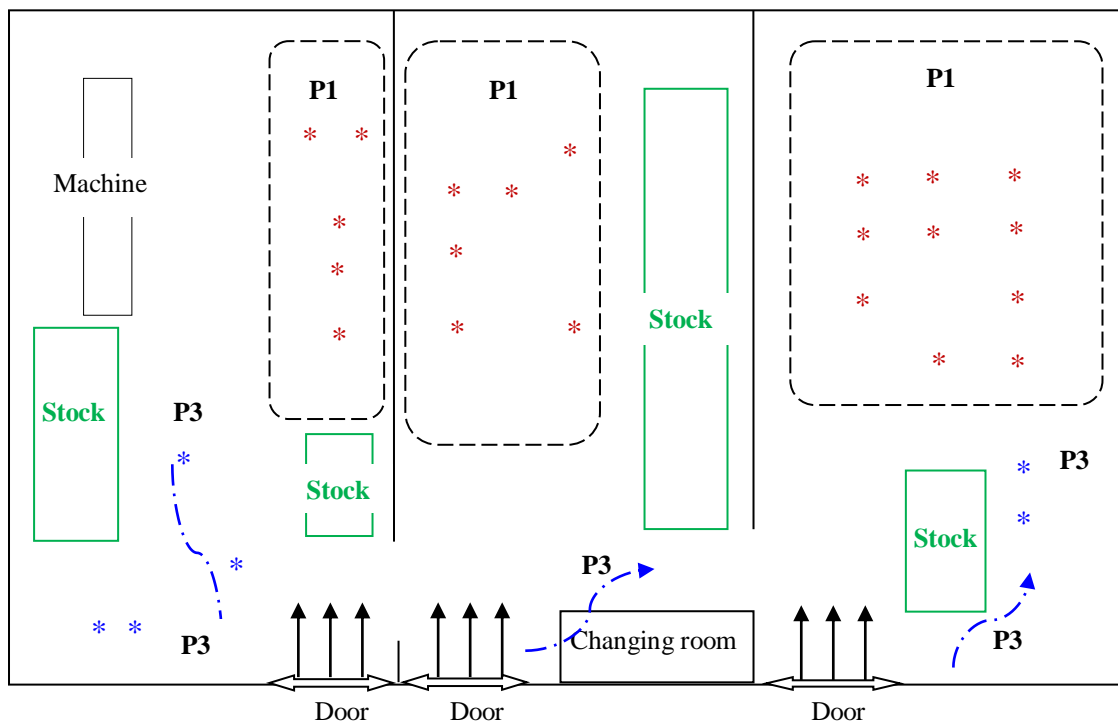
Figure 1.1: Scheme of workplace A1; P1: Press operator and P3: Packaging

*: fixed locations of workers,

*: Mobile positions, ⌒·▶ movement areas of mobile workers

The airflow rate nearby each worker is low. In this setting, we are using the near field/ far field model NF/FF with a constant emission rate. Hence, the workplace is going to be divided conceptually into two zones, the near field NF that includes a single emission source and the worker's breathing zone [3], and the far field FF being the rest of the workplace. Elsewhere, as presented in figure 1.1, the workplace A1 is separated in three compartments that are connected with large communicating openings. And, since only the total quantity of materials used in the process for the wholeA1 is provided, the volume-weighted average method is used to calculate the ventilation rate of A1, noted Q_{A1}.

- In the second situation, the workplace is named **A4** (figure 1.2). There are 4 steel cutting workers cutting steel both by sheering and by slitting metal sheets P6.

Every two of them are working continuously close to their machine for a four-hour shift. A4 is a relatively long workplace whose dimensions are 60*20 m. It is mainly ventilated by a front door. The air flow rate is remarkably lower in the vicinity of workers. Therefore, we are using the NF/FF model with a constant emission rate.

The values of the mass conservation ratios are 1.07 and 1.01, respectively, values close to 1 which means that mass conservation is confirmed.

➢ In the first job task P1, the NF is estimated as a parallelepiped box of air in front of a press machine. A worker is in seated position, so the height of the box is equal to the vertical distance between the metal workpiece press position, which represents the emission source, and about 15 cm above the worker's head to cover up the entire breathing zone as cited by INRS [62] according to the European norm. The length is equal to the distance between the worker and the metal workpiece press position. And the width is equal to the working surface of the metal workpiece press position (figure 3). It should be noted that the NF volume includes a little part of the machine which is estimated and subtracted in order to include only air.

Then, as the worker is in front of the press machine, the inter-box air flow rate β_{P1} does not flow through the front and about the half of the NF box bottom surface. Thus, only the remaining surfaces of a parallelepiped box are calculated in the FSA, which is equal to 2.775 m^2.
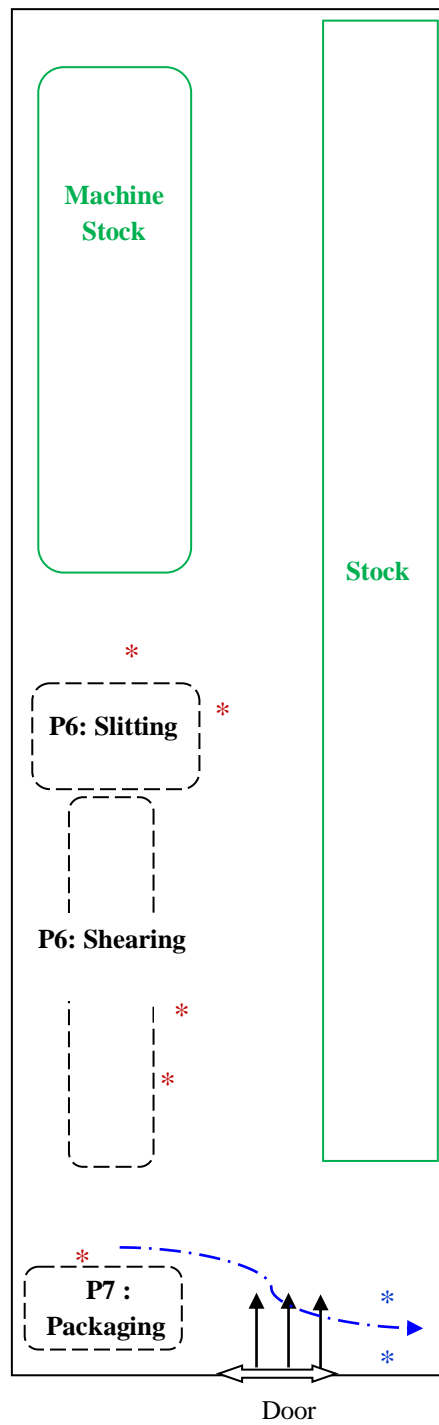
Figure 1.2: Scheme of workplace A4 *: fixed locations of workers,

*: Mobile positions, ⎯·▶ : movement area of mobile workers
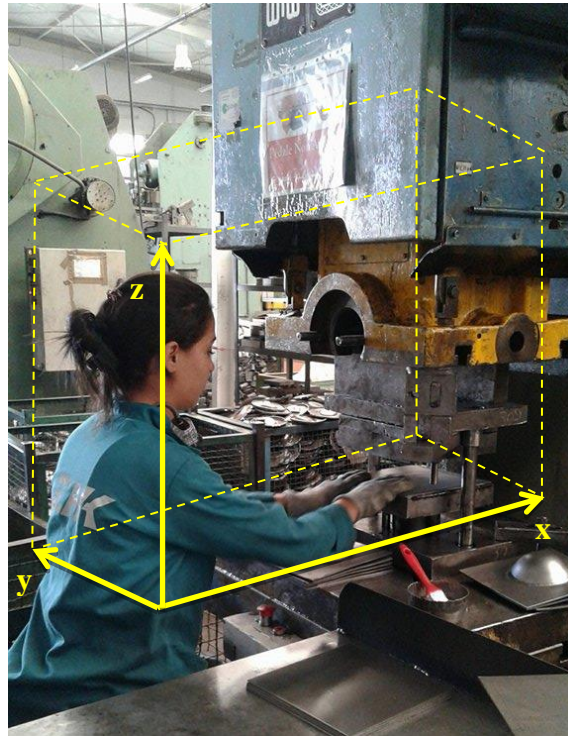
Figure 1.3: NF dimensions of P1 (steel sheets stamping):

x = 0.8 m, y = 0.5 m, z = 1 m

> ➤ In the second job task P6, the NF is estimated as a larger parallelepiped box because it covers the emission source which is a part of the machine where the steel cutting is taking place. During the cutting process, the steel sheets are introduced to the floor level; therefore the NF box is based on the floor.
>
> The NF also includes the two workers who are moving inside during a four-hour shift. They could be either in standing or in seated position in front of the machine. So, the height of the box is equal to the average height of a person with his entire breathing zone [62].
>
> The length and the width are equal to the distance covering the emission source (**figure 1.4**). The volume of the machine inside the NF is subtracted in order to include only air.

The inter-box air flow rate β_{P6} flows through all surfaces except the box bottom and the one side covered by the cutting machine. Thus, the FSA is equal to $37.67 m^2$.
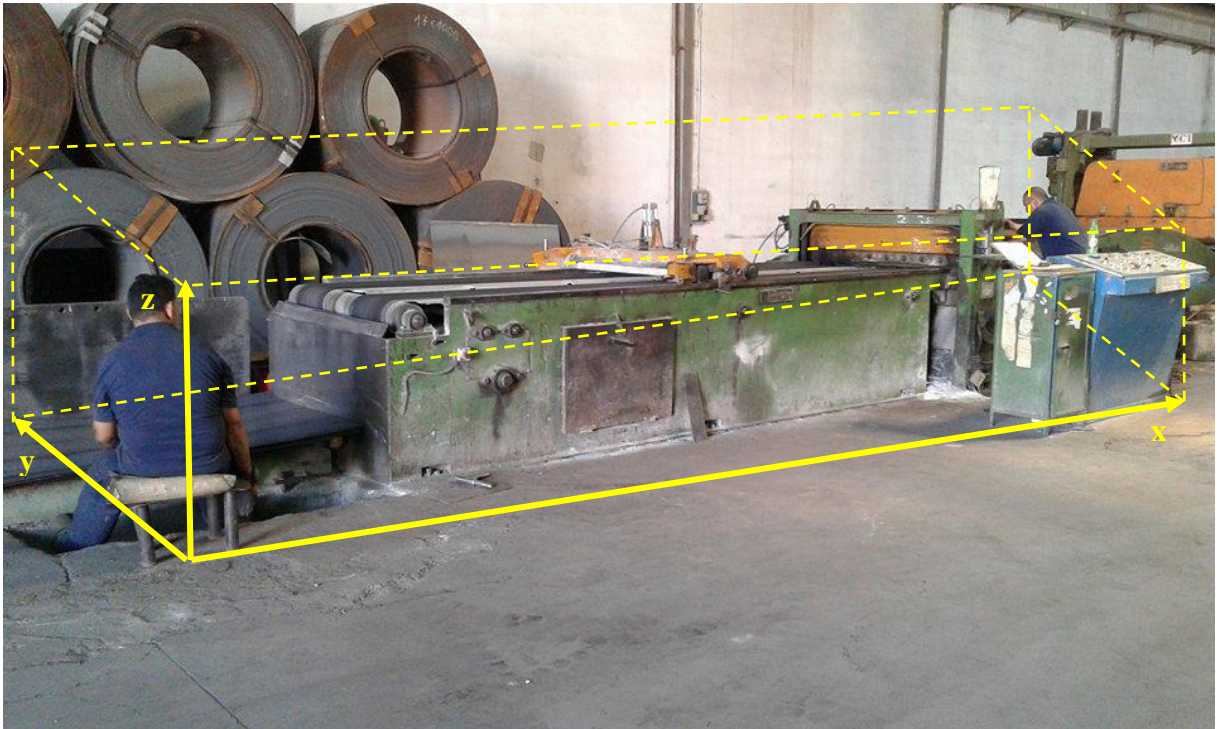
Figure 1.4: NF dimensions of P6 (steel sheering): x = 6.25 m, y = 1.6 m, z = 1.9 m

The average random air speed S is calculated for P1 and P4 and they are 0.565 and 0.023 m.s^{-1}, respectively.

β, Q and V are calculated as previously described for both situations. All model's parameters are in table 1.4.

The air changes per hour ACH were also calculated for both workplaces. ACH are equal to 0.85 and 4.77 for A1 and A4, respectively.

The exposure modeling is estimated along 4-hour shift. Then, machines are stopped for 1 hours-break.

In the context of steel cutting, the mass balance method is used to calculate the generation rate **G** in both workplaces. In fact, this approach doesn't consider the specific actions done in the job task. So, we are calculating G for the three types of cutting by stamping, sheering and slitting with the same method.

- In workplace A1, we have a single type of cutting. Whereas, in A4, we assume that sheering and slitting are emitting the same amount of metal dust and using the same quantities of metal sheets. This is an approximation, because we do not have enough information to calculate G for every different type of cutting.

Table 1.4: NF-FF model input values: constant emission rate of TMEs during steel sheet cutting

NF-FF Parameters	Situation 1: Stamping A1: P1	Situation 2: Sheering and slitting A4: P6
V (m^3)	38747.89	7476.81
V_{NF} (m^3)	0.36	7.00
β (m^3.min^{-1})	47.07	26.04
Q (m^3.min^{-1})	546.01	594.08
$G_{average}$ (mg. min^{-1})		
• Al	0.00628	0.0474
• Cu	0.00084	0.0785
• Ni	0.00758	0.0378
• Cr	0.01496	0.0860
• Zn	-	0.1049

Giving the available information, we can only calculate global emission rates $G_{A1,i}$ and $G_{A4,i}$ (i for each metal) for the whole workplaces. Therefore, to control over estimation of exposure, we use an average generation rate $G_{average}$ for every operational machine.

In the workplace A1, since, each press operator is doing the same operation onto his press machine, and using the same materials, we assume that he is emitting an individual amount of metals. Thus, the global emission rate G_{A1} is divided by the number of workers/ press machines in A1 to get an individual average generation rate $G_{averageA1}$. Actually, this estimation cannot be considered for many workers working at the same big machine that is emitting a global generation rate that induces exposure of everyone.

• As for workplace A4, every two workers are working on a larger machine. So, the global emission rate G_{A4} is divided by the number of the machines in the room to get an average generation rate $G_{averageA4}$ for both workers.
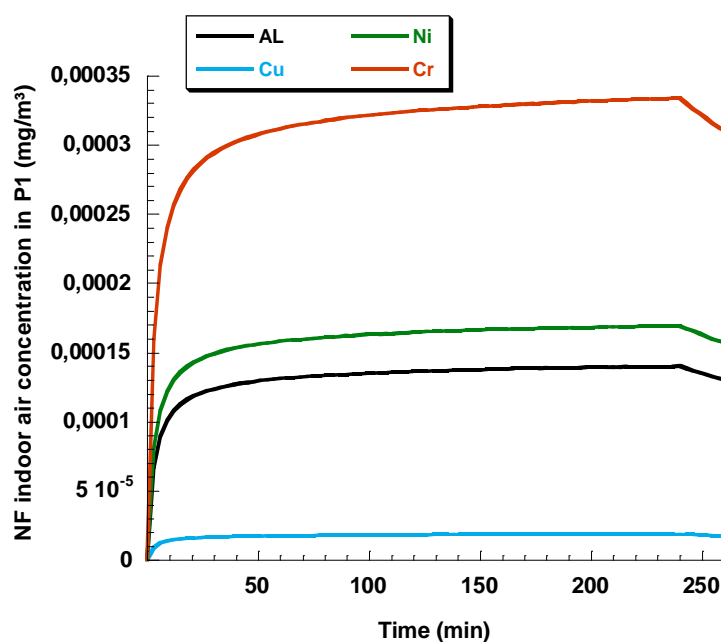
Figure 1.5: Modeled indoor air concentrations of Al, Cu, Ni and Cr in the NF of Steel sheet stamping (P1) during four-hour shift
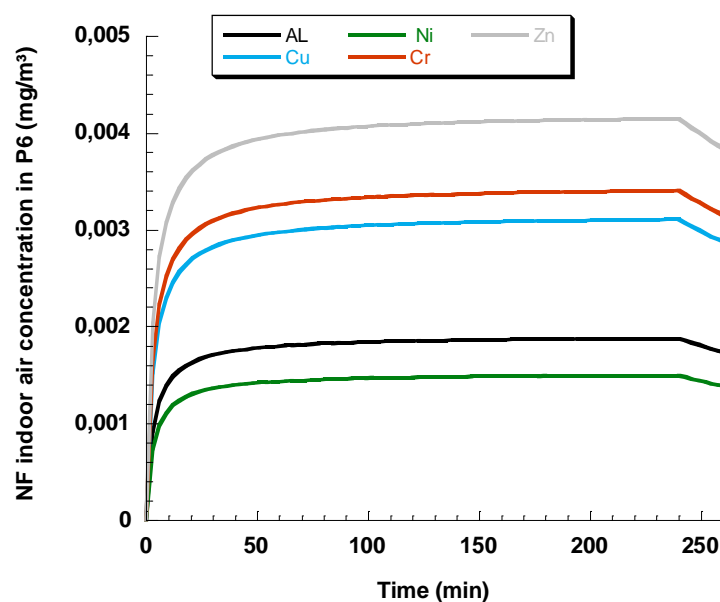
Figure 1.6: Modeled indoor air concentrations of Al, Cu, Ni, Cr and Zn in the NF of sheering and slitting (P6) during four-hour shift

Figure 1.5 shows NF model predictions of trace metallic elements concentrations in steel sheet stamping workplace. The NF concentration values quickly rise in the first 20 minutes.

Then, after nearly 90 min, concentrations almost reach steady state concentrations. Figure 1.6 shows corresponding data for steel sheet sheering and slitting workplace. The NF concentration values also quickly rise in the first 20 minutes. Then, after nearly 60 min, concentrations almost reach steady state concentrations. These steady state concentrations are exhibited in table 1.5.

Table 1.5: NF steady state concentrations $C_{NF,SS}$ during steel sheet cutting

NF steady state concentrations ($\mu g/m^3$), $C_{NF,SS}$ (240-min)	Situation 1: Stamping A1: P1	Situation 2: Sheering and slitting A4: P6
• Al	0.140	1.87
• Cu	0.019	3.10
• Ni	0.169	1.49
• Cr	0.334	3.40
• Zn	-	4.14

III.3.2. Welding modeling

III.3.2.1. Resistance spot welding

The Resistance spot welding RSW job task is noted as P4. As mapped in figure 1.7, there are between 3 to 5 RSW operators in the workplace A2. Every worker is welding workpieces using an individual RSW machine (see figure 1.7).

The room is ventilated thought the main door and a side opening. However, because A2 is located in the top floor of another room, the ventilation is poor. Another source of ventilation is the local exhaust ventilation that is integrated in each RSW machine. They are located just above the welding spot device and it was observed that it directly vacuums a great amount of welding fumes.
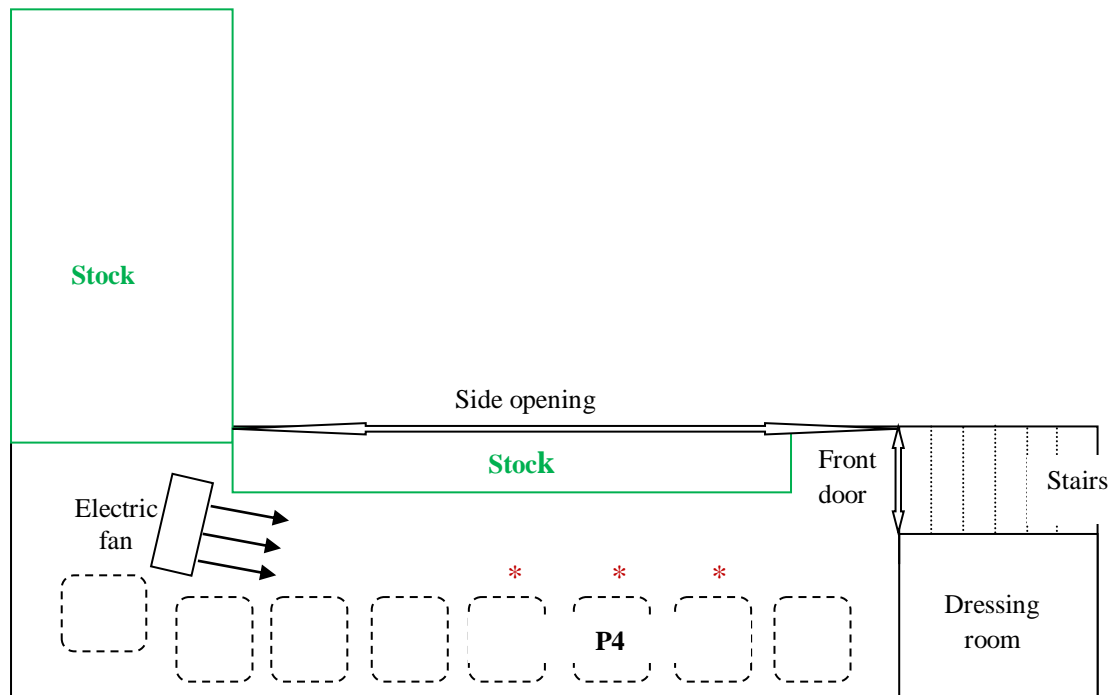
Figure 1.7: Scheme of workplace A2; P4: RSW

*: locations of workers

Nevertheless, air is evenly distributed in the A2 due to the setting up of a large electric fan (1m*1m) (figure 1.7). Indeed, the measured air velocity values were almost equal over the room. Therefore, we are assuming that the air is perfectly mixed. Consequently, we are using the WMB model.

The values of the mass conservation ratios for A2 and the value is 1.05. It is close to 1, so mass conservation is confirmed and the volumetric flow rate into the room must be equal to the one out of it. Subsequently, we can choose one of them to calculate Q_{A2}. So, we decided to calculate Q based on local exhaust ventilation in A2. Having this reliable information, we are able to calculate a Q_{A2} value with a sufficient confidence [34]. The intake velocity was calculated and is equal to 11.78 m.s^{-1}. As a result, the ACH is equal to 5.53.

In RSW task job, the generation rate $G_{averageA2,\ P4}$ is calculated based on the research studies that are interested in mass emission rate using RSW process. For non-coated steel sheets, G calculations are based on a study conducted by Pohlmann et al. [63]. The authors summarized mass emission rates for several welding processes. Among them, they considered the RSW process, and, they found that the mass emission rate for a non-coated steel sheet is between 0.0377- 0.0378 mg/s. The authors worked in many conditions and with several base materials to give us a more accurate interval of emission rates. This interval showed little variability, which help us to calculate G values with higher precision.

Thus, viewing the chemical composition of the used steel, we can calculate the mass emission rate for every metal.

Q and V are calculated as previously described.

In addition, C_0 is considered to be as null value because it is assumed that there are no TMEs in the workplace prior to the work shift. Because A2 is located at the top floor of A1 (the part in the far left) we can consider, as to C_{in}, that the air supply comprises an amount of TMEs. We assume this amount as cumulative FF concentrations of 7 press machines (located in the far left part) generated from the job task P1.

All models parameters are summarized in table 1.6.

Figure 1.8 shows the WMB model prediction of trace metallic element concentrations in RSW workplace. The concentration values rise in the first 35 minutes. Then, after nearly 90 min, concentrations reach the steady state concentrations cited for every metal in table 1.7.

Table 1.6: WMB model input values: constant emission rate of TMEs during RSW welding

WMB Parameters	Situation: RSW welding A2: P4
V_{A2} (m^3)	345.29
C_0(mg/ m^3)	0
C_{in} (mg/ m3)	0
• Al	0.0000574
• Cu	0.0000077
• Ni	0.0000693
• Cr	0.000137
Q_{A2} (m^3.min^{-1})	31.81
$G_{A4:\ P3,average}$ (mg. min^{-1})	
• Al	0.0084
• Cu	0.0032
• Ni	0
• Cr	0
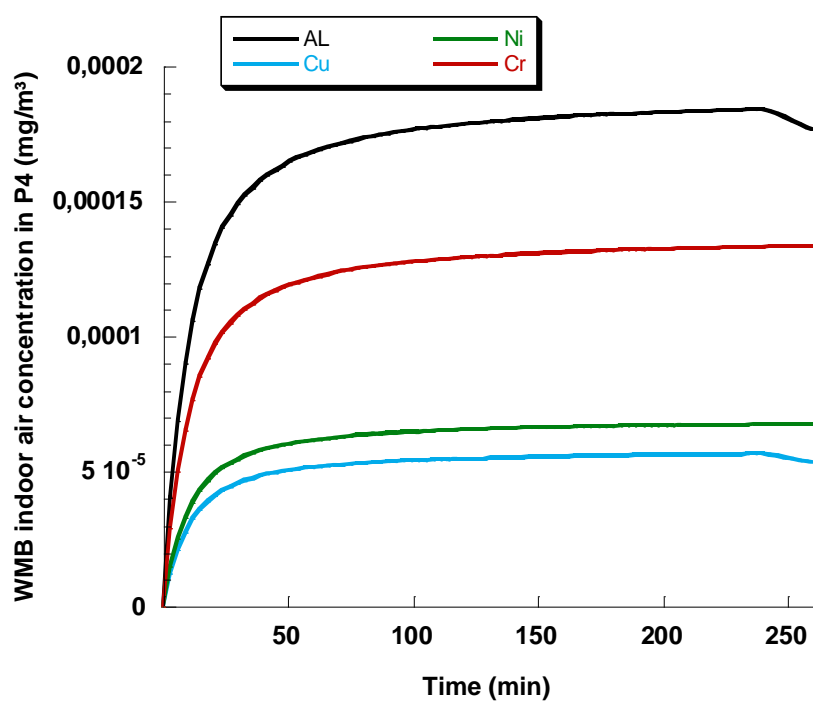
Figure 1.8: Modeled indoor air concentrations of Al, Cu, Ni and Cr in the whole workplace A2 for RSW (P4) during four-hour shift

Table 1.7: Steady state concentrations in the WMBC$_{WMB, SS}$ during RSW

WMB steady state concentrations (µg/m^3), C$_{WMB,SS}$ (240min)	Situation: RSW welding A2: P4
Al	0.305
Cu	0.103
Ni	0.067
Cr	0.133

III.3.2.2. Induction welding

The induction welding machine is placed all along the workplace A5 (mapped in figure 1.9).

There is a single induction welding machine operator, noted P9, who is controlling and supervising the induction welding process. He is positioned approximately in the middle of the room, in the vicinity of the welding area that is limited and tagged with a dashed line in figure 1.9.All other workers are far away from the welding area.

A5 is a quite long workplace (100*20 m) and mainly ventilated by a one side door and a one large lateral opening. They are situated in the room's two extremities (see figure 1.9). It was also observed that the airflow rate nearby P9 is lower. Therefore, we are using the NF/FF model with a constant emission rate. The NF includes the welding area and the induction welding machine operator.

The values of the mass conservation ratios in A5 is 1.03, confirming mass conservation.

In P9, the NF is estimated as a parallelepiped box on the top of the welding area. The worker is either in stand or seated position, so the height of the box is equal to the vertical distance between the induction welding setting, which represents the emission source, and about 15 cm above the worker's head to cover up the entire breathing zone in both positions. The length is equal to the distance between the worker and the induction welding setting. And the width is equal to the induction welding surface of the workpiece (**figure 1.9**).

Figure 1.9: Scheme of workplace A5
*: fixed locations of workers,
*: Mobile positions, .▶ : movement areas of mobile workers

As the NF box is on the top of induction welding setting, the inter-box air flow rate β does not flow through about the half of the bottom surface and the back surface that is affixed to the machine. Thus, the remaining surfaces of a parallelepiped box are calculated in the FSA, which is equal to 7.63 m^2.

The average random air speed S is calculated for P9 and is equal to 0.098 m.s^{-1}.

The air changes per hour ACH is also calculated and is to equal to 11.91 for A5.

To calculate the generation rate $\mathbf{G_{P9}}$ for induction welding, the mass balance method is used. In fact, using questionnaires, all information about the materials' quantities were collected. Indeed, galvanized steel sheets were used; their reference is DX51D+ Z. The chemical composition of the material was explored in literature [54,55].

β, Q and V are calculated as previously described. All models parameters summarized are in table 1.8.

Table 1.8: NF-FF model input values: constant emission rate of TMEs during induction welding

NF-FF Parameters	Situation: induction welding A5: P9
V_{A5} (m^3)	12812.25
$V_{NF, P9}$ (m^3)	1.88
β_{P9} (m^3.min^{-1})	22.42
Q_{A5} (m^3.min^{-1})	2543.42
$G_{A5: P9,average}$ (mg. min^{-1})	
• Al	0.0199
• Cu	0.0050
• Ni	0.0066
• Cr	0.0028
• Zn	0.0565

Figure 1.10 shows NF model prediction of trace metallic element concentrations in induction welding workplace. The NF concentration values quickly rises in the first 20 minutes. Then, after nearly 90 min, concentrations almost reach the steady state concentrations cited for every metal in table 1.9.
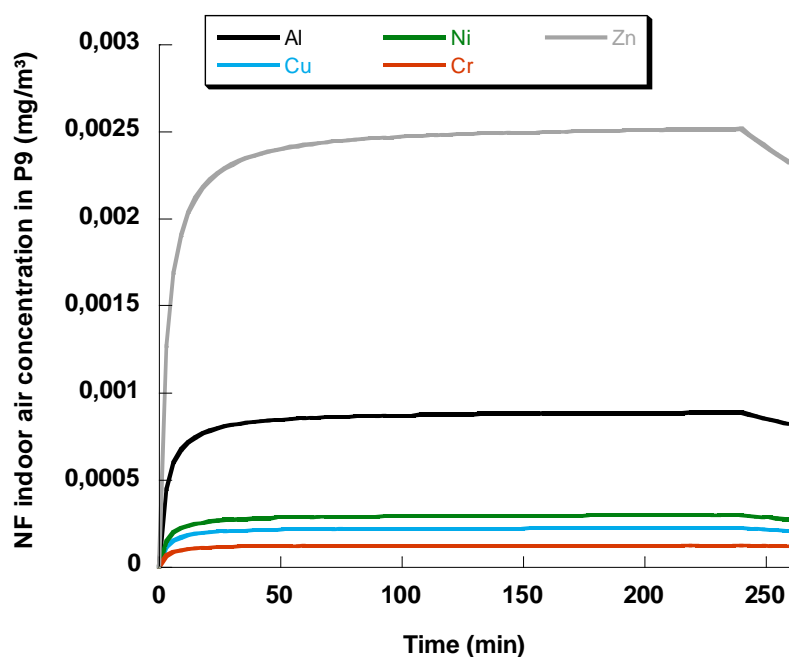
Figure 1.10: Modeled indoor air concentrations of Al, Cu, Ni, Cr and Zn in the NF of induction welding (P9) during four-hour shift

Table 1.9: NF steady state concentrations $C_{NF,SS}$ during induction welding

NF steady state concentrations ($\mu g/m^3$), $C_{NF,SS}$ (240 min)		Situation: induction welding A5: P9
•	Al	0.884
•	Cu	0.222
•	Ni	0.293
•	Cr	0.124
•	Zn	2.510

III.3.2.3.   Electric arc welding

- The first considered job task is Shielded Metal Arc Welding (SMAW) that is noted **P5**.

SMAW is taking place in the workplace A3 (figure 1.11). There is only one worker who is assumed to be continuously working for a four hour-shift; he takes less than a couple of minutes to position a new electrode when the prior one is totally consumed.

As showed in figure 1.11, the workplace is particularly full of products and old machine stocks. Even though A3 is jointly ventilated by two doors located against one another, there is neither a control system nor mechanical ventilation in our workroom. Hence a low airflow rate nearby the SMA welder. It was also observed that the welder is close to the emission source and the welding fumes are considerably concentrated in the surrounding area. Therefore, we are using the NF/FF model with a constant emission rate where the welder is exposed to the NF concentrations of TMEs.

- The second subtype of electric arc welding is GMAW.

GMAW process is occurring in the workplace named A5 (figure 1.9). In this particular situation, the job (noted **P16**) involves 2 different tasks; system control of the tube welding machine and periodic Gas metal arc welding (GMAW). P16 implicates 2 workers.

The main task job is the system controller task; the 2 workers are monitoring the machine for a four-hour-shift. The first one is regulating and checking the unrolling of the metal steel rolls. Next to him, the second one is controlling the quantity and the speed of the metal sheets that are introduced into the induction welding compartment.

Door

Front door
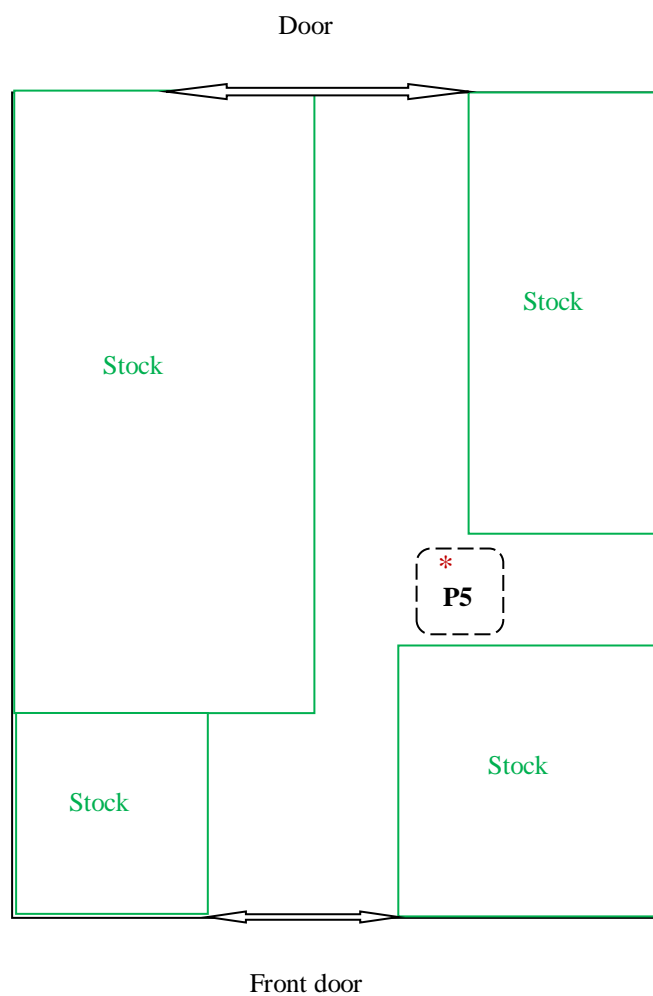
Figure 1.11: Scheme of workplace A3; P5: SMAW

*: worker's position

In addition, GMAW task is discontinuously realized to connect the steel sheets together for an average of 11 times during the four-hour shift. Each GMAW operation lasts for an average duration of 4 minutes.

Consequently, the 2 workers are co-exposed to two emission sources, the discontinuous emission of the GMAW and the continuous FF concentrations of the induction welding of P9 since they are sufficiently distant from the emission source (figure 1.9).

Hence, first of all, the GMAW task is modeled individually and noted later as **P16$_{GMAW}$.** Then, the concentrations of both emission sources will be summed to calculate the total predicted concentrations for P16 for each TME (i); C$_i$ as below:

$$C_i(P16) = C_{NF,i}(P16_{GMAW}) + C_{FF,i}(P9)$$

For GMAW exposure, the 2 operators are working next to each other and slightly moving in a restricted area. Indeed, it was observed that both workers are exposed to the GMAW fumes; the welder and his colleague. Therefore, we are using the NF/FF model where the NF includes both workers' breathing zones and the sitting where the emission is taking place. Moreover, the model's emission rate is considered cyclical over the four-hour shift; a constant emission rate during 4 minutes repetitively every 16 minutes.

The values of the mass conservation ratios for the workplace A3 and A5 are 1.005 and 1.03, respectively; mass conservation is confirmed.

➢ In the first job task **P5**, the SMA welder is working in a seated position. He is welding a metallic workpiece positioned in front of him (the emission source) that is at the same level as the seat of his chair. The NF is estimated as a half of a hemisphere. As shown in figure 1.12, its radius (1.15m) lies between the welder and the metallic workpiece being welded. Vertically, the radius actually covers the distance between the base seat of a chair up to 15 cm above the worker's head to cover up the entire breathing zone [62]. Besides, the inter-box flow rate β$_{A5}$ flows through all surfaces of the NF box.

➢ In the second job task **P16$_{GMAW}$**, the NF is estimated as a parallelepiped box that contains the GMAWelding setting. The length and the width are covering the space where both workers are moving and the emission source. The workers are in standing position, so, the height of the box is equal to the vertical distance between the welding setting level and about 15 cm above the worker's head to cover up the entire breathing zone. The inter-box air

flow rate β_{A16} flows through all surfaces except the little part of bottom surface overlapping with the welding setting on the machine.
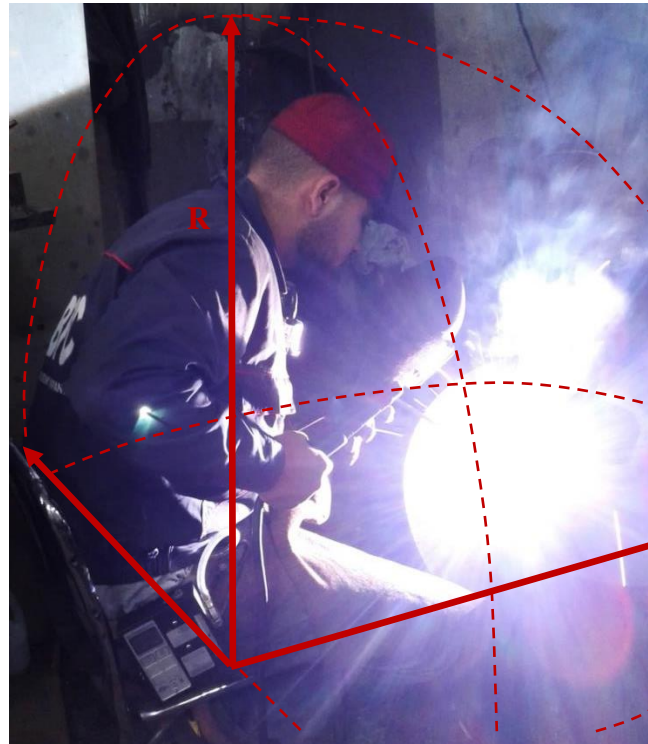
Figure 1.12: NF dimensions of P5 (SMAW): R = 1.15 m

Then, the FSAs are equal to 6.23 and 78.42m^2, for the NFs of P5 and P16$_{GMAW}$, respectively. And, to calculate β_{P5} and $\beta_{P16\ GMAW}$, S was calculated and is equal to 0.04 and 0.023 m.s^{-1}, respectively.

ACH are equal to 13.93 and 11.91. Thus, both workplaces A3 and A5 are adequately ventilated.

To calculate the generation rate **G** for electric arc welding, the emission factor EF method is used.

In the SMAWelding process, information about the base metal materials was not available. For electric arc welding, the greatest amount of the welding fume is originated by the electrodes compared to the basic metal material [64]. It was demonstrated that the welding fumes composition is the same as the consumed wire [36,64,65].
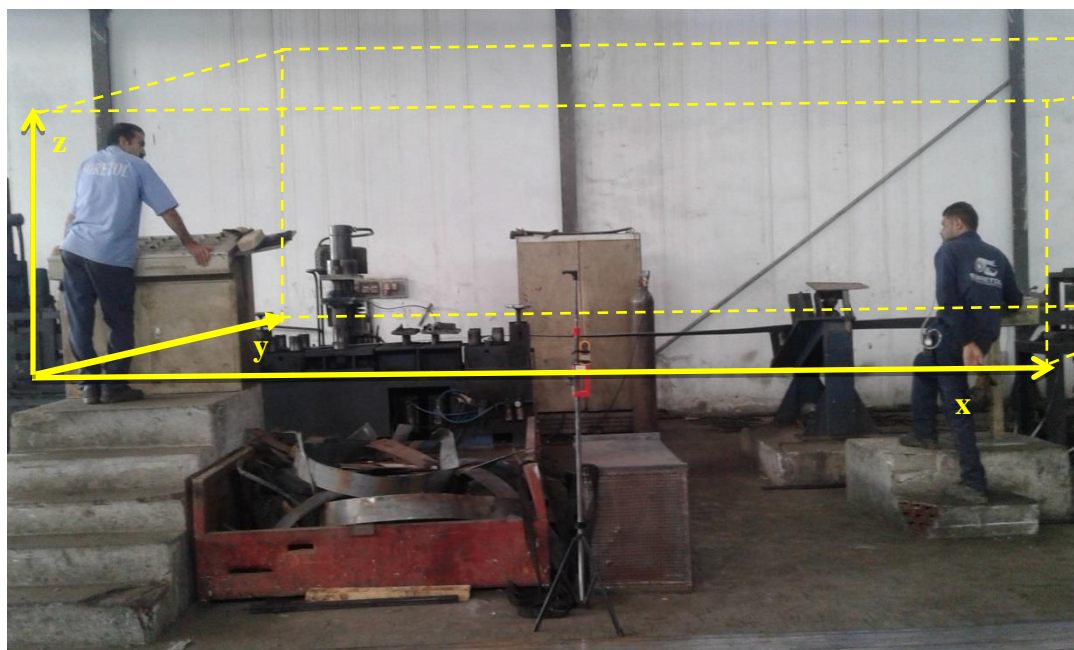
Figure 1.13: NF dimensions of P16$_{GMAW}$ (GMAW): x = 6 m, y = 3.7 m, z = 1.9 m

So, to calculate G, we decided to only consider the TMEs emitted from the consumable electrodes for both SMAW and GMAW.

In the section dedicated to electric arc welding in AP-42 by US EPA [66], SMAW and GMAW processes were both considered.

EFs were quantified for the electrodes used in P5and P16$_{GMAW}$ [37] and they are presented in table 1.10. The following emission factors are rated as excellent, above average and average factors, for E70S-6, E6013 and E7018, respectively. For the three of the electrodes, EFs were established only for Cr and Ni.

Table 1.10: AP 42- emission factors of total fume, Cr and Ni for electric arc welding processes [37]

Welding process	Electrode type	Emission factor (g/kg of electrode consumed)		
		Total fume	Cr	Ni
SMAW	E6013	19.7	0.004	0.002
	E7018	18.4	0.006	0.002
GMAW	E70S-6	5.2	0.001	0.001

The models parameters are presented in table 1.11.

Table 1.11: NF-FF model input values: constant emission rate of TMEs during SMAW: P5 (240 min) and GMAW: P16$_{GMAW}$ (4 min over 20 min)

NF-FF Parameters	Situation 1: SMAW A3: P5	Situation 2: GMAW A5: P16$_{GMAW}$
V (m^3)	593.57	12812.25
V$_{NF}$ (m^3)	1.59	42.18
β (m^3.min^{-1})	7.42	54.11
Q (m^3.min^{-1})	137.85	2543.42
G $_{average}$ (mg. min^{-1})		
• Al	0.0742	0.1006
• Cu	0.0140	1.8104
• Ni	0.0064	0.0007
• Cr	0.0180	0.0007
• Pb	0.0280	0.2514
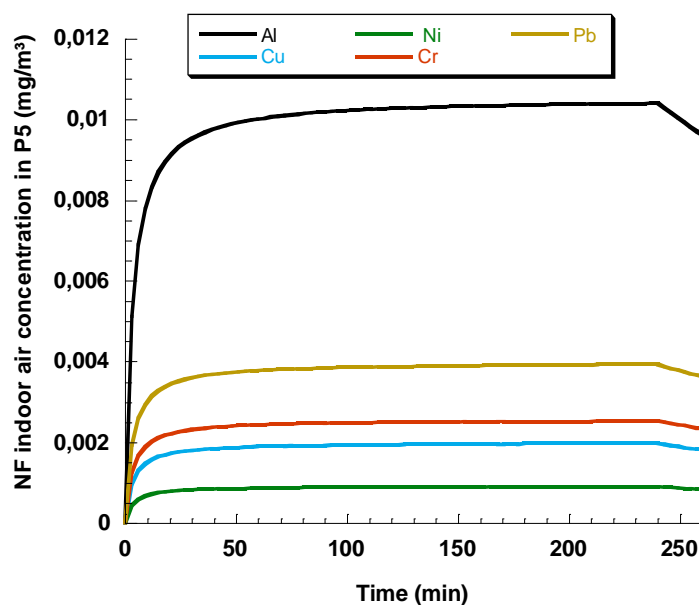
Figure 1.14: Modeled indoor air concentrations of Al, Cu, Ni, Cr and Pb in the NF of SMAW (P5) during four-hour shift
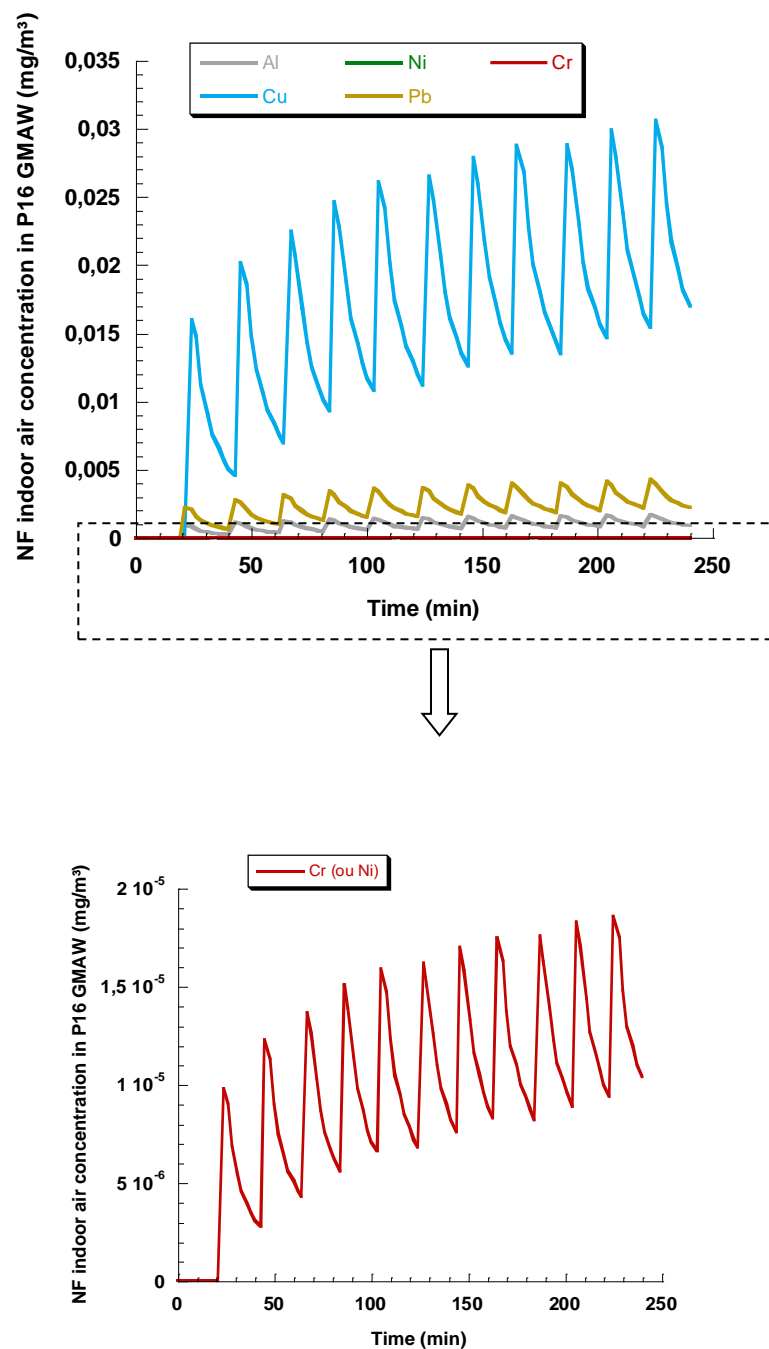
Figure 1.15: Modeled indoor air concentrations of Al, Cu, Ni, Cr and Pb in the NF of GMAW (P16$_{GMAW}$) during four-hour shift

Figure 1.14 shows trace metallic element concentrations in the NF where SMA welding is taking place. The NF concentrations values quickly rise in the first 20 minutes. Then, after nearly 50 min, concentrations almost reach the steady state concentrations cited for every metal in table 1.6.

Figure 1.15 shows cyclic exposure to trace metallic element concentrations in the NF where GMA welding is taking place. The following cycle is occurring before the TMEs can reach zero in the decay phase. So, the TME concentrations are increasing from cycle after the other. After fulfillment of eleven cycles, the steady state concentrations after the decay phase reach approximately the peak concentrations of the first exposure cycle.

Figure 1.16 shows the sum of trace metallic element concentrations for P16, where the NF concentrations of GMA welding and the FF of the induction welding are taking place.

The steady state concentrations are cited in table 1.12 for the identified metals.
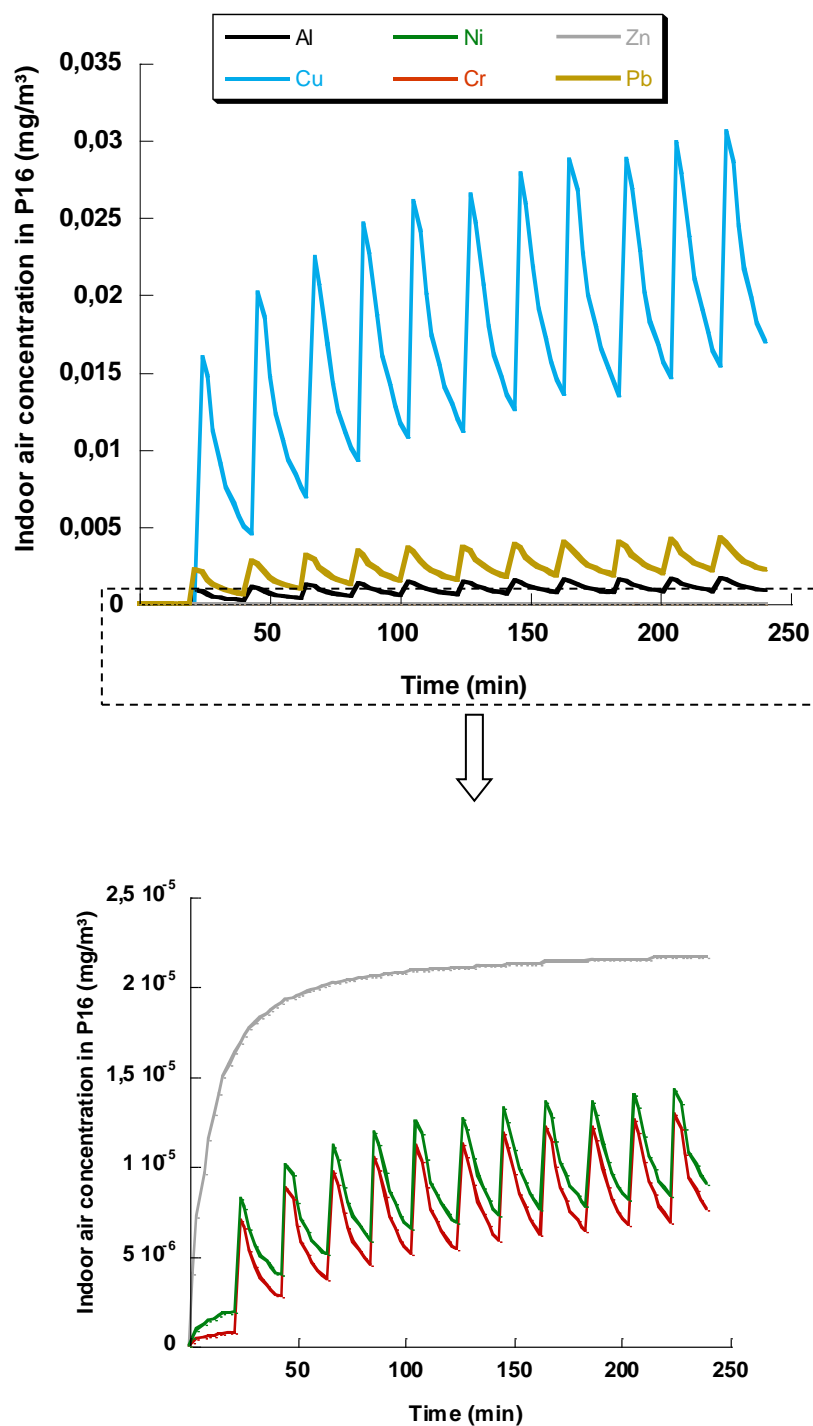
Figure 1.16: Modeled indoor air concentrations of Al, Cu, Ni, Cr, Zn and Pb for P16 (GMAW and system control of the tube welding machine) during four-hour shift

Table 1.12: NF steady state concentrations C$_{NF,SS}$ SMA welding process

NF steady state concentrations (µg/m^3), C$_{NF,SS}$ (240min)	Situation 1: SMAW A3: P5	Situation 3:A5: P16 NF GMAW + FF P9
• Al	10.401	0.897
• Cu	1.962	17.007
• Ni	0.897	0.009
• Cr	2.52	0.007
• Zn	-	0.022
• Pb	3.924	2.222

III.3.3. Electroplating modeling

III.3.3.1. Metal electroplating

In the workplace **A6** mapped in figure 1.17, there are two kinds of metal electroplating processes; zinc and nickel electroplating. Habitually, both zinc and nickel electroplating lines are active. In our study, we are adopting the scenario when both lines are functioning.

In the zinc-plating lines, the electroplating machine is an automated system which means nobody needs to be next to the plating baths. All the worker locations are in front of the lines, close to each other (positions indicated in figure 1.17). Therefore, all their job tasks are considered as a unique task named zinc-plating lines operator and noted **P10.** There are 7 workers.

The nickel-plating lines system has a different modus operandi; a system controller and two operators have to move all along between the two lines during the whole shift. This task job is named nickel-plating lines system controller and noted **P11** (positions indicated in blue in figure 1.14). There are also, lifting-hooks and quality control operators that are always working next to each other in the front of the lines and relatively away from the plating baths compared to **P11**. This task job is named nickel-plating lines lifting-hooks operator and noted **P12.** There are 4 workers.

The workplace is ventilated thought three doors; two side doors and a one at the back of the room; and some windows. Based on the second questionnaire, the room is also ventilated with

3 extractor fans having an individual average air flow rate value of 11 950m^3.h^{-1}. Air is also leaving the room through two local exhaust ventilation systems over the zinc-plating baths with an average air flow rate value of 17784 m^3.h^{-1}.

The air flow rates measured nearby the baths **(P10)** were low. Therefore, we are using the NF/FF model with a constant emission rate. The workers are considered to be in the FF because they are not closely next to the plating baths, even though the distance is not immense. In addition, since nickel-lines are simultaneously functioning, we are considering that **P10**is jointly exposed to the FF emissions from both zinc and nickel electroplating.

As for **P11**that is positioned closely next to the plating baths, we are considering that this task is exposed only to NF emissions of the nickel-plating lines. This is especially due to the low airflow rate that was observed between the lines where the workers were constantly circulating. So, we are using the NF/FF model with a constant emission ratein spite of the large dimensions of the emission sources.

Regarding **P12,** based on analogous reasoning with P10, workers should be jointly exposed to the FF emissions from both nickel-plating lines and zinc-plating lines. However, as previously mentioned, the zinc plating lines are equipped with local exhaust ventilation systems over the baths. That is why we are considering that P12 is exposed only to FF emissions from both nickel-plating lines.
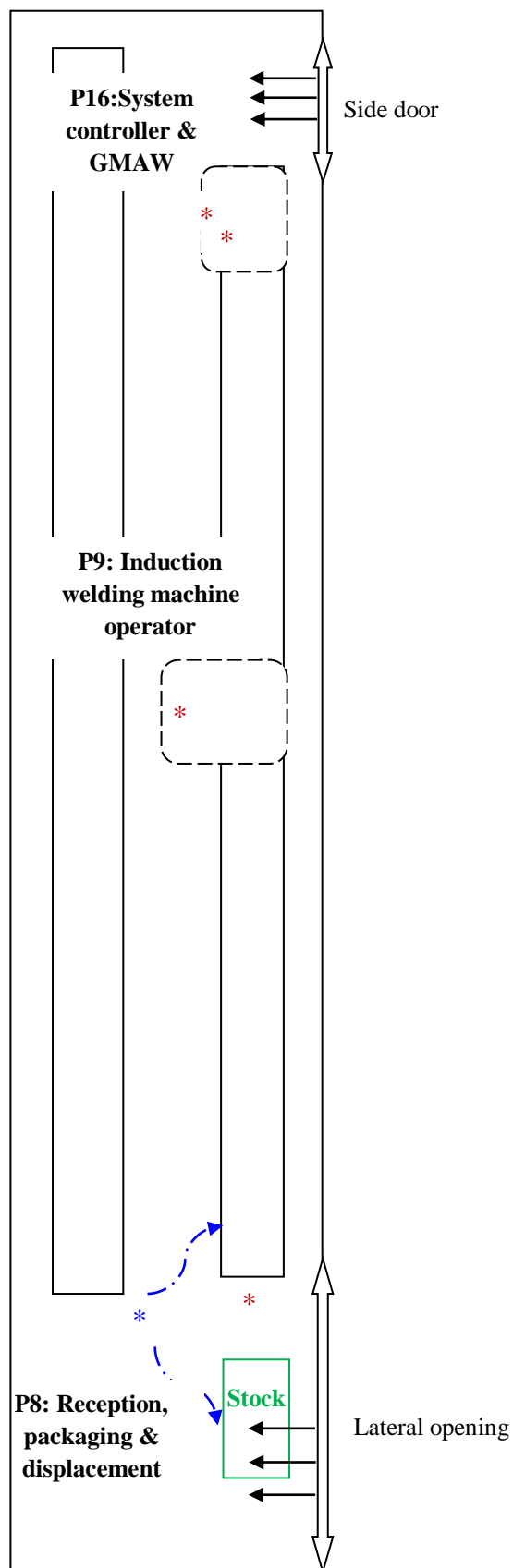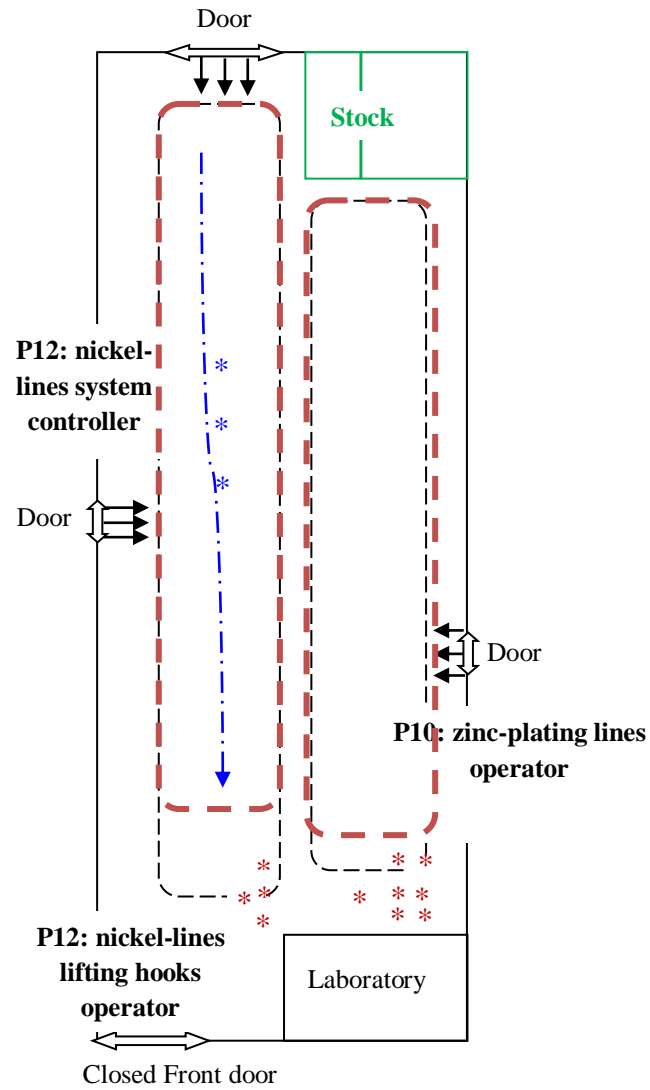
Figure 1.17: Scheme of workplace A6, *: fixed locations of workers,

***: Mobile positions,** ▸ : Movement area of mobile workers

- - - : NF lengths and widths

The values of the mass conservation ratio for the workplace A6 is 1.03, so the volumetric flow rate into the room must be equal to the one out of it. Therefore, we can choose one of them to calculate Q_{A6}. In the workplace A6, we decided to calculate Q based on local exhaust ventilation and the extractor fans flow rates. Having this reliable information, we are able to calculate a Q_{A6} value with a sufficient confidence [34]. As a result, the ACH is equal to 15.21.

- The two-nickel plating lines include 3 and 4 baths, respectively. Table 1.14 illustrates the different trace metallic element baths in A6.

In nickel-plating lines, we have two job tasks **P11** and **P12.** The first one is considered inside the NF and the second one is conceived to be exposed to lower concentrations in the FF.

The NF volume is rather big because the emission surface is wide. The NF is designed as a large parallelepiped box of air placed over the plating baths and covering the whole surface. The length of the NF is that of the nickel-lines and the width is that of both lines and the distance between them (figure 1.17). A worker is either in a standing position or walking, so the height of the box is equal to the vertical distance between the surface of the baths, which represents the emission source, and about 15 cm above the worker's head to cover up the entire breathing zone.

The inter-box air flow rate β flow through all surfaces except for the baths surfaces in the NF box bottom surface. So, FSA and S are calculated and are equal to 284.14 m^2 and 0.015 $m.s^{-1}$, respectively.

- In the zinc plating, each line includes one bath in each line (table 1.14).

As previously mentioned, **P10** is considered to be jointly exposed to the FF zinc-plating lines emissions and FF emissions from the nickel-plating lines.

The NF volume is quite big because the emission surface is wide. The NF is designed as a large parallelepiped box of air placed on the floor encompassing the two lines, but not the workers. The length of the NF is that of the zinc-lines and also the distance between the lines and the laboratory where P10 is located (see figure 1.14). The width is that of both lines and the distance between them. The height of the box is assumed as an average length of a worker and about 15 cm above the worker's head. This distance exceeds the bath surfaces of about 10 cm. It should be noted that the lines volumes are subtracted from the NF volume.

The inter-box air flow rate β flow through the top surface and also through the two side and back surfaces except for the bath dimensions. So, FSA and *S* are calculated and are equal to 192.73 m^2 and 0.022 $m.s^{-1}$, respectively.

Both models parameters are calculated and illustrated in table 1.13.

Table 1.13: NF-FF models input values: constant emission rate of TMEs electroplating

NF-FF Parameters	Situation 1: Nickel-plating lines system controller A6: P11	Situation 2: Nickel-plating lines lifting-hooks operator A6: P12	Situation 3: Zinc-plating lines operator A6: P10
V (m^3)		3526.03	
V_{NF} (m^3)	130.63	-	88.26
β ($m^3.min^{-1}$)	126.86	-	125.28
Q ($m^3.min^{-1}$)		894.00	
G *average* (mg. min^{-1})			
• Cr	125.500		-
• Ni	1.214		-
• Cu	0.276		-
• Zn	0.097		1.982

In the context of electroplating, the emission factor EF method is adopted to calculate the generation rates; $G_{A6: P10}$ and $G_{A6: P11}$ for zinc and nickel plating lines, respectively.

In the section dedicated to electroplating process in AP-42 [67], we are either using ready-established EFs to calculate the generation rates or calculating our own EFs using field based information.

- In nickel plating lines, except for Cr, all EFs were calculated using formula for uncontrolled electroplating tanks. On the other hand, for hard chromium electroplating bath, an EF for uncontrolled emissions of 0.12 grains/ A-hr was adopted from AP-42 [67].
- In zinc plating lines, EFs for Zn were calculated using the formula for controlled electroplating tanks.

All emission factors EFs and data used for EFs and generation rate calculations are in table 1.14.

Table 1.14: Trace metallic element baths in every line for both zinc and nickel electroplating in A6

Plating type	Zinc-plating lines		Nickel-plating lines						
Line number	Zn Line 1	Zn Line 2	Ni Line 1			Ni Line 2			
Bath number	B_1	B_1	B_1	B_2	B_3	B_1	B_2	B_3	
Metal-plating [a]	Zn	Zn	Cu	Ni	Cr	Cu	Ni	Zn	Cu
EE_m [b] (A-hr/mil-ft^2)	-	-	17.7	19.0	-	17.7	19.0	13.7	17.7
e_m [a] (%)	-	-	95	95	-	95	95	95	95
C_m [a] (g/L)	8-16	8-16	40-45*	80** +280***	-	40-45*	80** +300***	37	22
D_m [a] (A/dm^2)	-	-	1	0.3- 0.6	-	0.5-0.9	0.4- 0.9	0.35- 0.5	
$EF_{average}$ (mg/m^3)	5.18× 10^{-3} [d]	5.18 ×10^{-3} [d]	9.61 10^{-4} [d]	3.91×10^{-3} [d]	0.989 [c]	6.85 ×10^{-4} [d]	5.65 ×10^{-3} [d]	7.65× 10^{-4} [d]	5.32 × 10^{-4} [d]

[a]: Collected using questionnaires

[b]: [41]

[c]: Converted to mg/m^3 (developed by US EPA, AP 42- emission factors) [67]

[d]: Calculated

*: as $CuSO_4$, **: as $NiCl_2$, ***: as $NiSO_4$

Then, the predicted concentrations of Cu, Ni, Cr and Zn were computed using the IHMOD software tool. The models outputs are presented in figures 1.18 (for the job tasks A11and A12) and 16 (for A10).

Figure 1.18 shows the NF model predictions of trace metallic element concentrations in nickel-lines electroplating for electrodeposition onto metals. The NF concentration values quickly rises in the first 20 minutes. Then, for Cu and Zn after nearly 30 min, concentrations almost reach the C_{SS}. As to Ni and Cr, it took them 70 min to reach the C_{SS}.
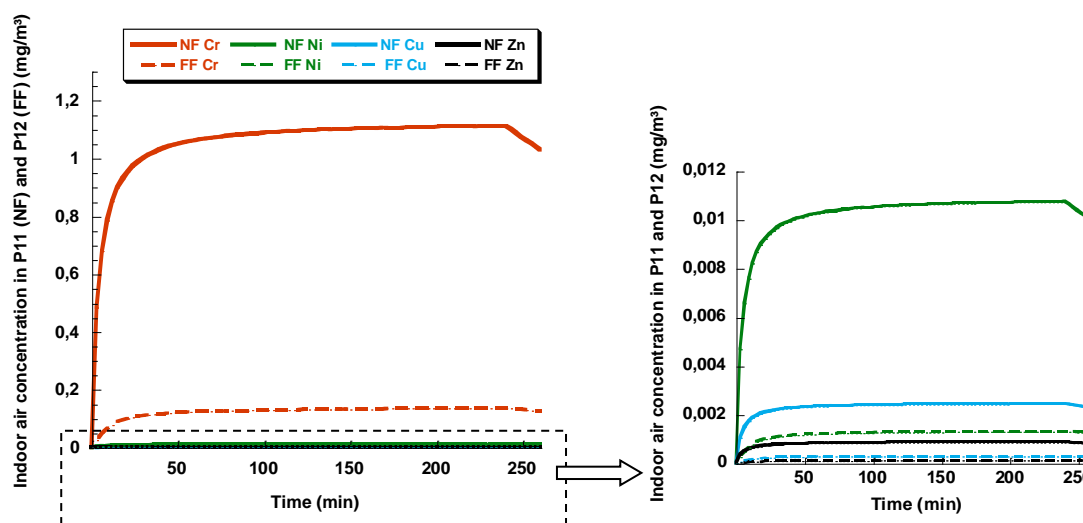
Figure 1.18: Modeled indoor air concentrations of Cu, Ni, Cr and Zn in NF (P11- solid lines) and FF (P12-dashed lines) for nickel-lines electroplating during four-hour shift
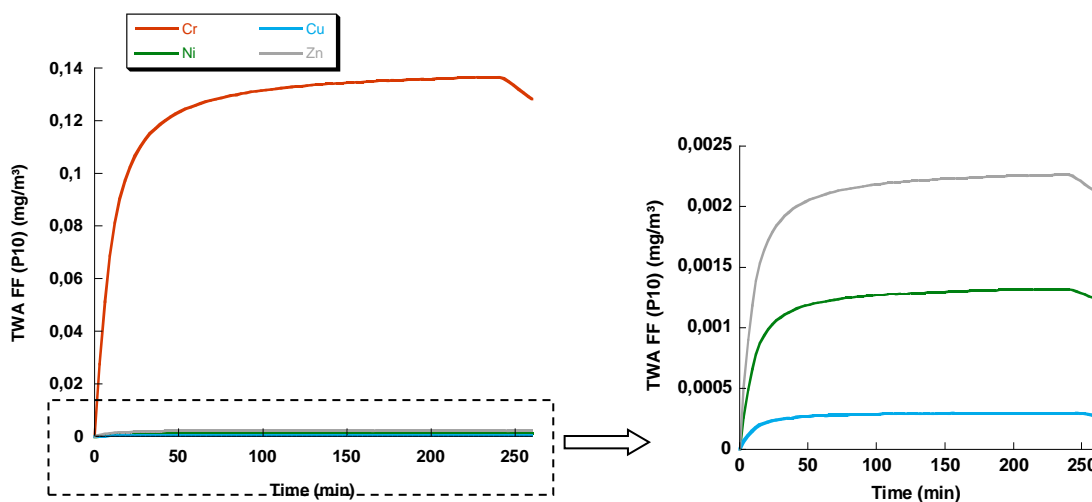
Figure 1.19: Modeled indoor air concentration (240-min) of Cu, Ni, Cr and Zn in FF for zinc-lines electroplating during four-hour shift

The estimated concentration of Cr is significantly higher than for other metals by a factor at least of100. This is could be due to the different approaches used to determine the EFs in the first place. Contrarily to Cu, Ni and Zn, the EF of Cr in uncontrolled chromium plating is already established in AP-42 and is considerably higher than our calculated EFs illustrated in table 1.8. This was justified by the fact that the cathode efficiency of chromium plating is very low compared to the other metals. Thus, the mist emission is higher because it is inversely proportional to cathode efficiency [67].

The steady state concentrations are cited in table 1.15.

Table 1.15: NF and FF steady state concentrations and the final predicted concentrations for each job task during metal electroplating

NF and FF steady state concentrations ($\mu g/m^3$), $C_{NF/FF,SS}$ (240-min)	Situation 1: Nickel-plating lines: NF	Situation 2: Nickel-plating lines: FF	Situation 3: Zinc-plating lines: FF
• Cr	1112	137	-
• Ni	10.7	1.32	-
• Cu	2.45	0.30	-
• Zn	0.86	0.11	2.22
Steady state concentrations ($\mu g/m^3$)	**Nickel-plating system controller A6: P11**	**Nickel-plating lifting-hooks operator A6: P12**	**Zinc-plating operator A6: P10**
• Cr	1112	137	137
• Ni	10.7	1.32	1.32
• Cu	2.45	0.30	0.30
• Zn	0.86	0.11	0.11+ 2.22 (=2.33)

III.3.3.2.   ABS plating:

The workplace **A7** is mapped in the figure 1.20, where the decorative chromium electroplating of ABS is taking place. The plating lines include numerous baths as indicated in table 1.17.

In the electroplating lines of ABS, the process is an automated system which means workers do not have to be next to the plating baths, but only occasionally for controls. The locations of the system controllers and the lifting hooks operators are all at the left side of the lines (positions indicated in figure 1.20). Hence, all these job tasks are considered as a unique job task named ABS plating lines operator and noted **P13**. There are 6 workers.

The workplace is mostly ventilated thought two side doors and barely through a communicating door with a hall. It was also reported that the A7is also ventilated with 2 extractor fans having an individual average air flow rate value of 11,950 $m^3.h^{-1}$. Moreover, the air is also leaving the room through local exhaust ventilation systems over the plating baths with an average air flow rate value of 11,088 $m^3.h^{-1}$.

The air flow rates measured nearby the workers **(P13)** were low. Therefore, we are using the NF/FF model with a constant emission rate. P13 are considered to be in the NF. Even though the NF volume is quite large, we estimated that P13 are more exposed because they are closer to the plating lines than the quality controllers (noted P14).

The values of the mass conservation ratios for the workplace A7 is 1.003. So, similarly to A6, we are calculating Q_{A7} based on local exhaust ventilation and the extractor fans flow rates. This reliable information can give us a ventilation rate result with a sufficient confidence [34]. Thereafter, the ACH is equal to 12.58.

The ABS plating lines include 7 baths. The table 1.11 illustrates the different trace metallic element baths in A7.

In ABS plating workplace, the NF volume is relatively big because of the emission surface and the consideration of the location of ABS lines operators. The NF is designed as a large parallelepiped box of air placed over the plating baths and the workers' location (illustrated in figure 1.17). The length of the NF is that of the ABS plating lines and the width is that of both lines, the distance between them and the distance between the workers and the lines (figure 1.17). All workers are in a standing position or walking, so the height of the box is equal to the vertical distance between the surface of the baths, which represents the emission source, and about 15 cm above the worker's head to cover up the entire breathing zone.

The inter-box air flow rate β flow through all surfaces except for the baths surfaces in the NF box bottom surface. So, FSA and *S* are calculated and are equal to 308.03 m^2 and 0.021 $m.s^{-1}$, respectively.
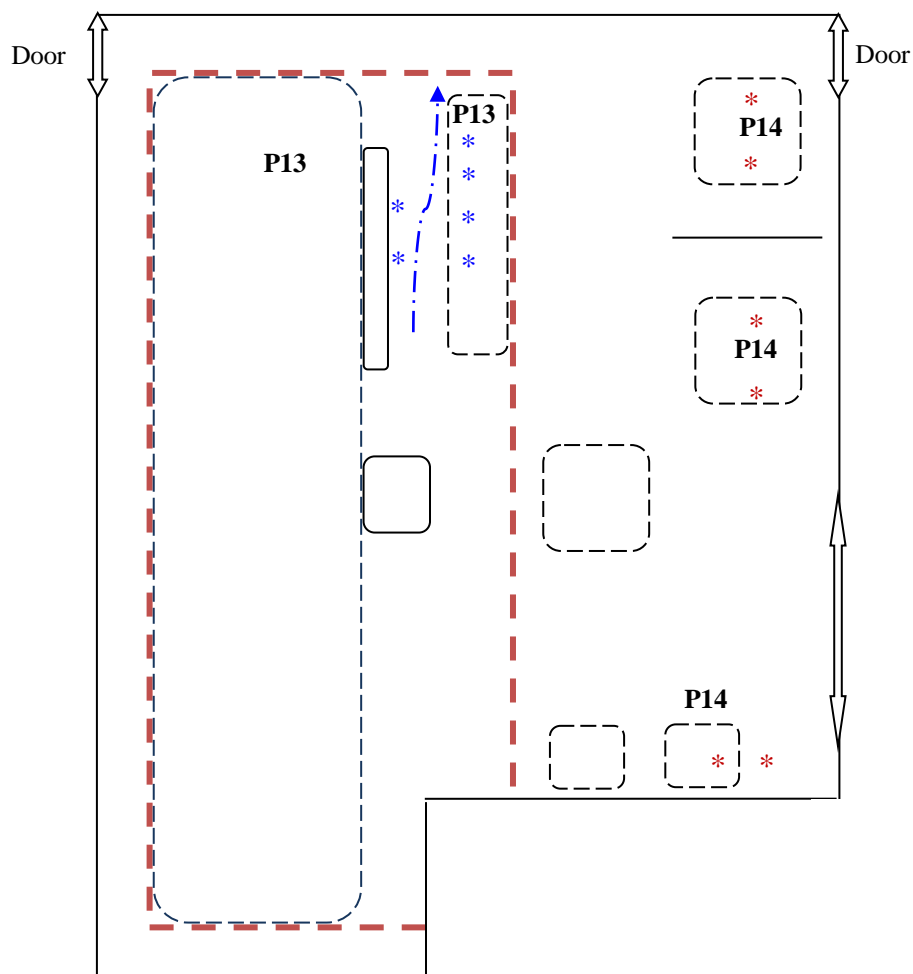
Figure 1.20: Scheme of workplace A7; P13: ABS plating line operator, P14: Quality controller

*: fixed locations of workers, *: Mobile positions,

: Movement area of mobile workers

: NF length and width of P13 modeling

The model parameters are calculated and illustrated in table 1.16.

Table 1.16: NF-FF models input values: constant emission rate of ABS plating

NF-FF Parameters	Situation 1: ABS plating line operator A7: P13
V (m^3)	2782.31
V$_{NF}$ (m^3)	86.88
β (m^3.min^{-1})	194.06
Q (m^3.min^{-1})	583.20
G $_{average}$ (mg. min^{-1})	
• Cr	0.998
• Ni	0.103
• Cu	0.056

In ABS plating lines, the generation rates G$_{A7:\ P13}$ is also calculated using the EF method; based on EFs calculation equations and established EFs from AP-42 [67].

Table 1.17: Trace metallic element baths in ABS plating lines in A7

Plating type	ABS plating lines						
Bath number	**B$_1$**	**B$_2$**	**B$_3$**	**B$_4$**	**B$_5$**	**B$_6$**	**B$_7$**
Metal in the bath [a]	CrH$_2$O$_4$	Cu	Ni	Ni	Ni	Ni	Cr
C$_m$ [a] (g/L)	-	[170-200]*	[40-65]** + [220-280]***	[60- 80]** + [260-300]***	[30- 40]** + [420-470]***	[200-260]**	-
EF$_{average}$	44.61[b]	2.88 10^{-4c}	4.63 10^{-4c}	5.38 10^{-4c}	7.21 10^{-4c}	4.07 10^{-4c}	10.43 10^{-4d}

[a]: Collected using questionnaires
[b]: Converted to **mg/hr-m^2** (developed by US EPAAP 42- emission factors) [67]
[c]: Calculated and expressed in **mg/m^3**
[d]: Converted to **mg/m^3** (developed by US EPA AP 42- emission factors) [67]
*: as CuSO$_4$, **: as NiCl$_2$, ***: as NiSO$_4$

For chromic acid and decorative chromium electroplating baths, EFs for controlled emissions using moisture extractors are not illustrated in AP-42 [67]. In fact, the Cr is considered as the reference element for electroplating in the EF approach. Therefore, we cannot calculate the EFs for Cr neither for decorative electroplating, nor chromic acid anodizing. That is why, as

an approximation, we decided to use the most similar EF values using another control mean. So, based on the EFs for hard chromium electroplating, among all the control means, the EF value of controlled emission with fume suppressant is the closest value (0.00016 grains/dscf) to the EF value with moisture extractor (0.00014 grains/dscf) and having the same order of magnitude.

For EFs for nickel and copper, the EF for decorative chromium electroplating was adapted as a reference value. All adapted emission factors EFs and data used for calculations are in table 1.17.

Then, the predicted concentrations of Cr, Ni and Cu were computed using the IHMOD tool. The model outputs are presented in figures 1.21 for the job task P13.
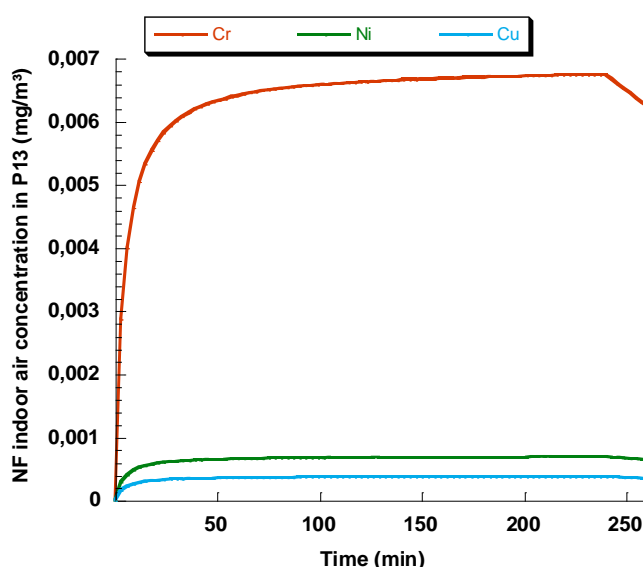
Figure 1.21: Modeled indoor air concentrations of Cr, Ni and Cu in the NF of decorative chromium electroplating of ABS (P13) during four-hour shift

Figure 1.21 shows the NF model predictions of trace metallic element concentrations in the electroplating of ABS. The NF concentration of Cr quickly rises in the first 30 minutes. As for Ni and Cu, after nearly 15 min, concentrations almost reach the C_{SS}.

Similarly to the model predictions in A6, the estimated concentration of Cr is higher than the other metals; this is also due to the fact that EFs of Cr are already established in AP-42 and not determined based on field based information.

The steady state concentrations are cited in table 1.18.

Table 1.18: NF steady state concentrations and the predicted concentrations C$_{NF,SS}$ during ABS plating

NF steady state concentrations ($\mu g/m^3$), C$_{NF,SS}$ (240 min)	Situation: ABS plating lines: P13: A7
• Cr	6.7
• Ni	0.696
• Cu	0.378

III.3.4. Modeling of indirect trace metallic element handling jobs in the same workplaces

III.3.4.1. Product packaging and displacement

The first indirect TME handling job task is product packaging and displacement. This job task is modeled in 3 different workplaces A1, A4 and A5.

Workers are moving around the room or working for a certain time in specific areas. However, it was observed that they are not close to the workers who are working on trace metallic element handling jobs; specifically, not inside or close to the NF where TMEs are emitted. Hence, these workers are considered to be in the FF of the workplaces.

Yet, it has to be noted that the FF of the room cumulates all FF concentrations C$_{FF}$ from all machines inside the workplace. Only steel cutting workplaces (A1 and A7) include multiple emission sources. So, exposure levels of the packaging workers ware calculated as the cumulative sum of all individual FF concentrations:

$$C_{FF, packaging} = C_{FF, steel\ cutting} \times Number_{emission\ source}$$

i. In a first situation, the packaging job task is noted as P3 in the workplace A1. There are 4 workers who are all moving around the workplace. They are sometimes remaining in a specific area in the far left of the workplace A1 (figure 1.1).

ii. In the second situation, the packaging job task is noted as P7 in the workplace A4 (figure 1.2). There are 3 workers.

iii. Lastly, in the third situation, the packaging job task is noted as P8 in the workplace A5 (figure 1.9). There are also3 workers.

The modeled indoor air concentrations of Al, Cu, Ni and Zn in FF for packaging & displacement in A1, A4 and A5 are graphically presented in figures 1.23, 1.24 and 1.25 respectively.
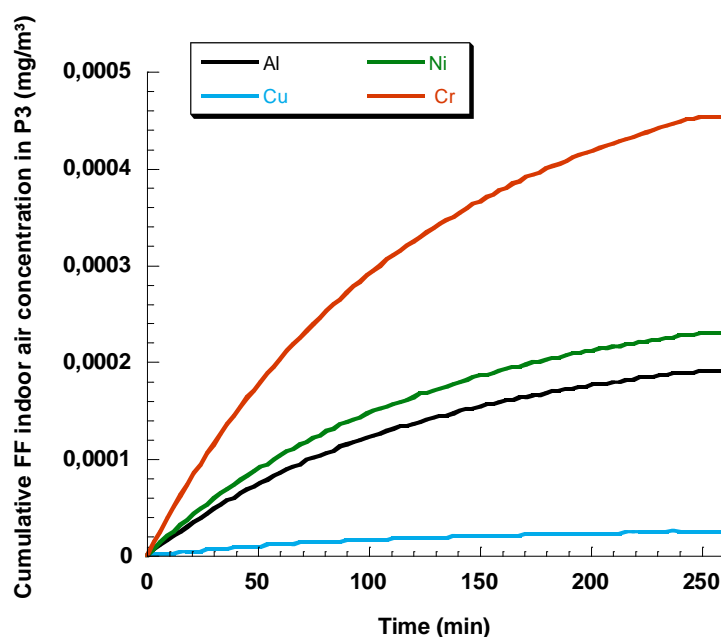
Figure 1.22: Modeled indoor air cumulative concentrations of Al, Cu, Ni and Zn in FF for packaging & displacement (P3) during four-hour shift in the workplace A1
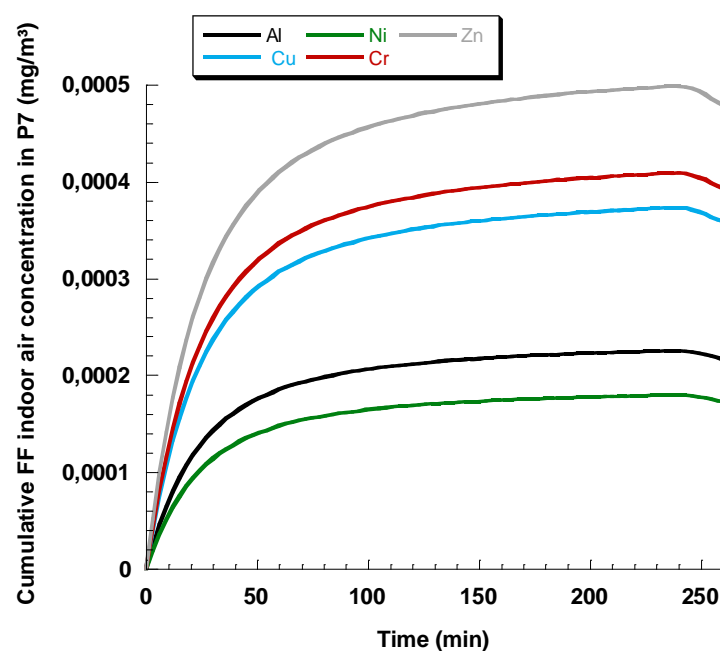
Figure 1.23: Modeled indoor air cumulative concentrations of Al, Cu, Ni, Cr and Zn in FF for packaging & displacement (P7) during four-hour shift in the workplace A4
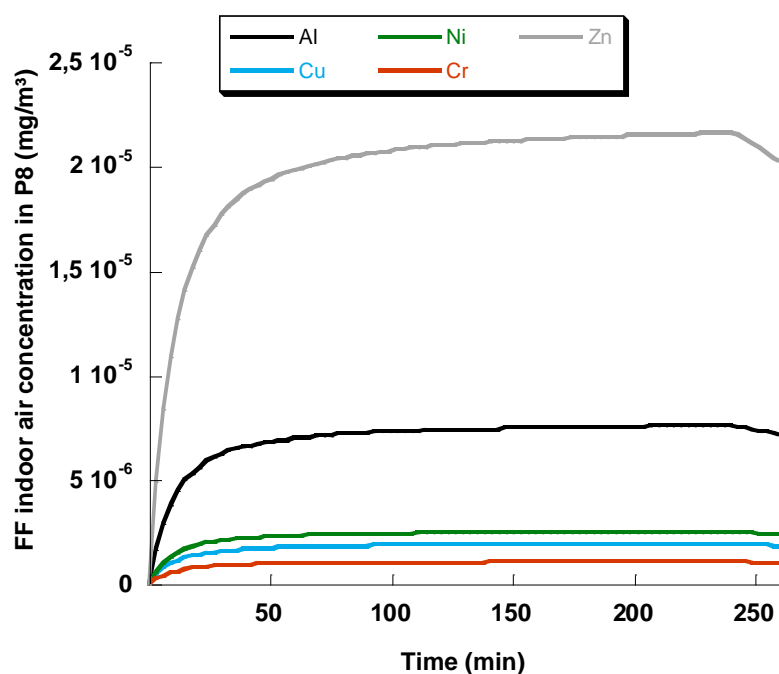
Figure 1.24: Modeled indoor air concentrations of Al, Cu, Ni, Cr and Zn in FF for reception & packaging (P8) during four-hour shift in the workplace A5

The steady state concentrations are cited in table 1.19.

Table 1.19: Cumulative FF steady state concentrations C$_{FF,SS}$ for P7 and P8, and cumulative FF concentrations at t = 240min C$_{FF(240)}$ for P3 during packaging & displacement

Cumulative FF concentrations (µg/m^3), (240min)	Situation 1: packaging & displacement A1: P3 (C$_{FF(240)}$)	Situation 2: packaging & displacement A4: P7 (C$_{FF,SS}$)	Situation 3: packaging & displacement A5: P8 (C$_{FF,SS}$)
• Al	0.189	0.225	0.0076
• Cu	0.025	0.373	0.0019
• Ni	0.225	0.179	0.0025
• Cr	0.446	0.409	0.0011
• Zn	-	0.498	0.0216

III.3.4.2.   Quality control

The second indirect TME handling job task is quality controlling noted as P14. There are 8 workers who are controlling the quality of the decorative chromium electroplating of ABS objects. As indicated in figure 1.20 of the workplace A7, P14 workers are relatively further away than P13, so they are considered to be in the FF of the room.

Figure 1.25 presents the predicted concentrations of Cr, Ni and Cu that are computed using the IHMOD tool.
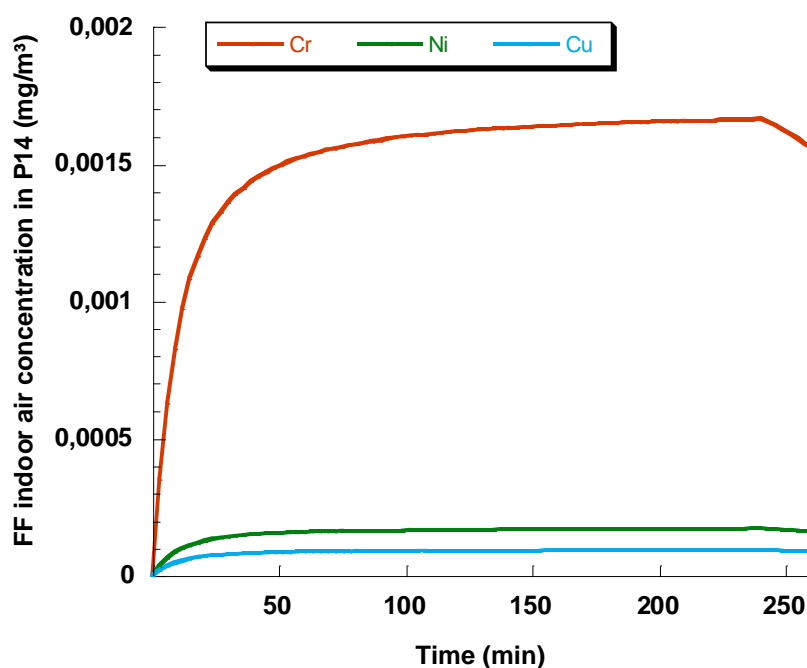
Figure 1.25: Modeled indoor air concentrations of Cr, Ni and Cu in FF for quality control (P14) during four-hour shift

Then, the time weighted average steady state concentrations in the FF ($C_{FF,\ SS}$) during ABS electroplating are illustrated in table 1.20.

Table 1.20: FF steady state concentrations $C_{FF,SS}$ during ABS electroplating

FF steady state concentrations ($\mu g/m^3$), $C_{FF,SS}$ (240-min)	Situation : Quality controller A7: P14
• Cr	1.66
• Ni	0.172
• Cu	0.093

III.3.4.3.   Plastic injection

The last job task is plastic injection operator noted P15. While in this job task, workers are not directly handling metallic materials or substances, the color masterbatches used in the process is suspected to contain trace amounts of TMEs [42]. Therefore, we included the plastic injection work job in our study even though TMEs are considered to be present in trace amounts.

Plastic injection operators are controlling the injection molding machines in the workplace named **A8** and mapped in figure 1.26. There are 5 to 6 workers. In P15, each worker is seated in front of a machine window in which the injection molding is taking place. The operator commands the thermoplastic injection while the window is closed, wait for the injection for a few seconds, and then open it to extract the plastic workpiece. He also checks it and adjusts it if there is an extra bit of plastic. In this modeling situation, we are considering the open window surface as the emission source.

The room is majorly ventilated through two main doors and windows just in front of them. Elsewhere, it was observed that there is a low airflow rate nearby each worker since they usually work behind the injection molding machines (figure 1.26). Thus, the near field/ far field model NF/FF with a constant emission rate is used.

Elsewhere, as we can notice in figure 1.26, A8 is separated in two compartments that are connected. Since only the total quantity used into process for both compartments is provided, a volume-weighted average of the ventilation rate is going to be calculated for A8.

The values of the mass conservation ratios for workplace A8 for both compartments are 0.98 and 0.99.

The NF includes a single emission source and the worker's breathing zone. The NF is estimated as a parallelepiped box of air affixed to the machine's window. It is presented in figure 1.23. The breathing zone is at the same level as the window, so the height and the width of the box are slightly greater to the height and the width of the window in order to cover the entire breathing zone. And the length is equal to the distance between the worker and the injection machine (figure 1.27).

The inter-box air flow rate β flows through all sides except for the front surface. Thus, the free surfaces of the parallelepiped box are calculated in the FSA, which is equal to 5.11 m^2. Moreover, the average random air speed S is calculated and it is 0.030m.s^{-1}.

To calculate the $G_{A8:\ P15}$, the mass balance method is used. Using questionnaires, only labels of the used products ware collected; no technical sheets were available to check their compositions. The official websites of the manufacturing companies do not mention the existence of TMEs [68,69]; they affirm that their "*heavy metal free products*" satisfy standard certification requirements [70].
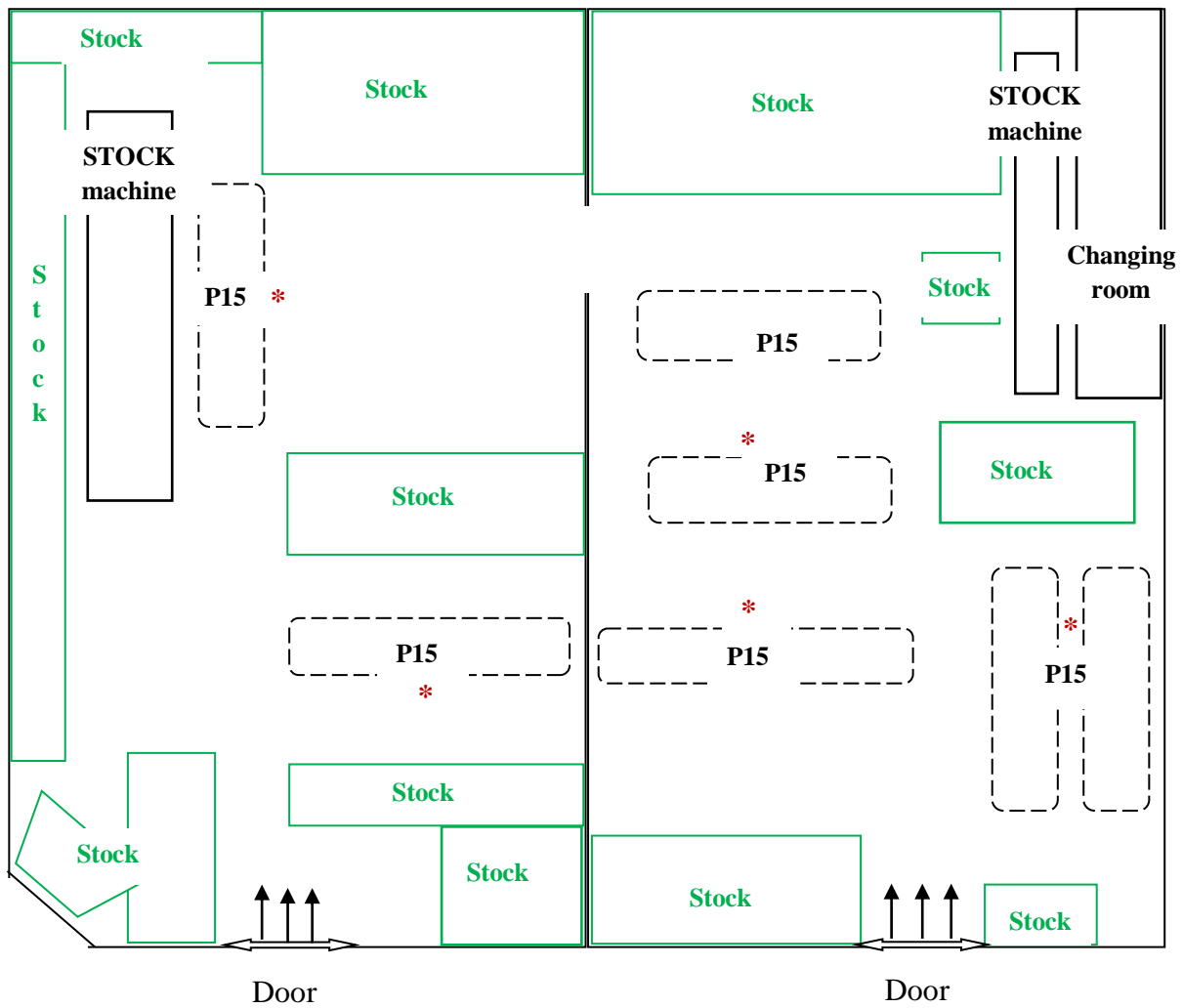
Figure 1.26: Scheme of workplace A8; P15: plastic injection operator

*: fixed locations of workers

Figure 1.27: NF dimensions of P15 (plastic injection): x = 1.15 m, y = 1m, z = 0.85 m

Consequently, we do not have an exact minimum percentage or amount of TMEs in the color masterbatches. Therefore, we are assuming this percentage as "*trace amounts*" which typically vary from 1 to 100 ppm.

In the other hand, the six TMEs are going to be considered because they were all mentioned in literature to be used as plastic pigments [44]. Still, the Pb is strictly controlled or substituted [44]. So, the percentage of Pb is assumed to be the lowest. Whereas, some zinc-additive compounds have been considered as non-toxic (need more reference) [44]. Thus, we assume that Zn is used in larger quantities than the other metals. For the rest of the metals, quantities are considered as equal amounts because of lack of information about the masterbatches color used into process.

Consequently, the percentage for Zn is considered as the highest, so an average generation rate is calculated based on emissions from 1 to 100 ppm. Then, for Cu, Cr, Ni and Al an average generation rate is calculated based on emissions from 10 to 100 ppm. Finally, the lowest generation rate of Pb is calculated based on emissions of 1 ppm.

$G_{A8: P15}$, β_{P15}, Q_{A8} and V_{A8} are calculated as previously described and are presented in table 1.21.

The air change per hour ACH was also calculated for A8 and is equal to 4.59.

Table 1.21: NF-FF model input values: constant emission rate of TMEs during plastic injection

NF-FF Parameters	Situation: Plastic injection operator: A8: P15
V_{A8} (m^3)	1677.99
$V_{NF,P15}$ (m^3)	0.98
β_{P15} (m^3.min^{-1})	4.65
Q_{A8} (m^3.min^{-1})	128.39
$G_{A8:\ P15,average}$ (mg. min^{-1})	
• **Al, Cu, Ni and Cr**	0.00041
• **Zn**	0.00372
• **Pb**	0.000074

Figure 1.28 presents the predicted concentrations of Al, Cu, Ni, Cr, Zn and Pb that are computed using the IHMOD tool.
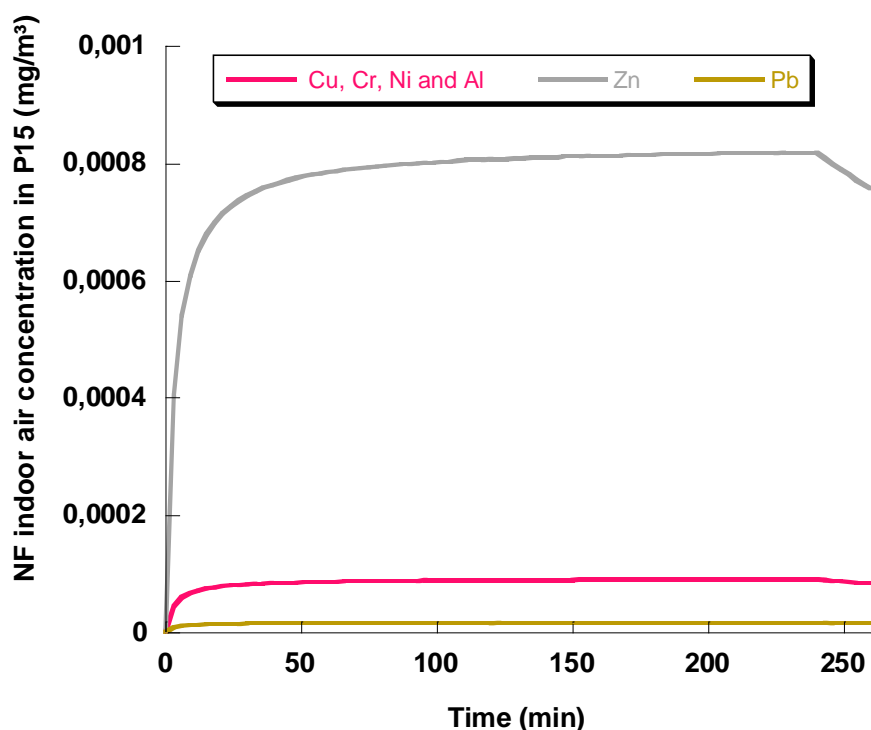
Figure 1.28: Modeled indoor air concentrations of Al, Cu, Ni, Cr, Zn and Pb in the NF of plastic injection molding (P15) during four-hour shift

Figure 1.28 shows NF model prediction of trace metallic element concentrations in plastic injection molding workplace. The NF concentration values quickly rises in the first 20 minutes. Then, after nearly 90 min, concentrations almost reach the steady state concentrations cited for every metal in table 1.22.

Table 1.22: NF steady state concentrations $C_{NF,SS}$ during plastic injection molding

NF steady state concentrations ($\mu g/m^3$), 240-min $C_{NF,SS}$	Situation: Plastic injection operator: A8: P15
• **Al, Cu, Ni and Cr**	0.090
• **Zn**	0.817
• **Pb**	0.016

IV. Discussion

IV.1. Contribution to modeling and comparisons

IV.1.1. WMB modeling: Several & identical emission sources

WMB model was only used in A2 for RSWelding process (P4). As defined, this model type is simpler than the NF-FF model. However, it assumes that air is perfectly mixed in the whole workplace, which is rare to find in real conditions, based on our observations, especially when the volume is quite large. So, we found that WMB model will be adequately used only if there is a mixing device, which is the case of A2 where a quite large mixing fan (1m× 1m) was used.

In order to verify the relevance of our choice, we wanted to compare the WMB results with those, if we had adopted a NF-FF model. So, we calculated the inter-box air flow rate β_{P4} near the NF box that includes one worker and his corresponding emission source. It was equal to 325.5 $m^3.min^{-1}$. Thus, if we compare it with the ventilation rate ($Q_{A2} = 31.81$ $m^3.min^{-1}$), we can clearly see that $\beta_{P4} \gg Q_{A2}$, which means that $C_{NF} \sim C_{FF}$ [35]. Consequently, there is no difference in TME concentrations near or far from the emission source, which backs the relevance of the WMB use.

On the other hand, in RSW task job, the generation rate $G_{averageA2}$ cannot be calculated by mass balance methods because the mass of product introduced into process is the same as the mass incorporated into the products and there is no wasted mass. In fact, it is a very small

amount that cannot be estimated by mass loss. On the other hand, US EPA did not consider this type of welding in AP-42 [66,71]. AP-42 illustrates emissions factors or methods to calculate the EFs only for Electric arc welding process. It considers neither the RSW type nor the induction welding process. The two former processes are different from the Electric arc welding in that they do not use any filler metal during the welding process. However, the choice of the emission factor for Electric arc welding is based on the use of the welding electrode type. Moreover, the EF for RSW suggested by the "**ChemTRAC**" method [72] does not consider the percentage of the metal in the materials, which is variable for each material even for Cr and Ni. So, we were constrained to use results of research studies. Our calculations were based on the study conducted by Pohlmann et al. where they used several types of materials and with many conditions to calculate mass emission ranges for several welding processes, including RSW [63].

In order to calculate the total emission from several RSW machines, we multiplied the personal G for each metal by the number of functioning machines. Then, we used this global generation rate G_{global} in the modeling calculations. In our case, only two machines were functioning in the monitoring week, so, G_{global} was the result of G multiplied by 2.

IV.1.2. NF-FF modeling

NF-FF models were applied for a number of exposure scenarios mainly for volatile organic compounds like we previously mentioned [2,3,73–76], and for organobromine compound [77]. Besides organic compounds, a newer study has also considered respirable dust and silica in some exposure scenarios [78]. Two studies had considered metal emissions [6,78] from electric arc welding and weighing and mixing of a cobalt containing powder. However, the common factor between all of these modeling scenarios is that they used former air sampling data to calculate the model's parameters. Moreover, they used a single emission source of a pollutant in their simulation designs, except for the most recent one [78] where a mean generation rate was calculated based on monitoring from multiple emission sources in silica exposure scenario.

Contrarily to the former studies, we are conducting modeling of TME emissions based only on field related information, literature and simple measurement like air velocity and temperature, in real workplaces' conditions. Hence, in real life situations, emission sources either be only unique or multiple and/or only similar or distinct. In fact, in some metalworking industries like steel cutting, it is common to find several machines in one

workplace setting, especially when these machines require one person or two in the work process. Sometimes, the same kinds of machines are functioning at the same time. Nevertheless, it is possible to find different processes that represent distinct emission sources of TMEs.

Therefore, we are presenting below, different exposure scenarios used in NF-FF models for predicting TME emissions.

IV.1.2.1. Unique emission source

a. Shielded Metal Arc Welding (SMAW)

Boelter et al. applied the NF-FF model to predict indoor air TME concentrations. They only considered Fe, Mn and total fume [6]. They calculated the generation rate G and the inter-box air flow rate β using the monitoring results. As an alternative cost effective and practical method, we calculated G using EFs from USEPA [67] for Ni and Cr and the corresponding fume correction factors FCF established by the SAN DIEGO Air Pollution Control District [65] for Al, Cu and Pb. Then, we will explore their predictive effectiveness.

In response to the study of boelter et al., Nicas has proposed a three zone model [79] because he believes that the total amount of the fume plume of welding is not totally well-mixed inside the NF. He elucidates that a fraction is leaving the NF to a third zone named the upper zone, other than the FF. He proposes three modified equations to calculate the concentrations in the 3 zones. In our study setting A3, there was only one worker who was performing SMAWelding (P5). That is why; we were only considering the NF zone. Nicas added a fraction $f_1 \times$ G that is mixing in the NF. At the steady state, the equation of the NF concentration is as below:

$$C_{NF,SS}(t) = \frac{f_1 \times G}{Q} + \frac{G}{\beta}$$

Obliviously, Boelter et al. have considered f_1=1. After verifications, Nicas found that f_1 was indeed approximately equal to 1 for total fumes [79]. And, since our calculations are based on total the EFs for total fumes, we estimated that we do not need to take into account this fraction in our calculations and assumed it as 1. Moreover, f_1 calculations were based on the monitoring concentrations, which could only be verified after monitoring. So, calculations of the C_{NF} were established using the basic equation.

b. Induction welding

In the workplace A5, there was a single induction welding emission source. This process is taking place with a quite large industrial machine. So, as indicated in Workplaces figure (figure 1.9). The operator noted P9 and the packaging job task noted as P8 are considered to be exclusively exposed to the TME concentrations from induction welding in the NF and FF, respectively. We acknowledge that the existence of another emission source, notably the GMAW at the back of the room, could affect the exposure intensity. However, there were great distances between them and the GMAW location especially for P8.Moreover, we assume that the side door next to GMAW location (figure 1.9) contributes to the non-spread of the TME emissions from the latter process. Still, our assumption's adequacy was explored by comparing the predicted concentrations with the air sampling concentrations.

As for G calculation, the mass balance method was adopted because there are no EFs available for the induction welding. Moreover, unlike the RSW, this process has known waste masses. So, the mass balance method was indeed the most suitable one for this process.

c. ABS plating

In A7, there was also a single emission source from ABS plating lines. There were seven baths but we considered them as a unique emission source. It is worth to mention that, even though there are 4 Ni baths (noted B3, B4, B5 and B6), only one of them is functioning during every shift. So, since we could not have information related to their functioning sequence, we calculated an average G for all Ni baths.

In A7 and also in A6, we are aware that the NF volumes are relatively big. This could minimize the difference of the exposure intensity between the NF and FF, which could be closer to the WMB approach. However, this cannot be adjusted because of the emission source extended surface. Moreover, we are convinced about our choice because β_{P13} (194.06 $m^3.min^{-1}$) is three times lower than Q_{A7} (583.20 $m^3.min^{-1}$).Consequently, this modeling scenario allows us to check the modeling performance of the NF-FF model in such circumstances.

IV.1.2.2. Several & similar emission sources

a. Steel cutting

In the steel cutting job task, we had two different workplaces. In A1, we have 23 personal stamping machines (P1) whereas, in A4, there are 3 sheering and slitting machine (P6). Each

worker was assumed to be exposed to its NF concentrations regardless to the other emission sources.

Packaging workers (P3 and P7in A1 and A6, respectively) are either moving in the FF of the workplace or mostly working in confined space where TME concentrations are assumed to be accumulating. Exposure of the packaging workers was calculated as the cumulative sum of all individual FF concentrations because of the poor ventilation of A1 and P7; their ACH is 0.85 and 4.77 (discussed later).

We combined the predicted concentrations in the NF and FF on the same figure. In figure 1.29 corresponding to A1, we can clearly notice that the C_{FF} concentrations increases slowly compared to the C_{NF}. But they surpass the C_{NF} after 120 min and do not reach a steady state but continue their increase until the end of the emission. This violates the definition of the NF-FF model. Therefore, we will wait for air monitoring to compare them with our approach results.
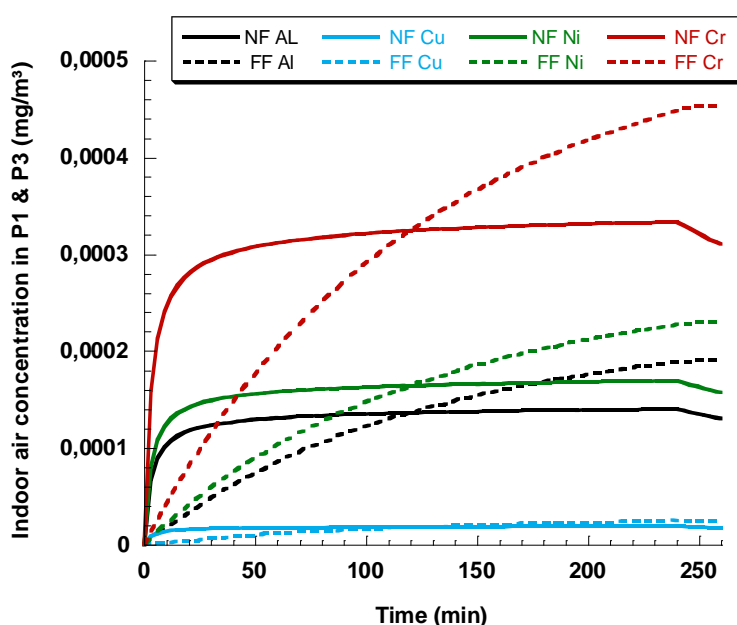
Figure 1.29: Modeled indoor air concentrations of Al, Cu, Ni and Cr in the NF of (stamping P1)
and the FF (packaging P3) during four-hour shift
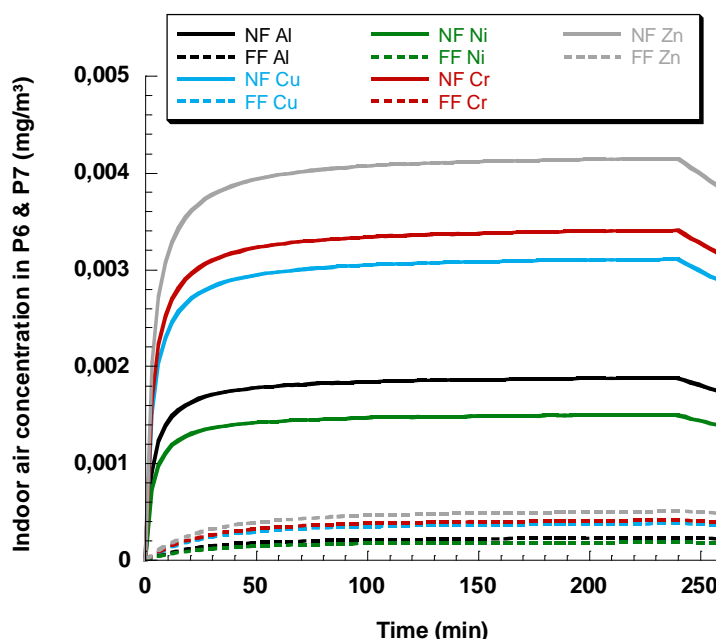
Figure 1.30: Modeled indoor air concentration (240-min) of Al, Cu, Ni, Cr and Zn in NF (for sheering and slitting P6) and FF (for packaging P7) during four-hour shift

As for figure 1.30, related to A7, the C_{NF} increases very slowly but they reach a steady state after about 60 min and the C_{FF} is always largely less than C_{NF}. Lastly, we can notice that the speed of increase of the C_{FF} accumulation is commensurate with the emission sources.

b. Plastic injection

In A8, there were 5 to 6 plastic injection machines (P15). We only considered the NF because of the workers' locations.

As we previously mentioned, this plastic injection industry does not pertain to the metalworking field, however, it is suspected to elicit TME emissions. All the materials' identification was based on literature [33,44]. And the G determinations were based on estimations [44]. Thus, air monitoring is necessary to confirm the presence of TMEs emissions and also check the order of magnitude of TME concentrations with the predicted results.

IV.1.2.3.   Two distinct emission sources

a. Job task noted P16

In A5, we encounter a quite complicated job post (P16) that includes two different tasks.

The exposure scenario of P16 was divided into NF emission from cyclic task P16 $_{GMAW}$ and FF emissions from the induction welding machine (P9). Each emission amount was calculated separately, and then summed.

> b. Metal electroplating

In A6, there were two different electroplating lines. Zinc-plating lines operator noted P10 who were assumed to be exposed to the FF zinc plating and FF from nickel plating P11. As we can see in figure 1.17, workers are next to the NF. However, we cannot consider them in it because of the low air velocity nearby. The same holds true about nickel-plating lines lifting-hooks operators (P12), assumed to be exposed to the FF from nickel plating. The FF zinc plating emissions were denied because zinc plating lines are equipped with local exhaust ventilation systems over the baths. We acknowledge that P12 is also close to nickel-plating lines but we cannot consider it is a same job task as P11 because the latter is moving between the lines and is working in the vicinity of plating baths. Still, we are eager to know if our modeling approach is comparable with the air monitoring results.

Another potential concern is the use of ready to use EFs of Cr. It was observed that these EFs have higher of magnitude compared to the calculated EFs.

IV.1.3.   Adaptation of the mass balance equation

The original mass balance equation [80] does not consider the quantity of deposited metallic dust, which could yield overestimation of exposure, especially when considerable quantities of deposited dust are observed (particularly in steel cutting job tasks).

Aerosol deposition was considered by Schneider et al. [81] in a NF-FF model. He described dust deposition as an equivalent air exchange rate that leads to mass loss of particulate matter from air to the floor or other surfaces. This notion was also discussed by Reinke et al. in *Mathematical Models for Estimating Occupational Exposure to Chemicals* [82] and was named a "sink" or non-ventilatory loss of mass. They considered it as a proportional factor to the estimated pollutant concentration. However, they highlighted that it is usually disregarded because it is extremely difficult to estimate.

Thus, in order to remedy overestimation and to quantify the mass loss of dust, we consider this mass loss as a fixed amount when computing the generation rate G. Thus, we collected the dust in the two companies where the mass balance method is adopted (workplace 1 and 5),

at the end of the week shift, and weighed it for integration in the mass balance equation. As an approximation, we neglected the contribution of outdoor airborne particle sources (due to the small air exchanges in the workplaces) and we assumed that the collected dust contains only metallic dust; this yields overestimation of this dust-associated metallic sink.

We acknowledge the limitations of this approach, although we are suggesting a simpler and more accurate approach to assess the impact of deposited dust when estimating workplace air concentrations of metals.

IV.1.4. Ventilation rate method

In our study, we predominantly used the anemometer technique which is considered one of the main methods to determine Q [34]. It was chosen because we have previously assumed that the open doors and windows are the only or major source of ventilation; air comes in and out of these two openings, generally located at opposite ends of the rooms [34]. So, after verification of the mass conservation, we can calculate the Q_{in} that is equal to Q_{out}. In addition, this technique is cost effective compared to other methods.

There is another effective method to calculate Q which is the tracer gas technique. This technique requires expensive technical instruments. Boelter et al. used both techniques to calculate the ventilation rate in a workplace in order to use it in a NF-FF model [6]. Comparing the two values, they found that the anemometer technique moderately overestimated Q. In order to correct this and to consider the variability during and between the days, we adopted the measurement approach previously exposed over 3 days a week and then we calculated average values.

In addition, we also used another method to calculate Q based on local exhaust ventilation systems. It is considered a more accurate method because we have a precise value of the exhaust rate. Keil confirms that if the exhaust rate of local exhaust ventilation is available, we are able to calculate a ventilation value Q with a sufficient confidence [34]. Sometimes, the anemometer method is quite difficult to establish. For example, the workplace A2 (where RSW was taking place) is located at the top floor and is already inside another room and is ventilated through wide surfaces. Also, in the workplaces A6 and A7 (where electroplating of metal and ABS was respectively taking place), the natural ventilation was supplied by 3 doors from different directions and many other little openings. So, calculations based on the anemometer method is more sophisticated and with a higher margin of error. Thus, since we

have an alternative method using the local exhaust ventilation rates; we chose to calculate Qs with it, as long as the mass conservation is confirmed.

In our study, air changes per hour ACH were calculated for the workplaces. They ranged from 0.85 in A1 (steel cutting workplace) to 15.21 in A6 (metal electroplating). If we compare our values with those found by Bolter et al. (20.4) [6]; in all our workplaces, ACH were smaller than it. In fact, the common general ventilation is typically between 1.2 - 12 ACH [83]. Still, ventilation rate can even reach 0.3 ACH for a closed window dwelling [34].

For instance, ACH is under 5 in A1, A6 and A8; their values are 0.85, 4.77 and 4.59, respectively. These values are relatively small particularly for A1. The latter is poorly ventilated; its ACH is even smaller than the common general ventilation, which is probably due to the large volume of the workplace (38747.89 m^3).

When it comes to the other workplaces, in 3 posts (P5, P6 and P7) in 3 different workplaces, the ACH exceed the maximum value for the common general ventilation (13.93, 15.21 and 12.58, respectively).

IV.2. Difficulties and challenges

IV.2.1. Companies contact and participation

The first difficulty was in seeking the approval of the companies to participate. Occupational exposure assessment is not mandatory in Tunisia. So, the majority of the companies' managers do not feel concerned.

Some companies denied participation categorically at the first contact and refused to have an appointment. They just expressed that they were not interested.

Others had expressed their concern about the monitoring results and were anxious either about publications of the results or potential problems with the corresponding authority structure, even though, we had confirmed that all identities and names are were to be confidential.

For the rest, they were worried about the reactions of their employees towards the study. They claimed that workers would probably think their job tasks are extremely harmful.

Furthermore, few companies have given us their principle agreement; we had several appointments and did some field visits to the workplaces. However, after up to 6 months, they finally pulled out from the study.

IV.2.2. Information availability

The second challenge was the information collection using the questionnaires in order to establish the models' parameters. All companies did not have complete information about the names and the mass amounts of the used materials. So, we took several appointments to have all the required information.

Some of them did not have the exact references and sometimes products had only local references. So we had to do supplementary research to gather all the exact references in order to look for their metal compositions. Moreover, data and safety sheets were not provided by the companies, we explored all chemical compositions like previously mentioned.

In one case, it took up to 24 months to obtain the required information.

IV.3. Limitations and bias

IV.3.1. Uncertainty analyses

Modeling can involve uncertainty in exposure estimation. Input data are frequently not precise. Uncertainty can be due to natural variability or lack of knowledge [84].

Natural variability is commonly referred to as "type 1" in risk assessment [84]. For example, it is due to variability in hourly /daily air velocity in calculations of ventilation rates. As for lack of knowledge, it is commonly called as "type 2" [84]. It represents the uncertainty in measurement devices and shortage of information.

Therefore, in order to quantify the uncertainty in parameters estimate, a Monte Carlo simulation was conducted [85,86]. This approach was used in some studies to estimate volatile organic compounds concentrations [2–4]. Moreover, this approach will offer a confidence interval range of the output and a distribution, not only one value.

Therefore, as a perspective, an uncertainty analysis will be conducted using the Monte Carlo simulation in order to publish our findings.

IV.3.2. Margin of error due to global information

We noticed that the collected information about the materials' types could present a margin of error. The available information could sometimes bear on annual consumption. So, the proportion of a specific material usage in the monitoring week may be different than the proportion during the whole year. Consequently, the amount of a particular metal can vary.

Thus, we believe that more precise information within a specific period of time could lead to more exact predicted concentrations with a better range of confidence.

IV.3.3. Emission factors' ratings

In electric arc electroplating, the used emission factors EFs are rated as "*excellent*", "*above average*" and "*average*" factors, for E70S-6, E6013 and E7018, respectively. AP-42, emission factors are tested and divided into 5 ratings according to the quality of the studies and methodologies and according to the representativeness of the EFs for a number of facilities [87].

The EFs that were used for metal electroplating were rated as "*above average*", which means that these factors were established from a "reasonably number" of research occupational studies about electroplating facilities [87]. This rating is based on shortage of information about random collection of these facilities. But we found no particular preference.

As for EFs used for ABS modeling, both factors are rated as "*below average*". According to AP-42, this rating means that they were established from a limited number of research occupational studies. So, these facilities are probably not randomly collected, and then they could encompass variability in calculations.

IV.3.4. Average Generation rate calculation

The generation rate G was always considered as an average value calculated from maximum and minimum values. These ranges are due to two main factors. According to the collected information from the companies' managers, the mass amounts were usually provided as intervals. In addition, steel chemical compositions are not presented as point values in data sheets but often as requirements of specific metals in an interval range. And sometimes, these ranges are slightly different in research studies that have actually analyzed the material. So, we decided to work with the mean value of the generation rate, noted as $G_{average}$. We acknowledge that this will increase the confidence range, but this is one of our challenges because companies' managers could not provide us with more accurate information and steel chemical compositions are variable. In a perspective, and in order to remedy that, this interval will be considered to estimate the uncertainty of our modeling approach using the Monte Carlo approach.

IV.3.5.   Exhaustive Trace metallic elements identification

We identified a potential deficiency in occupational exposure modeling. Unlike indoor air monitoring that is using analytical chemical instruments to identify TME presence; occasionally models cannot predict the presence of all trace metallic elements despite of their existence, notably for ultra small amounts. And this is in effect of the non-exhaustive available information in data sheets. This could be considered as a shortcoming but it was not frequently encountered.

V.   Conclusion of part 1

In this first part, our main objective was to use, in lieu of systematic measurements, an alternative and reliable method to predict indoor air TME concentrations without costly measurements and using available field–related information and literature. We used mathematical models for estimating occupational exposure to TMEs in several metalworking industries. Moreover, we strive to assess the models' effectiveness not in simulation designs but in real-life exposure scenarios where there are many workers, notably with more than one job task and one emission source at the same workplace. Yet, we faced some challenges and difficulties and we observed some limitations and will discuss future perspectives. Finally, we believe that workplace air monitoring is a crucial and determinant step to validate the predicted concentrations and to check the effectiveness of our modeling approaches.

VI.   Bibliography

1. Jayjock MA, Chaisson CF, Arnold S, Dederick EJ. Modeling framework for human exposure assessment. J Expo Sci Environ Epidemiol. 2007;17:S81–9.

2. Nicas M, Neuhaus J. Predicting Benzene Vapor Concentrations with a Near Field/Far Field Model. J Occup Environ Hyg. 2008;5:599–608.

3. Nicas M, Plisko MJ, Spencer JW. Estimating Benzene Exposure at a Solvent Parts Washer. J Occup Environ Hyg. 2006;3:284–91.

4. Spencer JW, Plisko MJ. A Comparison Study Using a Mathematical Model and Actual Exposure Monitoring for Estimating Solvent Exposures During the Disassembly of Metal Parts. J Occup Environ Hyg. 2007;4:253–9.

5. AIHA, Charles B. Keil, Cathrine E. Simmons, T. Renée Anthony. Mathematical Models for Estimating Occupational Exposure to Chemicals. 2nd edition. AIHA press; 2009.

6. Boelter FW, Simmons CE, Berman L, Scheff P. Two-Zone Model Application to Breathing Zone and Area Welding Fume Concentration Data. J Occup Environ Hyg. 2009;6:298–306.

7. Feki-Tounsi M, Olmedo P, Gil F, Khlifi R, Mhiri M-N, Rebai A, et al. Cadmium in blood of Tunisian men and risk of bladder cancer: interactions with arsenic exposure and smoking. Environ Sci Pollut Res. 2013;20:7204–13.

8. Smaoui-Damak W, Rebai T, Berthet B, Hamza-Chaffai A. Does cadmium pollution affect reproduction in the clam Ruditapes decussatus? A one-year case study. Comp Biochem Physiol Part C Toxicol Pharmacol. 2006;143:252–61.

9. Smaoui-Damak W, Berthet B, Hamza-Chaffai A. In situ potential use of metallothionein as a biomarker of cadmium contamination in Ruditapes decussatus. Ecotoxicol Environ Saf. 2009;72:1489–98.

10. Ketata I, Smaoui-Damak W, Guermazi F, Rebai T, Hamza-Chaffai A. In situ endocrine disrupting effects of cadmium on the reproduction of Ruditapes decussatus. Comp Biochem Physiol Part C Toxicol Pharmacol. 2007;146:415–30.

11. Smaoui-Damak W, Berthet B, Rebai T, Hamza-Chaffai A. Effets de la pollution par les metaux sur le potentiel reproducteur de la palourde Ruditapes decussatus (L.) issue du Golfe de Gabes (Tunisie). Bull Société Zool Fr. 2008;133:131–139.

12. Kessabi K, Kerkeni A, Saïd K, Messaoudi I. Involvement of Cd Bioaccumulation in Spinal Deformities Occurrence in Natural Populations of Mediterranean Killifish. Biol Trace Elem Res. 2008;128:72–81.

13. Kessabi K, Annabi A, Hassine AIH, Bazin I, Mnif W, Said K, et al. Possible chemical causes of skeletal deformities in natural populations of Aphanius fasciatus collected from the Tunisian coast. Chemosphere. 2013;90:2683–9.

14. Hamza-Chaffai A, Cosson RP, Amiard-Triquet C, El Abed A. Physico-chemical forms of storage of metals (Cd, Cu and Zn) and metallothionein-like proteins in gills and liver of

marine fish from the Tunisian coast: ecotoxicological consequences. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol. 1995;111:329–41.

15. Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Hammami B, Rebai A, et al. Risk of laryngeal and nasopharyngeal cancer associated with arsenic and cadmium in the Tunisian population. Environ Sci Pollut Res. 2013;21:2032–42.

16. Khlifi R, Hamza-Chaffai A. Head and neck cancer due to heavy metal exposure via tobacco smoking and professional exposure: A review. Toxicol Appl Pharmacol. 2010;248:71–88.

17. Hentati O, Chaker S, Wali A, Ayoub T, Ksibi M. Effects of long-term irrigation with treated wastewater on soil quality, soil-borne pathogens, and living organisms: case study of the vicinity of El Hajeb (Tunisia). Environ Monit Assess [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s10661-013-3570-z

18. Ben Fredj F, Wali A, Khadhraoui M, Han J, Funamizu N, Ksibi M, et al. Risk assessment of heavy metal toxicity of soil irrigated with treated wastewater using heat shock proteins stress responses: case of El Hajeb, Sfax, Tunisia. Environ Sci Pollut Res [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s11356-013-2411-5

19. Gargouri D, Azri C, Serbaji MM, Jedoui Y, Montacer M. Heavy metal concentrations in the surface marine sediments of Sfax Coast, Tunisia. Environ Monit Assess. 2010;175:519–30.

20. Annabi A, Said K, Messaoudi I. Heavy metal levels in gonad and liver tissues—effects on the reproductive parameters of natural populations of Aphanius facsiatus. Environ Sci Pollut Res. 2013;20:7309–19.

21. Serbaji MM, Azri C, Medhioub K. Anthropogenic Contributions to Heavy Metal Distributions in the Surface and Sub-surface Sediments of the Northern Coast of Sfax, Tunisia. Int J Environ Res. 2012;6:613–26.

22. El Ati-Hellal M, Hedhili A, Hellal F, Boujlel K, Dachraoui M, Bousnina M, et al. Lead and cadmium concentrations in seawater and algae of the Tunisian coast. Arch Inst Pasteur Tunis. 2005;82:75–82.

23. Kessabi K, Navarro A, Casado M, Saïd K, Messaoudi I, Piña B. Evaluation of environmental impact on natural populations of the Mediterranean killifish Aphanius fasciatus by quantitative RNA biomarkers. Mar Environ Res. 2010;70:327–33.

24. Hamza-Chaffai A, Roméo M, el Abed A. Heavy metals in different fishes from the middle eastern coast of Tunisia. Bull Environ Contam Toxicol. 1996;56:766–73.

25. Barhoumi S, Messaoudi I, Deli T, Saïd K, Kerkeni A. Cadmium bioaccumulation in three benthic fish species, Salaria basilisca, Zosterisessor ophiocephalus and Solea vulgaris collected from the Gulf of Gabes in Tunisia. J Environ Sci. 2009;21:980–4.

26. Lahbib Y, Mleiki A, Marigomez I, Trigui El Menif N. Copper, zinc, and cadmium body concentrations in Hexaplex trunculus collected from the Tunisian coast. Environ Monit Assess. 2013;185:8967–75.

27. Banni M, Jebali J, Daubeze M, Clerandau C, Guerbej H, Narbonne JF, et al. Monitoring pollution in Tunisian coasts: application of a classification scale based on biochemical markers. Biomarkers. 2005;10:105–16.

28. Saïdi SA, Azaza MS, Windmolders P, van Pelt J, El-Feki A. Cytotoxicity evaluation and antioxidant enzyme expression related to heavy metals found in tuna by-products meal: An in vitro study in human and rat liver cell lines. Exp Toxicol Pathol. 2013;65:1025–33.

29. Khlifi R, Olmedo P, Gil F, Hammami B, Chakroun A, Rebai A, et al. Arsenic, cadmium, chromium and nickel in cancerous and healthy tissues from patients with head and neck cancer. Sci Total Environ. 2013;452–453:58–67.

30. Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Chakroun A, Rebai A, et al. Blood nickel and chromium levels in association with smoking and occupational exposure among head and neck cancer patients in Tunisia. Environ Sci Pollut Res. 2013;20:8282–94.

31. Mezghani-Chaari S, Hamza A, Hamza-Chaffai A. Mercury contamination in human hair and some marine species from Sfax coasts of Tunisia: levels and risk assessment. Environ Monit Assess. 2011;180:477–87.

32. Chambre de commerce et d'industrie de Sfax, Tunisie. Guide des exportateurs de Sfax. Tunisie; 2010.

33. Lauwerys R. Toxicologie industrielle et intoxications professionnelles. 3 éme édition. Paris: Masson; 1990.

34. Charles B. Keil. chapter 2: General principals of physical-chemical models. Math Models Estim Occup Expo Chem. USA; 2009.

35. Mark Nicas. Chapter 6: The Near Field/ Far Field (two box) Model with a constant contaminant emission rate. Math Models Estim Occup Expo Chem. USA: AIHA press; 2009. p. 47–52.

36. Golbabaei F, Khadem M. Chapter 2: Air Pollution in Welding Processes — Assessment and Control Methods. In: Nejadkoorki F, editor. Curr Air Qual Issues [Internet]. InTech; 2015 [cited 2016 May 12]. Available from: http://www.intechopen.com/books/current-air-quality-issues/air-pollution-in-welding-processes-assessment-and-control-methods

37. US EPA Office of Air Quality Planning and Standards, US EPA. Chapter 12: Metallurgical Industry, section 19: Electric Arc Welding. AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1995. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

38. Larry F. Jeffus. Chapter 6: related processes and technology. Weld Princ Appl. USA: Cengage Learning; 2004.

39. Weman K. Chapter 8 - Pressure welding methods. Weld Process Handb [Internet]. Woodhead Publishing; 2003 [cited 2018 Mar 16]. p. 80–92. Available from: https://www.sciencedirect.com/science/article/pii/B9781855736894500114

40. de Santana IJ, Paulo B, Modenesi PJ. High frequency induction welding simulating on ferritic stainless steels. J Mater Process Technol. 2006;179:225–30.

41. US EPA. Emission Factor Documentation for AP-42 Section 12.20 Electroplating Final Report [Internet]. 1996 Jul. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/bgdocs/b12s20.pdf

42. Abrams R, Ali M, Denton P, Igualada J, Groen M, Gschwind E. Colouring plastics: fundamentals and trends. Plast Addit Compd. 2001;3:18–25.

43. Bolgar M, Hubball J, Groeger J, Meronek S. Handbook for the Chemical Analysis of Plastic and Polymer Additives, Second Edition. CRC Press; 2015.

44. Murphy J. Additives for Plastics Handbook. Elsevier; 2001.

45. Akkas N, Varol F, Ferik E, Ilhan E, Ozsarac U, Aslanlar S. Effect of Welding Current on Mechanical Properties of Welding Joints in S235JR(Cu) Steel Sheets in Resistance Spot Welding. Acta Phys Pol A. 2014;125:500–2.

46. Total Materia - La Base de Données sur les Matériels la Plus Complète au Monde [Internet]. [cited 2016 Mar 24]. Available from: http://www.totalmateria.com/page.aspx?ID=Home&LN=FR

47. en_S235JR.pdf [Internet]. [cited 2016 Apr 21]. Available from: http://www.atrspa.eu/allegati/prodotti/en/en_S235JR.pdf

48. s235jren42.pdf [Internet]. [cited 2016 Apr 21]. Available from: http://www.lucefin.com/wp-content/files_mf/s235jren42.pdf

49. S235JR.pdf [Internet]. [cited 2016 Apr 21]. Available from: https://www.metaldata.info/reports/S235JR.pdf

50. S235JR Chemical Composition, S235JR Mechanical Properties, S235JR Heat Treatment [Internet]. Longhai Spec. Steel. [cited 2016 May 1]. Available from: http://www.steelgr.com

51. S235JR Steel Grade, Mechanical Properties, Chemical Composition, Grade Equivalent [Internet]. [cited 2016 May 1]. Available from: http://www.b2bmetal.eu/en/pages/index/index/id/141/

52. DigitalCavalry. Firstinox : acier inoxydableFirstinox, acier inoxydable, aluminium damier. Inox : 304, 304L,316L, 4307 [Internet]. [cited 2016 Jun 20]. Available from: http://www.firstinox.fr/inox-composition-chimique-acier-inoxydable/

53. INOX 304-316-FT-FINAL.pdf [Internet]. [cited 2016 Jun 12]. Available from: http://docs.indigo-group.be/catalogs/cat01/INOX%20304-316-FT-FINAL.pdf

54. Mucha J, Witkowski W. The clinching joints strength analysis in the aspects of changes in the forming technology and load conditions. Thin-Walled Struct. 2014;82:55–66.

55. Kaščák Ľ, Viňáš J, Spišák E. Deltaspot as an innovative method of resistance spot welding. Sci Lett Rzesz Univ Technol - Mech. 2012;84:43–53.

56. OK With ESAB [Internet]. [cited 2016 May 18]. Available from: http://www.esab.fr/france-benelux/fr/okwithesab/

57. AWS E6013 Welding Electrode [Internet]. [cited 2016 Oct 12]. Available from: http://www.tenweld.com/aws-e6013-welding-electrode.html

58. Ebrahimnia M, Goodarzi M, Nouri M, Sheikhi M. Study of the effect of shielding gas composition on the mechanical weld properties of steel ST 37-2 in gas metal arc welding. Mater Des. 2009;30:3891–5.

59. Ramirez JE. Characterization of high-strength steel weld metals: chemical composition, microstructure, and nonmetallic inclusions. Weld J-N Y-. 2008;87:65.

60. ER70S-6 [Internet]. WeldWire. [cited 2017 Nov 21]. Available from: http://www.weldwire.net/weld_products/ww70s-6/

61. MSMildSteel.pdf [Internet]. [cited 2017 Nov 22]. Available from: https://www.mathesongas.com/industrialgas/pdfs/MSMildSteel.pdf

62. INRS. Principe général et mise en œuvre pratique du prélèvement [Internet]. 2015 [cited 2016 Sep 16]. Available from: http://www.inrs.fr/dms/inrs/PDF/metropol-prelevement-principe.pdf

63. Gerhard Pohlmann, Charly Holzinger, Vilia Elena Spiegel-Ciobanu. Comparative investigations in order to characterise ultrafine particles in fumes in the case of welding and allied processes. Weldingand Cut [Internet]. 2013;12. Available from: https://www.bghm.de/fileadmin/user_upload/Arbeitsschuetzer/Fachinformationen/Schweissen/00_WC2_SpA_w20000014__.pdf

64. Antonini JM. Health Effects of Welding. Crit Rev Toxicol. 2003;33:61–103.

65. SAN DIEGO Air Pollution Control District, editor. WELDING OPERATIONS [Internet]. 1998 [cited 2018 Jan 9]. Available from: http://www.sdapcd.org/content/dam/sdc/apcd/PDF/Toxics_Program/APCD_welding1.pdf

66. US EPA. AP-42: Compilation of Air Emissions Factors [Internet]. US EPA. 2016 [cited 2018 Mar 26]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emissions-factors

67. US EPA Office of Air Quality Planning and Standards. Chapter 12: Metallurgical Industry, section 20: Electroplating. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1996. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

68. EnerPlastics. EnerPlastics – Masters in the art of colouring [Internet]. [cited 2018 Feb 16]. Available from: http://www.enerplastics.com/

69. Product List: | ICC Chemical Corporation [Internet]. [cited 2018 Feb 16]. Available from: https://www.iccchem.com/products

70. Euromaster Spa. Euromaster Spa Masterbatches and compounds [Internet]. Euromaster Spa. [cited 2018 Feb 16]. Available from: https://www.euromasterspa.com/en/

71. US EPA O. AP-42: Compilation of Air Emission Factors [Internet]. 1995 [cited 2018 Jan 12]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

72. ChemTRAC - Environmental Health - Toronto Public Health | [Internet]. [cited 2016 May 11]. Available from: http://www1.toronto.ca/wps/portal/contentonly?vgnextoid=8e00ebfc2bb31410VgnVCM10000 0071d60f89RCRD

73. Arnold SF, Shao Y, Ramachandran G. Evaluating well-mixed room and near-field–far-field model performance under highly controlled conditions. J Occup Environ Hyg. 2017;14:427–37.

74. Jayjock MA, Armstrong T, Taylor M. The Daubert Standard as Applied to Exposure Assessment Modeling Using the Two-Zone (NF/FF) Model Estimation of Indoor Air Breathing Zone Concentration as an Example. J Occup Environ Hyg. 2011;8:D114–22.

75. Keil CB, Nicas M. Predicting Room Vapor Concentrations Due to Spills of Organic Solvents. AIHA J. 2003;64:445–54.

76. Robbins CA, Krause MW, Atallah RH, Plisko MJ. Comparison of exposure measurements to near field–far field modeled results for benzene and base solvents during a cleaning process using plain or 0.1% benzene spiked toluene and xylene. J Chem Health Saf. 2012;19:3–11.

77. Nicas M. Estimating Methyl Bromide Exposure Due to Offgassing from Fumigated Commodities. Appl Occup Environ Hyg. 2003;18:200–10.

78. Arnold SF, Shao Y, Ramachandran G. Evaluation of the well mixed room and near-field far-field models in occupational settings. J Occup Environ Hyg. 2017;14:694–702.

79. Nicas M, Boelter FW, Simmons CE, Scheff P, Berman L. Letter to the Editor. J Occup Environ Hyg. 2009;6:D69–71.

80. Charles B. Keil. Chapter 3: Modeling Pollutant Generation Rates. Math Models Estim Occup Expo Chem. USA; 2009.

81. Schneider T, Kildes J, Breum NO. A two compartment model for determining the contribution of sources, surface deposition and resuspension to air and surface dust concentration levels in occupied rooms. Build Environ. 1999;34:583–95.

82. Patricia H. Reinke, Charles B. Keil. Chapter 4: Well-Mixed Box Model. Math Models Estim Occup Expo Chem. USA; 2009.

83. Laboratory Ventilation ACH Rates Standards and Guidelines [Internet]. 2012 Jan. Available from: http://www.aircuity.com/wp-content/uploads/Aircuity-White-Paper_Lab-Ventilation-ACH-Rates_Standards-Guidelines_ACHWP_20120103-2.pdf

84. Michael Jayjock, Gumurthy Ramachandran, Susan F. Arnold. Chapter 10: Uncertainty. Math Models Estim Occup Expo Chem. USA; 2009.

85. Jayjock MA. Uncertainty Analysis in the Estimation of Exposure. Am Ind Hyg Assoc J. 1997;58:380–2.

86. Nicas M, Jayjock M. Uncertainty in Exposure Estimates Made by Modeling Versus Monitoring. AIHA J. 2002;63:275–83.

87. US EPA Office of Air Quality Planning and Standards. Intoduction. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

2nd PART:

Validation of Mathematical Models for Estimating Occupational Exposure to Trace Metallic Elements in Metalworking Industries (Indoor Air Monitoring)

& Biomonitoring

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Validation of Mathematical Models for Estimating Occupational Exposure to Trace Metallic Elements in Metalworking Industries (Indoor Air Monitoring)

& Biomonitoring

I. Introduction

As stated in part 1, these mathematical models were initially developed and applied to solvents and other volatile compounds and. several studies demonstrated that their predicted concentrations are "reasonably" comparable to air monitoring measurements within a factor of 0.5 to 2 folds [1].

With regards to metals, only two studies have used this kind of models for metal contaminants. The first one was dealing with arc welding process, where the author considered only iron and manganese [2]. The second one was dealing with two job tasks involving weighing and mixing of a cobalt containing powder [3]. In contrast to both studies, our modeling approach does not use air monitoring measurements to calculate any models' parameters. Therefore, in our study, a validation step is necessary to evaluate our models estimations.

For purposes of comparison between the modeled indoor air concentrations and the measured ones, we are using statistical tools that are bringing to light the relationships and discrepancies between them.

On the other hand, a biomonitoring study is conducted to explore the relationships between the internal and external doses. With the aim of investigating the contribution of the occupational pathway to the internal urinary metallic concentrations, we included administration workers in the biomonitoring survey from the same companies.

II. Materials and methods

II.1. Air monitoring

II.1.1. Equipment and material acquisition

In order to conduct the indoor air measurements, a complete material package for active monitoring was looked for. We used the database "*MétroPol*" illustrated by INRS [4] to choose the suitable sampling means (Quartz Filters). In addition, we used the official site of the equipment supplier [5] to properly choose the adequate pumps and the complementary equipment and accessories.

The package contains: (see figure 2.1)

- 2 personal sampling Pump SKC®: PCMTX4KV ATEX(figure 2.1, b, 5)

- 2 lots of 50 Filter Cassettes, Blank, 37 mm, Clear Styrene, SKC®, include 3 sections of clear styrene filter cassette, with a diameter of 37 mm (Cassette SKC® SKC2253050LF) [6,7] (figure 2.1, a, 1)

- 2 lots of 100 Quartz Filters, 37 mm, Type R-100 (100% quartz) SKC®, with porosity of 1.2 μm SCS225 1827 [8] (figure 2.1, a, 2)

- 2 Filter Cassette Holders(figure 2.1, b, 6)

- Sure Seal cassette opener(figure 2.1, a, 3)

- Calibrator: type M5(figure 2.1, c)

Figure 2.1: Equipment and materials for TME indoor air monitoring; a: Cassettes and quartz filters, b: sampling pump, c: calibrator

II.1.2. Air monitoring methodology

Indoor air TMEs concentrations were measured using (i) personal samplers set up near the worker's breathing zone, or (ii) fixed samplers placed in the workplace at average height corresponding to the breathing zone of the worker.

For statistical considerations and in order to minimize the natural variability of concentration measures, we conducted six replicate measurements, as recommended in *Mathematical models for estimating occupational exposure to chemicals* [1].

Air monitoring was conducted over 10 weeks. For each job task, the six replicates were carried out through 3 days in the middle of the week; Tuesday, Wednesday and Thursday, in order to get an idea of the exposure variability between days.

The air flow rate of the personal sampling pump Pump SKC® was regulated to 2L/min using the method provided by INRS [9–11]. Air monitoring covered a four-hour shift [7,12].

Afterward, statistical analyses of the air monitoring data was carried out to evaluate distribution normality (or log-normality) of the six replicate measurements. Hence, if the distribution of the six replicates is normal, the mean value is adopted, otherwise, the median is selected. Either way, the selected values were noted as the "*location measures*" (LM) of the measured TME concentrations. Statistical analyses were realized using IBM SPSS Statistics, version 20.

II.1.3. Indoor air concentration calculations

Since the collection of trace metallic elements was performed onto quartz fiber filters, we had to take into account the matrix effect of our collecting substrate. Indeed, they contain a non-negligible amount of the considered metals. Thus, the mean filter blanks $\bar{C}_{Filter\ Blank}$ were calculated for every metal in both lots. Typically, their values should exceed the quantification limits of our analytical method in order to be able de subtract them from the sample results [13].

The indoor air concentrations $C_{in\ air}$ were then calculated using the average sample flow rate and sampling time for each workstation. The average sample flow rate is the mean between the initial Q_i and final Q_f flow rates. These measurements were conducted before and after each use of pumps to make sure of their stability over time [11] using a Mini-Buck flow calibrator M5 which is a soap bubble flow meter.

The final formula is the following [11,13]:

$$C_{in\ air} = \frac{(C_x - \bar{C}_{Filter\ Blank}) \cdot v_{samp}}{\left(Q_i + Q_f/2\right) \cdot t}$$

Where:

$\bar{C}_{Filter\ Blank}$: Mean filter blanks concentration of the considered metal

C_x: mass concentration provided by the ICP-MS

v_{samp}: sampling volume

Q_i and Q_f: initial and final flow rates

t:monitoring time

II.2. Biomonitoring: Urinary sampling

In order to assess TMEs excretion in the urine of workers and to check the influence of occupational exposure, urinary sampling was chosen for biomonitoring purposes. Urinary metals can be viewed as an indicator for the airborne exposure. Moreover, it is easier to convince workers to have a urinary sampling than a blood one. However, this is not always valid. For example, urinary aluminum was showed to be a better indicator than the serum aluminum of inhalation occupational exposure [14,15]. It is also considered to be a good indicator of occupational exposure for Ni and Zn [16,17]. However, urinary analyses of Pb are considered as weak exposure indicator of the internal dose of lead because urinary sampling for Pb could be biased by external contamination [18].

Spot urinary sampling was conducted at the end of the shift and the end of the week (Friday noon or afternoon, depending on the work schedule of the company).This timing was chosen based on the data base Biotox illustrated by INRS [19]. In the Biotox documents for all the six selected metals Cr [20], Ni [17], Cu [21], Zn [16] and Pb [18], the privileged time stated for occupational exposure is end of the shift, end of the day. Whereas, for Al, this timing could more represent the recent exposure [14].

Workers from the five companies were solicited to participate; among them 61 volunteer workers accepted to provide urinary sampling.

Urines were collected in polypropylene bottles (50 ml), immediately transported to the laboratory (time elapsed between 10 and 25 minutes) and kept at -80°C until analysis.

II.3.   Sample analysis

TME quantification was conducted by ICP-MS (Agilent Technologies 7700 Series ICP-MS). The purity of the plasma torch argon was around 99.999%.

An external multi-element standard was used for direct calibration (Environmental calibration Standard), from Agilent Technologies (USA). And, purified water was used by means of Milli-Q Direct 8 system (Millipore, SAS, Molsheim, France).We chose the most predominant isotopes; Al 27, Cr 53, Ni 60, Cu 63, Zn 66 and Pb 208.

We followed the analytical procedures provided by INRS [7] to determine TMEs airborne concentrations. As for, urine sample analyses were conducted using multi-elementary ICP-MS method by Goullé et al. [22]; aliquots of urine (0.4 ml) were diluted in 3.6 ml of HNO_3(0.65%, SIGMA–ALDRICH, Germany).

II.4.   Comparison of exposure measurements to modeled results for trace metallic elements in metalworking industry

We compared the values of the modeled TME concentrations with the *location measures* of the measured ones. The *location measures* values are defined as mentioned above.

Additionally, to avoid underestimation or overestimation of some situations where exposure is significantly higher or lower due to the natural variability, we decided to validate a second scenario where we compare the modeled values with the arithmetic mean of the measured values. To this intent, statistical analyses of all data are evaluated to check the normality of distribution for both validation scenarios.

To evaluate the match between measured and predicted TME exposure levels, different methods were used in literature. They vary from value comparisons [2,23,24] to statistical tests [25,26]. Though, the correlation approach is judged as a statistically more informative method for such models [1,25], thus, we adopted it.

In all our statistical testing, we are considering the significance level at α = 0.05. Thus, if p-value is lower than 0.05, the null hypothesis is rejected. All statistical analyses were achieved using IBM SPSS statistics, version 20.

Normality tests are also conducted for all the samples when the correlations are explored. The null hypothesis of the Shapiro-Wilk test is that distribution is normal. If both samples are not, a log-transformation is conducted and the normality is checked again.

Pearson correlations are used when one of the samples is normally distributed. Otherwise, the non parametric Spearman is used.

Then, the calculations of the statistical significance of the correlations are automatically achieved by the SPSS statistics software. The null hypothesis of the performed test is that no significant correlation is observed. In addition, we also adopted other methods used for comparison by testing the difference between the paired values (the modeled TMEs concentrations and the mean/median of measured ones), with dependent *Student's t*-test or nonparametric Wilcoxon signed-rank tests, as appropriate.

The dependent *Student's t*-test is testing the mean difference between the predicted and the measured concentrations samples. The null hypothesis of this test is that the mean difference could be zero. So, the predicted and measured values could be equal. Thus, when the significance p-values are higher than 0.05, the null hypothesis is accepted.

First of all, we decided to compare all the predicted concentrations (all metals in all task jobs) with the measured ones for the metalworking industries, in order to check the models global predictive ability. Then, we compared the predicted concentrations depending on the process and the modeling scenario because every type is based on different calculations. Similar task jobs are gathered together.

We will compare the following data;

(i)   WMB modeled concentration for RSW

(ii)   NF predictions in the steel cutting industry

(iii)   NF modeled concentration for plastic injection

(iv)   Modeled concentration for welding industry: NF predictions in SMAW and induction welding process, and combination predictions for P16

(v)   Modeled concentration for electroplating industry: NF predictions for Ni and ABS plating, and combination predictions for metal electroplating

II.5.   Correlation analysis

Urinary metals can be related to occupational exposure via inhalation; for instance, for Al, 85% of inhaled amount is excreted in urines [14]. For zinc also, a correlation has been demonstrated between airborne concentration and urinary metals, in a study where workers

were exposed to cutting fluids [16]. Soluble compounds of Ni, showed also good correlations [17].

Therefore, we explored if the correlation between the airborne measured concentrations and the urinary metals.

III.   Results

III.1.   Indoor air monitoring results

In table 2.1, statistical analyses of the air monitoring data are shown for the six replicate measurements for every metal and every task job P.

If we consider the LM values, we can notice that the highest Al concentrations are from P5 and P16; corresponding to SMAW process and the combinations of GMAW and induction welding, respectively.

Then, the highest Cr LM concentrations are also P5, P6 and P10 corresponding to the SMAW, steel shearing/ slitting and the combination of GMAW and zinc plating.

As for Ni, the majority of the task jobs have the same level; around 0.5 $\mu g/m^3$, except for P1, P4, P7, P8 and P15 that are corresponding to stamping, RSW, packaging in the stamping and induction welding workplaces and plastic injection.

For Cu, the LM concentration in P5 is considerably higher than all job tasks. Also, for Pb, P5 has the highest concentration, and then comes P6 and P3 that have almost a half lower concentrations than P5.

Lastly for Zn, P6 has highest concentration, and then all job tasks have almost the same level except for P4 and P13; corresponding to RSW and quality control in ABS plating workplace.

So, we observe that highest concentrations are generally in P5, P6, P16 and P10. Therefore according to air monitoring these are the most exposing job tasks.

Table 2.1: Statistical analysis of indoor air measured concentrations of the selected TMEs for each task job

Task jobs	Al				Cu				Cr			
	LM(μg/m^3)	M (μg/m^3)	SD	Range	LM (μg/m^3)	M (μg/m^3)	SD	Range	LM (μg/m^3)	M (μg/m^3)	SD	Range
P1	0.078	0.154	0.218	0.023 to 0.541	0.008	0.015	0.019	0.001 to 0.48	0.017*		0.007	0.010 to 0.027
P3	0.818*		0.452	0.013 to 1.322	0.178	0.927	1.306	0.011 to 2.902	0.034	0.124	0.177	0.017 to 0.461
P4	0.391*		0.247	0.057 to 0.663	0.170	0.619	1.148	0.005 to 2.946	0.009*		0.005	0.001 to 0.014
P5	4.325	6.233	4.976	2.553 to 16.103	1.935*		1.092	0.407 to 3.626	0.467	0.545	0.382	0.143 to 1.278
P6	1.731	2.206	0.932	1.335 to 3.467	0.191	0.601	0.678	0.094 to 1.498	1.277	4.193	7.917	0.387 to 20.324
P7	1.376*		1.215	0.185 to 3.681	0.021		-	-	0.049	0.098	0.140	0.004 to 0.346
P8	0.775*		0.235	0.518 to 1.125	0.022		0.014	0.012 to 0.032	0.091*		0.086	0.012 to 0.176
P9	0.751*		0.278	0.380 to 1.071	0.258*		0.307	0.025 to 0.789	0.075*		0.018	0.047 to 0.094
P10	0.455*		0.336	0.029 to 0.992	0.757*		0.567	0.044 to 1.614	0.432*		0.152	0.246 to 0.604
P11	0.687		0.845	0.089 to 1.284	0.437*		0.237	0.156 to 0.814	0.247*		0.182	0.033 to 0.496
P12	0.124*		0.129	0.030 to 0.333	0.279	0.499	0.493	0.050 to 1.139	0.130	0.691	1.374	0.012 to 3.481
P13	0.362*		0.124	0.193 to 0.558	0.315*		0.156	0.084 to 0.473	0.188*		0.013	0.169 to 0.205
P14	0.375*		0.015	0.355 to 0.390	0.245	0.289	0.102	0.226 to 0.442	0.181*		0.028	0.144 to 0.213
P15	0.267*		0.384	0.006 to 0.836	~ 0		-	-	0.002*		0.0007	0.02 to 0.003
P16	3.423*		4.495	0.067 to 11.914	0.341*		0.293	0.053 to 0.734	0.190*		0.131	0.080 to 0.359

Task jobs	Ni LM (µg/m3)	M (µg/m3)	SD	Range	Pb LM (µg/m3)	M (µg/m3)	SD	Range	Zn LM (µg/m3)	M (µg/m3)	SD	Range
P1	0.151*		0.127	0.036 to 0.338	0.039	0.286	0.443	0.000 to 1.078	0.774	0.711	0.172	0.362 to 0.816
P3	0.383*		0.363	0.107 to 0.955	0.163*		0.133	0.029 to 0.351	1.485*		1.662	0.119 to 4.681
P4	0.125	0.220	0.253	0.080 to 0.735	0.045	0.086	0.108	0.026 to 0.304	0.240	0.516	0.576	0.035 to 1.296
P5	0.649*		0.325	0.194 to 1.135	0.365*		0.302	0.080 to 0.928	1.310	2.056	2.457	0.212 to 6.965
P6	0.523	2.059	4.150	0.072 to 10.515	0.137*		0.174	0.010 to 0.425	3.819*		1.911	2.100 to 6.915
P7	0.100	0.134	0.099	0.065 to 0.332	0.011		0.008	0.005 to 0.017	1.371*		0.782	0.432 to 2.646
P8	0.183*		0.174	0.029 to 0.487	0.034*		0.020	0.006 to 0.054	0.804*		0.310	0.500 to 1.270
P9	0.489*		0.259	0.126 to 0.792	0.004		0.003	0.002 to 0.006	1.796*		0.891	0.975 to 2.927
P10	0.444*		0.225	0.084 to 0.643	0.067		0.005	0.064 to 0.070	2.235*		1.033	0.911 to 3.792
P11	0.700*		0.451	0.251 to 1.315	0.002		0.002	0.001 to 0.004	0.626*		0.302	0.222 to 1.077
P12	0.585*		0.335	0.136 to 1.023	0.009*		0.008	0.001 to 0.017	1.612*		1.098	0.234 to 2.922
P13	0.595*		0.168	0.305 to 0.757	~ 0		-	-	0.206	0.349	0.388	0.079 to 1.125
P14	0.585*		0.190	0.365 to 0.781	0.007		-	-	0.432	0.846	0.911	0.313 to 2.207
P15	0.088*		0.030	0.053 to 0.120	0.073*		0.034	0.035 to 0.120	0.865*		0.353	0.356 to 1.195
P16	0.311*		0.128	0.108 to 0.504	0.042	0.329	0.583	0.027 to 1.203	1.725*		0.666	0.659 to 2.529

Note: LM: Location measure value: mean if normal distribution/ median if not, M: arithmetic Mean, SD: Standard deviation,
*: Normal distribution (p-value of the Shapiro-Wilk test is >0.05)

III.2. Comparison of modeled and measured concentrations of airborne trace metallic elements in metalworking industry

Table 2.2 shows the predicted indoor air concentrations of TMEs versus the mean and LM of the measured concentrations.

Table 2.2: Indoor air measured and predicted concentrations of the selected TMEs for each task job

Task jobs	Al			Cu			Cr			Ni			Pb			Zn		
	LM($\mu g/m^3$)	M ($\mu g/m^3$)	P ($\mu g/m^3$)	LM($\mu g/m^3$)	M ($\mu g/m^3$)	P ($\mu g/m^3$)	LM($\mu g/m^3$)	M ($\mu g/m^3$)	Pr ($\mu g/m^3$)	LM($\mu g/m^3$)	M ($\mu g/m^3$)	P ($\mu g/m^3$)	LM($\mu g/m^3$)	M ($\mu g/m^3$)	P ($\mu g/m^3$)	LM($\mu g/m^3$)	M ($\mu g/m^3$)	P ($\mu g/m^3$)
P1	0.078	0.154	**0.140**	0.008	0.015	**0.019**	0.017		**0.334**	0.151		**0.169**	0.039	0.286	-	0.774	0.711	-
P3	0.818		**0.189**	0.178	0.927	**0.025**	0.034	0.124	**0.446**	0.383		**0.225**	0.163		-	1.485		-
P4	0.391		**0.301**	0.170	0.619	**0.103**	0.009		**0.133**	0.125	0.220	**0.067**	0.045	0.086	-	0.240	0.516	-
P5	4.325	6.233	**10.401**	1.935		**1.962**	0.467	0.545	**2.52**	0.649		**0.897**	0.365		**3.924**	1.310	2.056	-
P6	1.731	2.206	**1.87**	0.191	0.601	**3.10**	1.277	4.193	**3.40**	0.523	2.059	**1.49**	0.137		**4.14**	3.819		-
P7	1.376		**0.225**	0.021		**0.373**	0.049	0.098	**0.409**	0.100	0.134	**0.179**	0.011		-	1.371		**0.498**
P8	0.775		**0.008**	0.022		**0.002**	0.091		**0.001**	0.183		**0.003**	0.034		-	0.804		**0.022**
P9	0.751		**0.884**	0.258		**0.222**	0.075		**0.124**	0.489		**0.293**	0.004		-	1.796		**2.510**
P10	0.455		-	0.757		**0.30**	0.432		137	0.444		**1.32**	0.067		-	2.235		**2.33**
P11	0.687		-	0.437		**2.45**	0.247		1112	0.700		**10.7**	0.002		-	0.626		**0.86**
P12	0.124		-	0.279	0.499	**0.30**	0.130	0.691	137	0.585		**1.32**	0.009		-	1.612		**0.11**
P13	0.362		-	0.315		**0.378**	0.188		6.7	0.595		**0.696**	~ 0		-	0.206	0.349	
P14	0.375			0.245	0.289	**0.093**	0.181		1.66	0.585		**0.172**	0.007		-	0.432	0.846	-
P15	0.267		**0.09**	~ 0		**0.09**	0.002		**0.09**	0.088		**0.09**	0.073		**0.016**	0.865		**0.817**
P16	3.423		**0.897**	0.341		**17.007**	0.190		**0.007**	0.311		**0.009**	0.042	0.329	**2.222**	1.725		**0.022**

P: Predicted concentrations

III.2.1. Normality tests

We checked normality of the distribution of all HMs concentrations of the predicted values, the location measures LM of the measured values and the Mean of the measured values before all the correlation analyses. The following **table 2.3** shows the Shapiro-Wilk p-values of the normality tests for all concentration samples. If none of the three variable distributions was normal, a log-transformation was conducted to seek normality. The new log-transformed variables will be noted as Ln(LM), Ln(Mean) and Ln(Predicted) for the log-transformation of the measured *location measures* values, measured Mean values and the predicted values, respectively. Thus, the new p-values of the Shapiro-Wilk test of the log-transformed samples are also presented.

Table 2.3: The Shapiro-Wilk p-values of the normality tests for original and log-transformed variables

Modeling	Normality test of the original data			Normality test of log-transformed data		
	LM measured ($\mu g/m^3$)	Mean measured ($\mu g/m^3$)	Predicted ($\mu g/m^3$)	LM measured ($\mu g/m^3$)	Mean measured ($\mu g/m^3$)	Predicted ($\mu g/m^3$)
All selected companies	0.00	0.00	0.00	0.02	0.00	0.20
All selected companies(without outliers)	-	-	-	0.11*	0.04	0.21*
WMB for RSW	0.72*	0.10*	0.23*	-	-	-
NF for steel cutting	0.00	0.04	0.01	0.81*	0.14*	0.19*
NF for plastic injection	0.33*		0.00	-	-	-
NF for welding	0.00	0.00	0.00	0.92*	0.93*	0.81*
Combination in welding	0.03	0.01	0.00	0.81*	0.12*	0.30*
NF for electroplating	0.50*		0.00	-	-	-
FF for electroplating	0.00	0.00	0.00	0.85*	0.68*	0.03
FF for packaging	0.01	0.02	0.03	0.19*	0.11*	0.02

* p-value of the Shapiro-Wilk is >0.05: normal distribution

III.2.2. Comparing measured versus predicted concentrations in all selected companies

III.2.2.1. Distributions

The three box plots show the presence of many outliers. Figure 2.2 shows that these points were considerably far away from the majority of the values, so, the boxplots were reduced to lines.
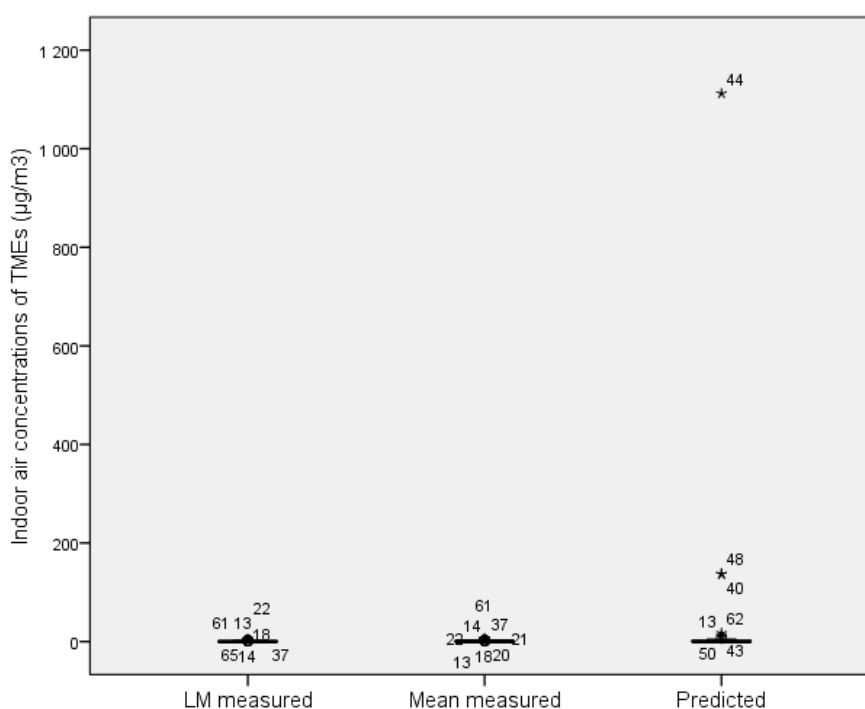
Figure 2.2: Boxplots for the *location measures* and Mean of the measured TMEs concentrations and the predicted TMEs concentrations

After the log transformation, only the predicted values are log-normally distributed (table 2.3). Moreover, Q-Q plots (quantile-quantile plot) of the *location measures* values and the Mean values showed improvements compared to the non-transformed data; they become more linearly distributed except for a couple of points. For example, figure 2.3 shows the distribution modification in Q-Q plots for the measured *location measures* values before and after log transformation. This indicates that the presence of some outliers possibly precludes normality of the distribution.

(a)

(b)
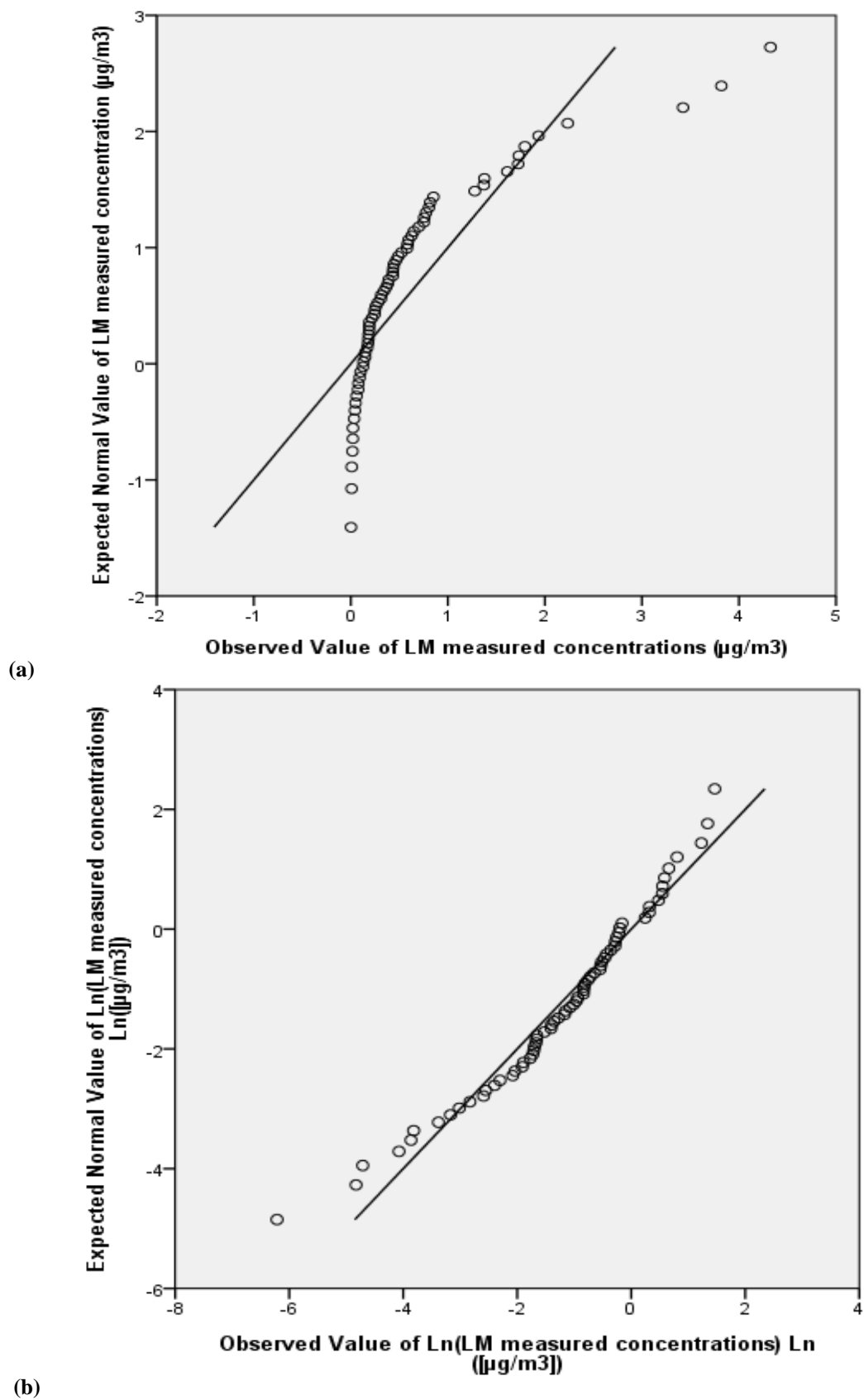
Figure 2.3: Normal Q-Q plots for the measured *location measures* values; (a) real data before transformation, (b) data after log transformation of TMEs concentrations

The boxplots showed the presence of the same single outlier point (point 59 in figure 2.4) that is relatively far away from the lower whisker which means that this is highly affecting the distribution. This point corresponds to the concentration of Cr in the Plastic injection job task. The prediction of the latter was absolutely based on literature among other metals, which means that its removal would not affect the correlation verification. Consequently, we decided to remove it.
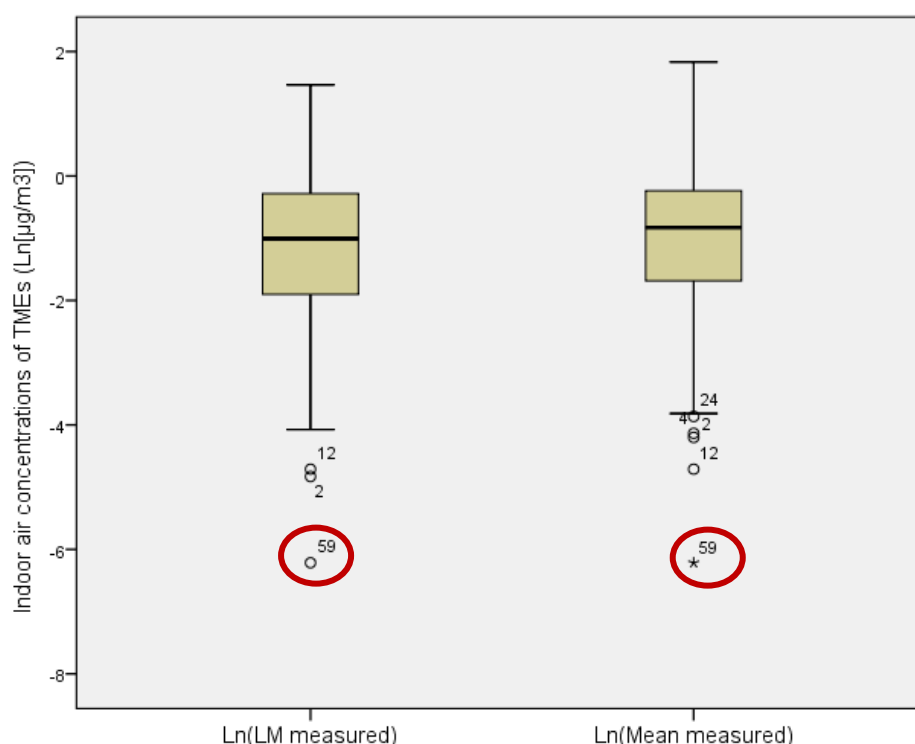
Figure 2.4: Boxplots for the log transformed *location measures* values and log transformed Mean values

Normality results show that the predicted values and the *location measures* values are log-normally distributed. Therefore, we chose to use of parametric tests that are adequate if at least one of the variables is normally distributed. In our case, only Ln(Mean) is not normally distributed. But from the Q-Q plots observation, we can assume that the Ln(Mean) distribution is close to normal.

Moreover, figure 2.5 shows the new distributions of the transformed data and their improvements compared to the distributions of initial data in figure 2.5 (boxplots). Boxplots still encompass outliers, but we can ignore them since the distributions are normal for Ln(LM) and Ln(Predicted). This will allow using parametric methods: Pearson's correlation for correlation calculations and Student's *t*-test for paired difference tests, using the log-transformed data. Student's *t*-test will also provide confidence intervals of the mean

differences, which is an additional tool to evaluate the deviation between the predicted and the measured concentrations.
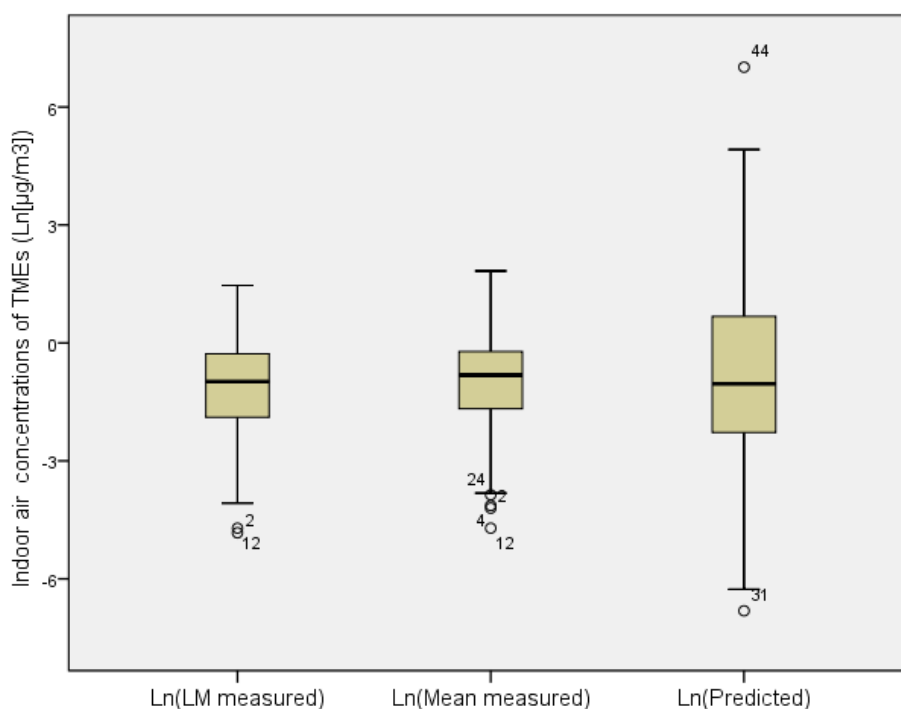
Figure 2.5: **Boxplots for the Ln(*location measures*), Ln(Mean) of the measured TMEs concentrations, and the Ln(Predicted) TMEs concentrations**

These boxplots can also be used for initial comparison of the distributions of the three variables: Ln(LM), Ln(Mean) and Ln(Predicted), in metalworking industry.

We can notice that Ln(Predicted) distribution is larger than both distributions of Ln(measured). However, the bottom whisker of the Ln(Predicted) boxplot shows that in some cases our modeling approaches underestimate the exposure level of trace metallic elements. Therefore, more modeling-specific comparisons will show which models are better in predicting exposure.

III.2.2.2.   Correlation

First, scatter dots were plotted as showed in figure 2.6 and 2.7 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively. We can clearly notice that the concentration values are highly dispersed and do not follow the linear function in both figures.
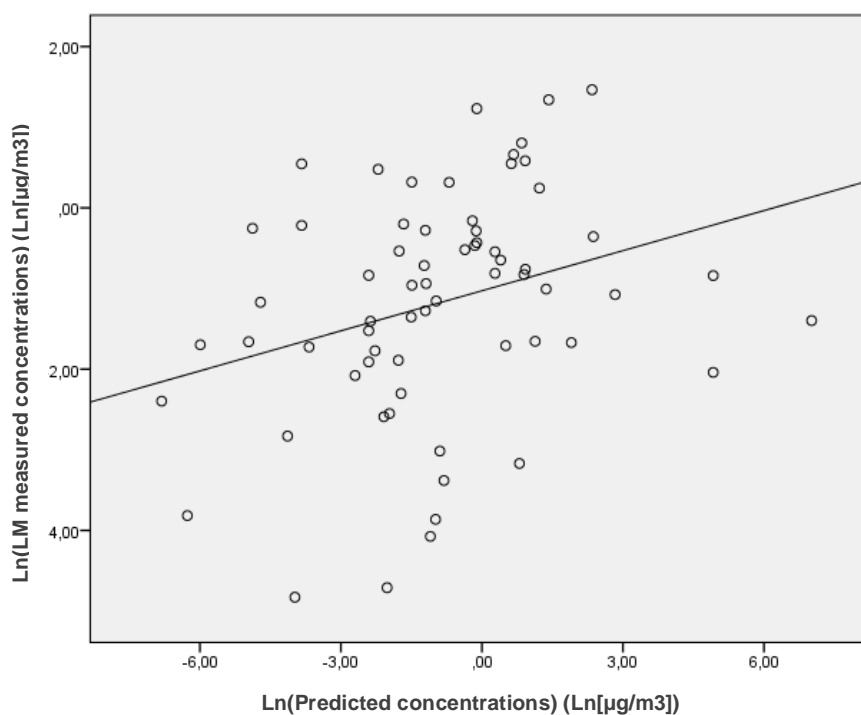
Figure 2.6: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(*location measures of the measured of the TMEs concentrations*) across the fifteen job tasks (n=66)
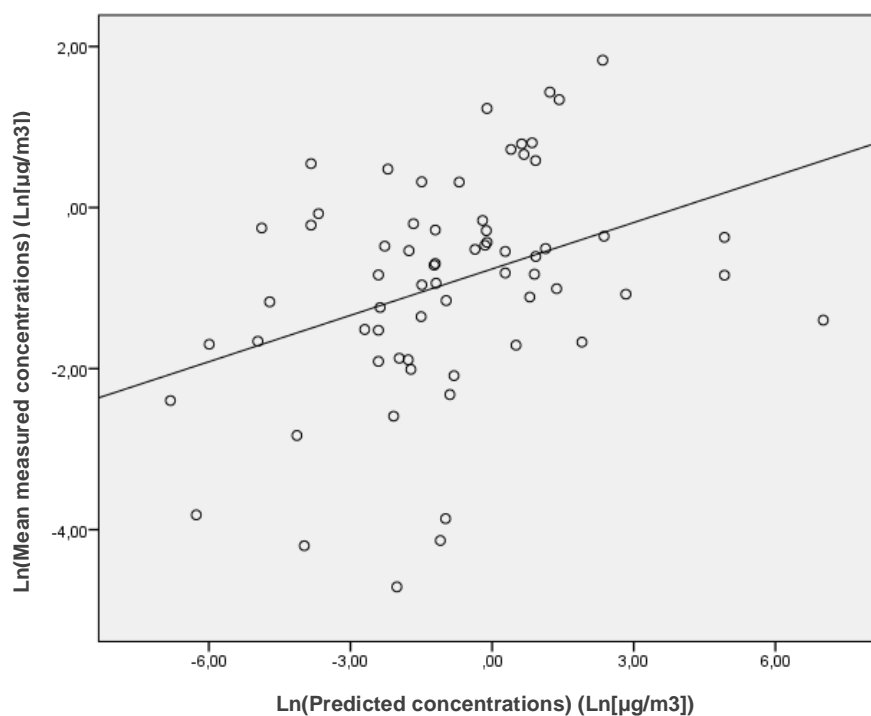
Figure 2.7: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) across the fifteen job tasks (n=66)

The p-values of Pearson's correlation coefficients(r) (table 2.4) are lower than 0.05 for Ln(measured LM) *vs* Ln(Predicted) and for Ln(measured Mean) *vs* Ln(Predicted). This means that the correlations are significant between the Predicted concentrations and both measured LM and measured Mean concentrations. Further, the correlation's significance is stronger between the Predicted concentrations and the measured LM concentrations (p-value <0.01).

However, Pearson's coefficients (r) are relatively low. So, we believe that global correlation is not enough for comparison, which is also confirmed visually by the scatter dots (figure 2.6 and 2.7). This is probably due to the non-homogeneity of the global sample.

Table 2.4: Pearson's correlation coefficients and their corresponding p-values for metalworking industry modeling

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Pearson's (r)	0.30*	0.36**
Correlation significance: P-value	0.01	0.003

Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

III.2.2.3.   Paired difference tests

In a second step, we established the dependant samples *Student's* Test for Ln(LM) and Ln(Predicted), and Ln(Mean), Ln(Predicted). Table 2.5 shows the mean values of the calculated difference (Ln(Predicted) minus Ln(measured LM or Mean)), their 95% confidence intervals and the p-values of the difference.

Table 2.5: The Means of differences and their corresponding p-values for metalworking industry modeling

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Mean difference	0.268	0.026
Confidence interval	[-0.353 to 0.889]	[-0.572 to 0.624]
Difference significance: P-value	0.39	0.93

The difference significance p-values are higher than 0.05 for both Ln(measured LM) *vs* Ln(Predicted) and for Ln(measured Mean) *vs* Ln(Predicted)suggesting these values can be considered as statistically close. The mean differences are presented with their 95% confidence interval. The mean difference of Ln(measured Mean) minus Ln(Predicted) is about ten times lower than the mean difference between Ln(measured LM) minus Ln(Predicted). However, the 95% confidence intervals have almost the same size.

III.2.3. Comparing measured versus WMB predicted concentrations

III.2.3.1. Distributions

Since the three p-values of the Shapiro-Wilk they are higher than 0.05, the three distributions are normal and the Pearson's correlation method will be used along with the Student's *t*-test.

We present an initial comparison using boxplots of the distributions of the three variables: LM measured, Mean measured and Predicted concentrations, for RSW process. The Predicted concentrations distribution is smaller than both distributions of measured ones. On the other hand, Mean measured distribution is larger than the LM measured distribution, which shows the high variability in exposure levels in this particular job task.
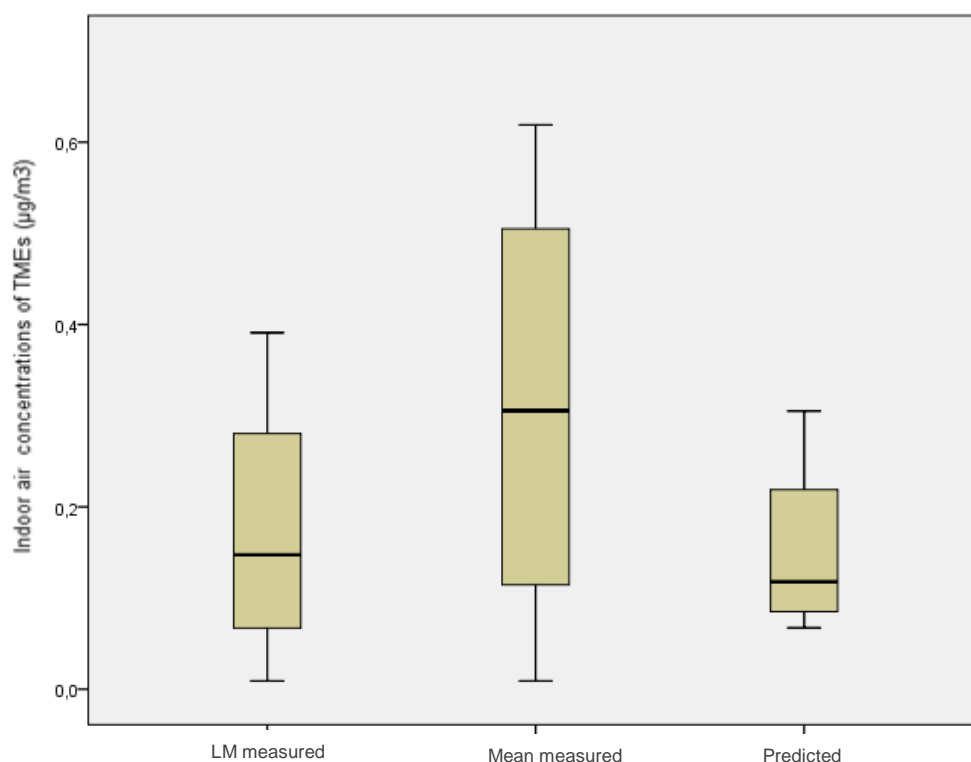
Figure 2.8: Distribution comparison of LM measured concentrations of TMEs, Mean measured concentrations and modeled concentrations for of the RSW modeling (P4)

III.2.3.2.   Correlation

Scatter dots were plotted as showed in figure 2.9 and 2.10 in order to check the degree of association between LM and Predicted values, and Mean and Predicted values, respectively.

Pearson's correlation coefficients (r) and the p-values for their significance are shown in table 2.6.Both p-values are higher than 0.05. So, even though the Pearson's (r) is high for Ln(measured LM) *vs* Ln(Predicted), the correlation is not significant.

This could be due to the small size of this sample; so we decided to conduct a non parametric method to evaluate the correlation. Spearman's correlation coefficients (r) and the p-values for their significance are shown also in table 2.4 Both p-values are higher than 0.05, showing no significant correlation between the Predicted concentrations and Ln(measured LM/Mean).

Therefore, it is useless to conduct the *Student's* Test.
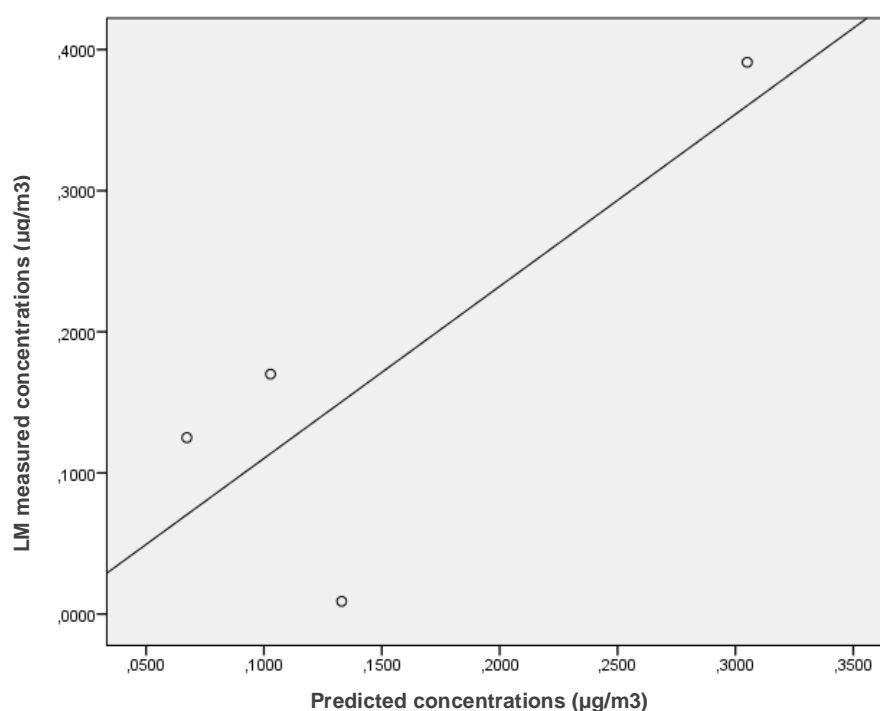
Figure 2.9: Linear regression of the Predicted TMEs concentrations against the LM of the measured of the TMEs concentrations of the RSW modeling (P4)

Figure 2.10: Linear regression of the Predicted TMEs concentrations against the Mean of the measured of the TMEs concentrations of the RSW modeling (P4)

Table 2.6: Pearson's correlation coefficients and their corresponding p-values for the RSW modeling (P4)

	Measured LM *vs* Predicted	Measured Mean *vs* Predicted
Pearson's (r)	0.80	0.13
Parametric Correlation significance: P-value	0.20	0.87
Spearman's (r)	0.40	0.00
Non-parametric Correlation significance: P-value	0.60	1.00

III.2.4. Comparing measured versus to NF predicted concentrations in steel cutting industry

III.2.4.1. Distributions

The log-transformed variables showed normality of the distributions. Consequently, the Pearson's correlation method will be used, and the Student's *t*-test.

An initial comparison is presented using boxplots of the distributions of the three variables; Ln(LM), Ln(Mean) and Ln(Predicted), for steel cutting job tasks. The distribution ranges of the Ln(Predicted) distribution and Ln(Mean) measured distribution coincide and are similar, whereas the bottom whisker of the boxplot of Ln(LM) measured is a bit longer. This means that in some cases, the model mildly overestimates the exposure levels.
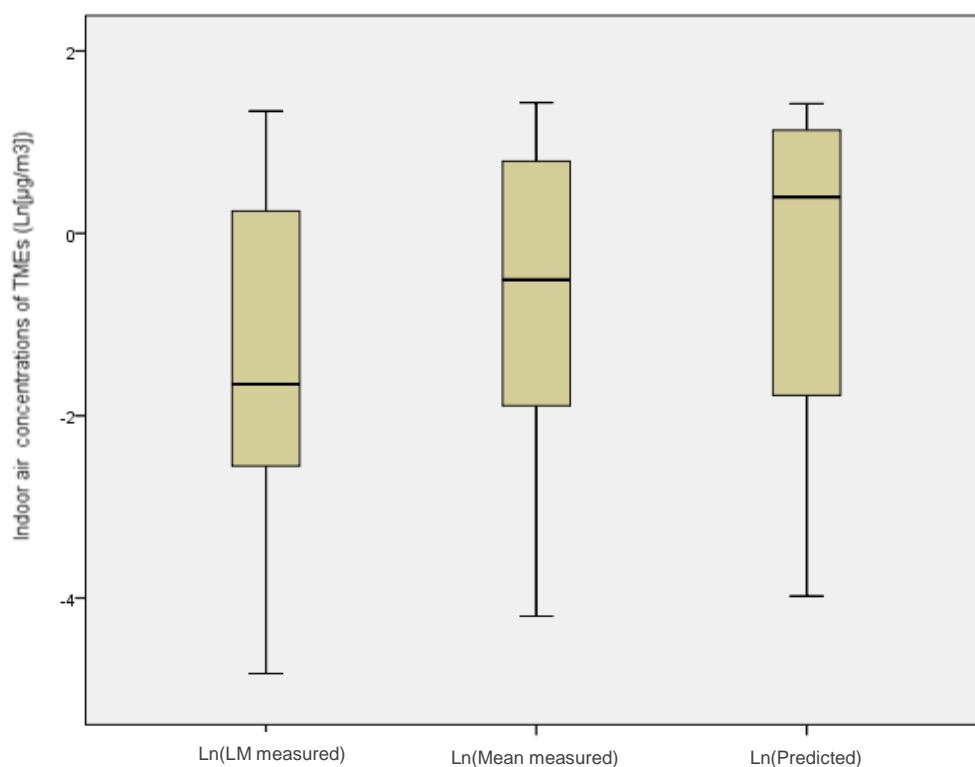
Figure 2.11: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) of the steel cutting job tasks (NF in P1 and P6)

III.2.4.2. Correlation

Scatter dots were plotted as showed in figures 2.12 and 2.13 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively.

Pearson's correlation coefficients (r) and their significance levels are shown is table 2.7 The p-values are lower than 0.01; 0.004 and 0.003 for Ln(measured LM) *vs* Ln(Predicted) and for Ln(measured Mean) *vs* Ln(Predicted), respectively, showing that correlations are strongly significant between the Predicted concentrations and both LM of the measured concentrations and the Mean measured concentrations.
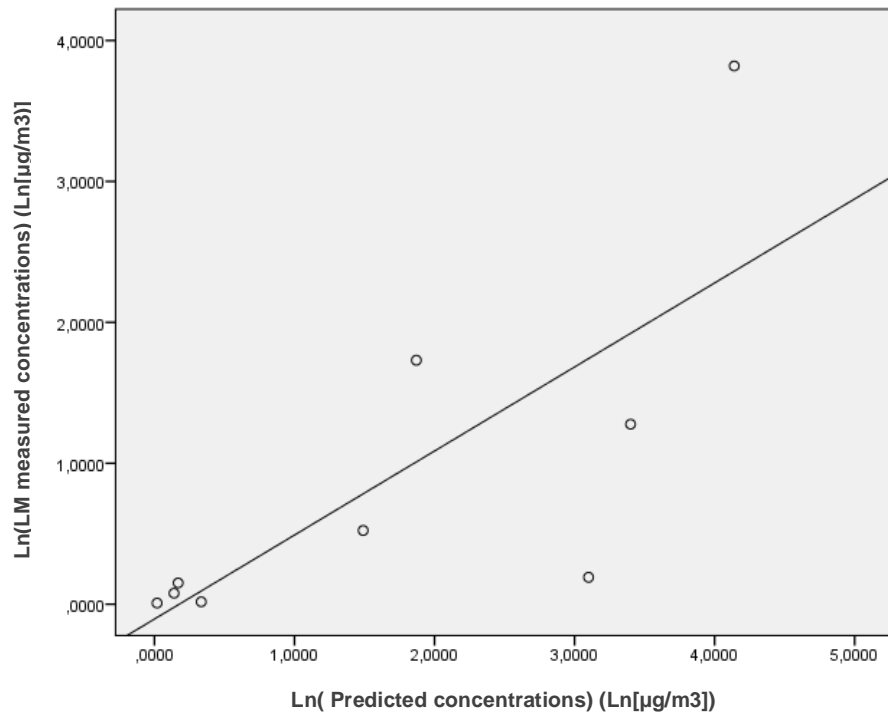
Figure 2.12: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(LM of the measured of the TMEs concentrations) of the steel cutting job tasks (NF in P1 and P6) (n=9)
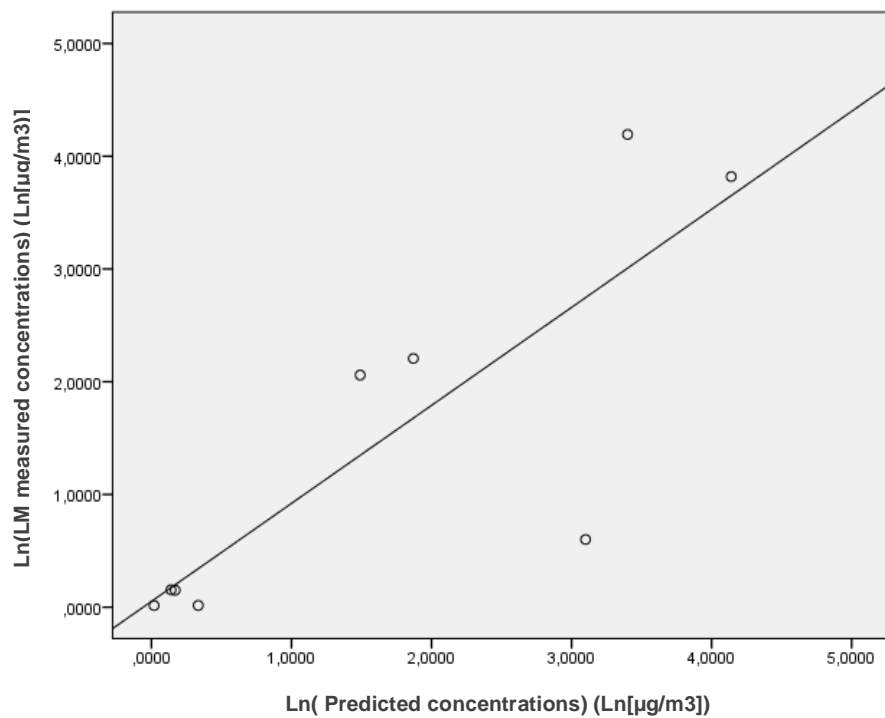
Figure 2.13: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of the steel cutting job tasks (NF in P1 and P6) (n=9)

In addition, both Pearson's coefficients (r) are relatively high and close to each other (~0.85). We consider that the NF Predicted TMEs concentrations are strongly and significantly correlated with both LM and Mean of the measured of the TMEs concentrations released in steel cutting job tasks (P1 and P6).

Table 2.7: Pearson's correlation coefficients and their corresponding p-values for the steel cutting job tasks (P1 and P6)

	Ln(measured LM) vs Ln(Predicted)	Ln(measured Mean) vs Ln(Predicted)
Pearson's (r)	0.85	0.86
Correlation significance: P-value	0.004**	0.003**

** *Correlation is significant at the 0.01 level*

III.2.4.3. Paired difference tests

We established the *Student's* Test for Ln(LM) and Ln(Predicted), and Ln(Mean), Ln(Predicted). Table 2.8 shows the mean values of the calculated difference (Ln(Predicted) minus Ln(measured LM or Mean)), their 95% confidence intervals and the p-values of the difference.

Table 2.8: The Means of differences and their corresponding p-values for the steel cutting job tasks (P1 and P6)

	Ln(measured LM) vs Ln(Predicted)	Ln(measured Mean) vs Ln(Predicted)
Mean difference	1.055	0.478
Confidence interval	[0.206 to 1.904]	[-0.387 to 1.342]
Difference significance: P-value	0.02	0.24

The correlation significance p-value is lower than 0.05 for Ln(measured LM) *vs* Ln(Predicted), showing the values are probably different, even though Ln(measured LM) and Ln(Predicted) are significantly correlated.

Whereas, for Ln(measured LM) *vs* Ln(Predicted), p-value is higher than 0.05, showing that the two values are close and could be identical. This is confirmed because zero is included in its confidence interval of the mean difference.

III.2.5. Comparing measured versus to NF predicted concentrations in plastic injection

III.2.5.1. Distributions

In this case, the six replicates for all metals were normally distributed, so, the *location measures* are the same as the Mean values.

Normality tests showed that LC/Mean values are normally distributed. Thus, we used the Pearson's correlation method and the Student's *t*-test.

III.2.5.2. Correlation

The scatter dot was plotted as showed in figure 2.14 in order to check the degree of association between LC/ Mean measured concentrations and Predicted concentrations values.

Pearson's correlation coefficients (r) and the p-values for their significance are shown is table 2.9. The p-values are lower than 0.05for measured LM/ Mean values *vs* Predicted values. Pearson's coefficients (r) is also remarkably high (0.923), showing that the NF Predicted TMEs concentrations are highly correlated with both LM and Mean of the measured of the TMEs concentrations released in plastic injection.
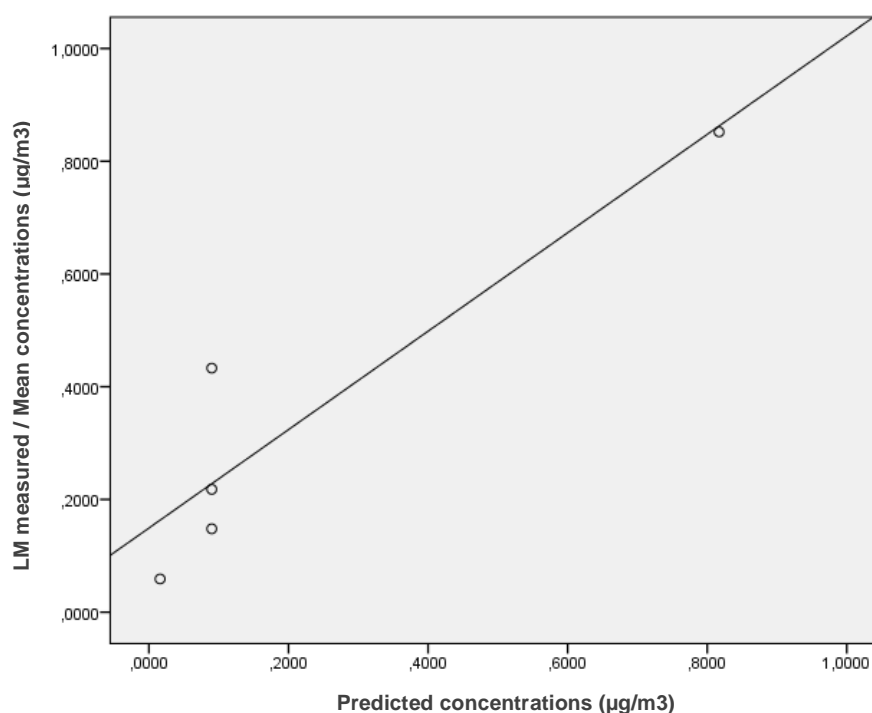
Figure 2.14: Linear regression of Predicted TMEs concentrations against the LC/ Mean of the measured of the TMEs concentrations of the plastic injection job tasks (P15)

Table 2.9: Pearson's correlation coefficients and their corresponding p-values for the plastic injection job tasks (P15)

	Measured LM/ Mean *vs* Predicted
Pearson's (r)	0.92
Correlation significance: P-value	0.03*

* Correlation is significant at the 0.05 level

III.2.5.3.   Paired difference tests

Student's test was also established for LM values and Predicted values. Table 2.10 shows the mean values of the calculated difference (Predicted values minus measured LM values), their 95% confidence intervals and the p-values of the difference.

Table 2.10: The Means of differences and their corresponding p-values for the plastic injection job tasks (P15)

	Measured LM/ Mean *vs* Predicted
Mean difference	-0.121
Confidence interval	[-0.282 to 0.039]
Difference significance: P-value	0.10

Table 2.9 shows a fairly good overlap between measured LM concentrations and Predicted concentrations.

III.2.6.   Comparing measured versus to NF-FF model predicted concentrations in welding industry

III.2.6.1.   Measured vs NF predicted concentrations in welding

a.   Distributions

The NF predicted concentrations in welding includes the SMAW (P5) and induction welding (P9) processes.

After log-transformation of the three variables, all distributions become normal, allowing using the Pearson's correlation and the Student's *t*-test.

Initial comparison is presented using boxplots of the distributions of the variables: Ln(LM), Ln(Mean) and Ln(Predicted), for welding job tasks (exposure in NF). The three distribution ranges are quite similar. The bottom whiskers of the boxplots of Ln(LM) measured and Ln(Mean) measured are a bit longer, meaning that in some cases, the model mildly overestimates exposure.
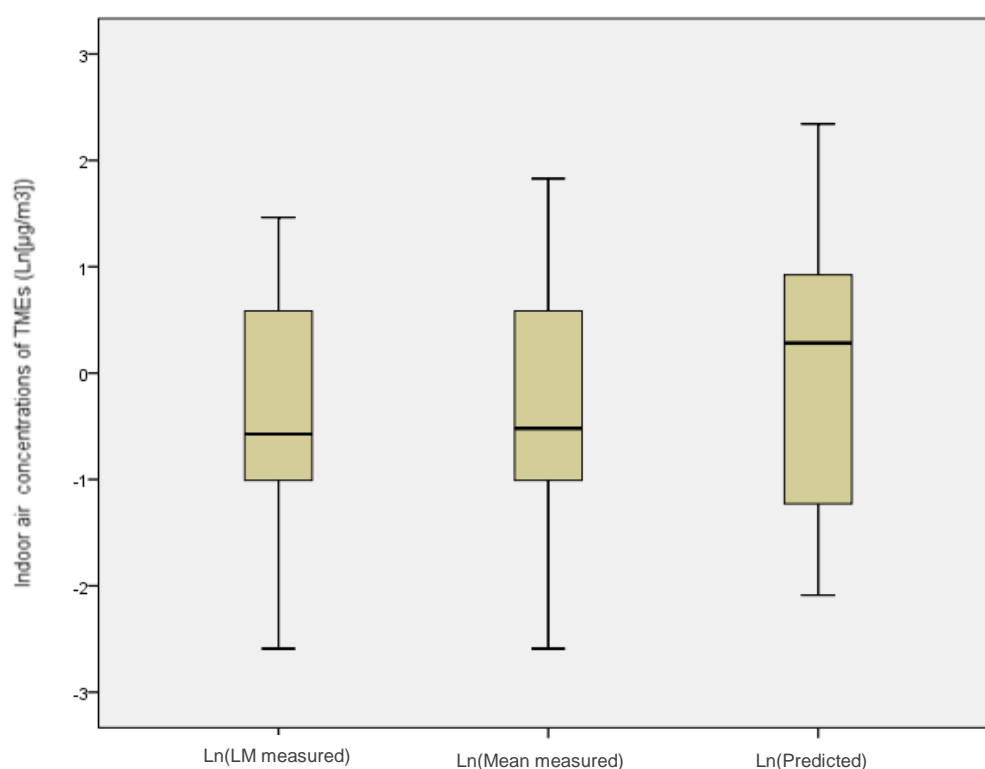
Figure 2.15: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) of welding job tasks (NF in P5 and P9)

      b.   Correlation

Scatter dots were plotted as showed in figure 2.16 and 2.17 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively.

The p-values of the Shapiro-Wilk tests are much lower than 0.01 (table 2.11), showing significant correlations between the Predicted concentrations and both LM of the measured concentrations and the Mean measured concentrations.
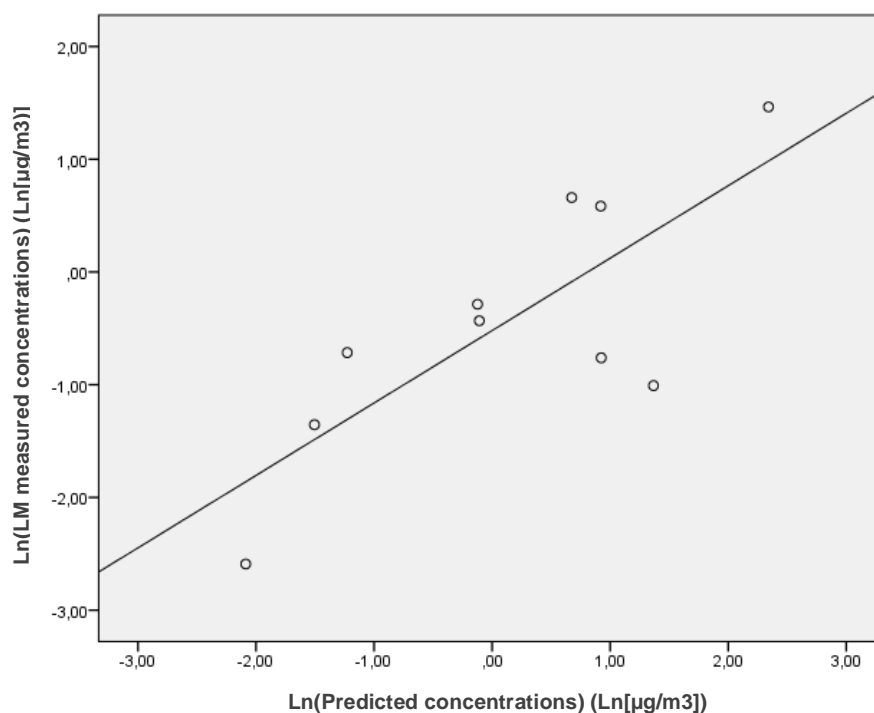
Figure 2.16: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(LM of the measured of the TMEs concentrations) of welding job tasks (NF in P5 and P9)
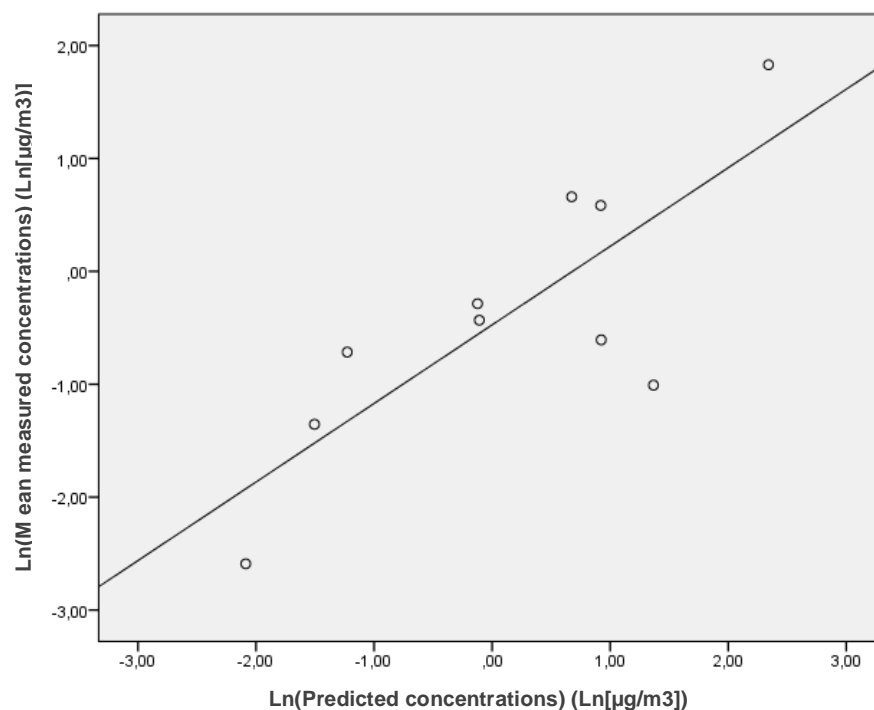
Figure 2.17: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of welding job tasks (NF in P5 and P9)

In addition, both Pearson's coefficients (r) are relatively high and close to each other (~0.78) , so, we consider that the NF Predicted TMEs concentrations is highly and significantly correlated with both LM and Mean of the measured of the TMEs concentrations released in welding job tasks (P5 and P9).

Table 2.11: Pearson's correlation coefficients and their corresponding p-values for welding job tasks (NF in P5 and P9)

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Pearson's (r)	0.78	0.80
Correlation significance: P-value	0.008**	0.006**

*** Correlation is significant at the 0.01 level*

c.   Paired difference tests

The *Student's* Test for the mean difference (Ln(Predicted) minus Ln(LM measured) or Ln(Mean)), (table 2.12) show high p-values, confirming the results of the regression method: the predicted and measured Ln values are close and could be similar in some cases.

Table 2.12: The Means of differences and their corresponding p-values for the welding job tasks (NF in P5 and P9)

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Mean difference	0.562	0.510
Confidence interval	[-0.064 to 1.187]	[-0.095 to 1.114]
Difference significance: P-value	0.07	0.09

III.2.6.2.   Measured vs predicted concentrations combination in welding

a.   Distributions

This particular job task P16 is the combination of the exposure to the C_{NF} from the GMAW and the C_{FF} from induction welding P9.

With low p-values of the Shapiro-Wilk test (0.03, 0.01 and 0.000for LM values, Mean values and Predicted values, respectively), we conclude that the three variable distributions were not normal for the welding task jobs P16.

After log-transformation, the three p-values become 0.81, 0.12 and 0.30 for Ln(LM), Ln(Mean) and Ln(Predicted), respectively, showing normality is acceptable. Thus, the Pearson's correlation method and the Student's *t*-test will be used.

A distribution comparison is presented using boxplots of the three variables: the Ln(Predicted) distribution is lot wider than Ln(Mean measured) and Ln(LC measured) distributions. Moreover, its box of Ln(Predicted) is quite large and exceeds the bottom whiskers of the Ln(Mean measured) and Ln(LC measured) boxplots, suggesting the model is often underestimating exposure.
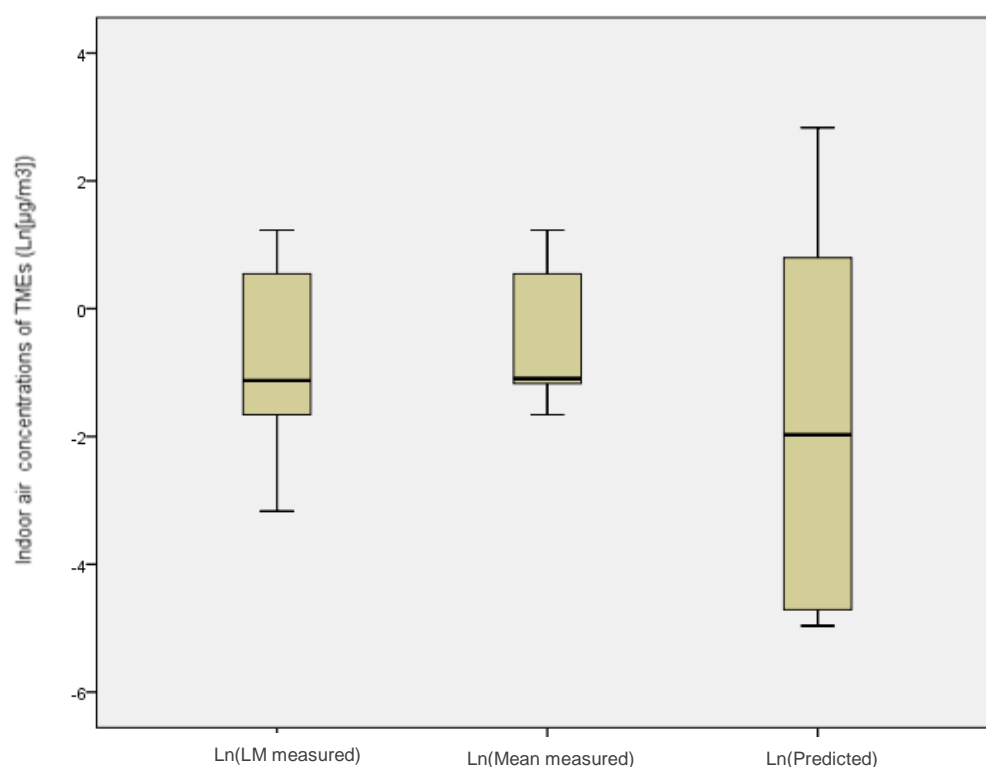
Figure 2.18: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) of welding job tasks (combined exposure in P16)

    b.   Correlation

Scatter dots were plotted as showed in figure 2.19 and 2.20 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively.
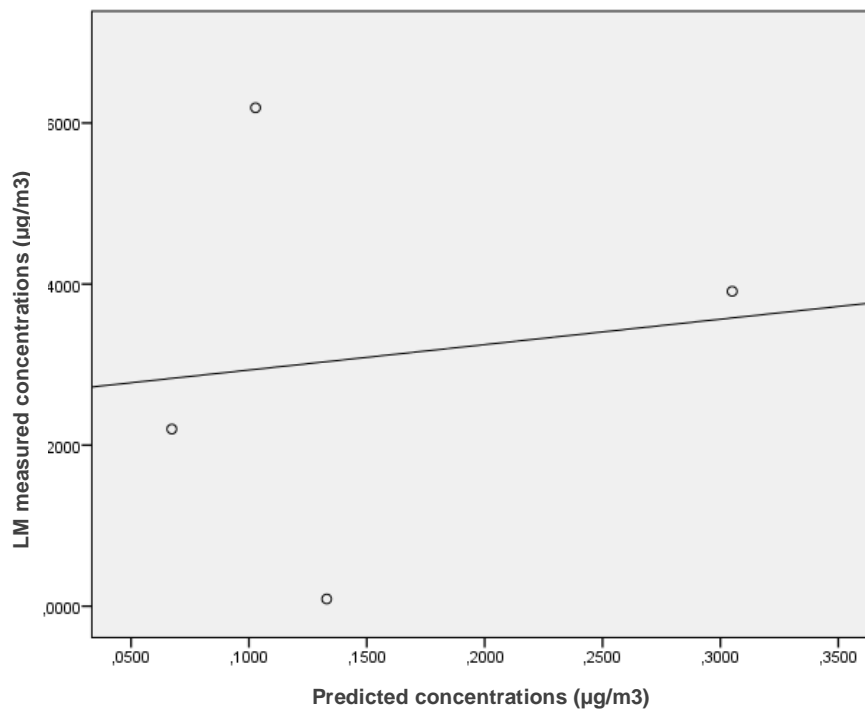
Pearson's correlation coefficients (r) and the p-values for their significance are shown is table 2.12.

Pearson's (r) are very low (~0.11) and both p-values are higher than 0.05. So, there is no correlation between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted). So, it useless to conduct the *Student's* Test.

We tried the non-parametric correlation method. Spearman's correlation coefficients (r) and the p-values for their significance is also shown is table 2.13. The p-values are high, confirming that no correlation between the Predicted values and measured LM and Mean.
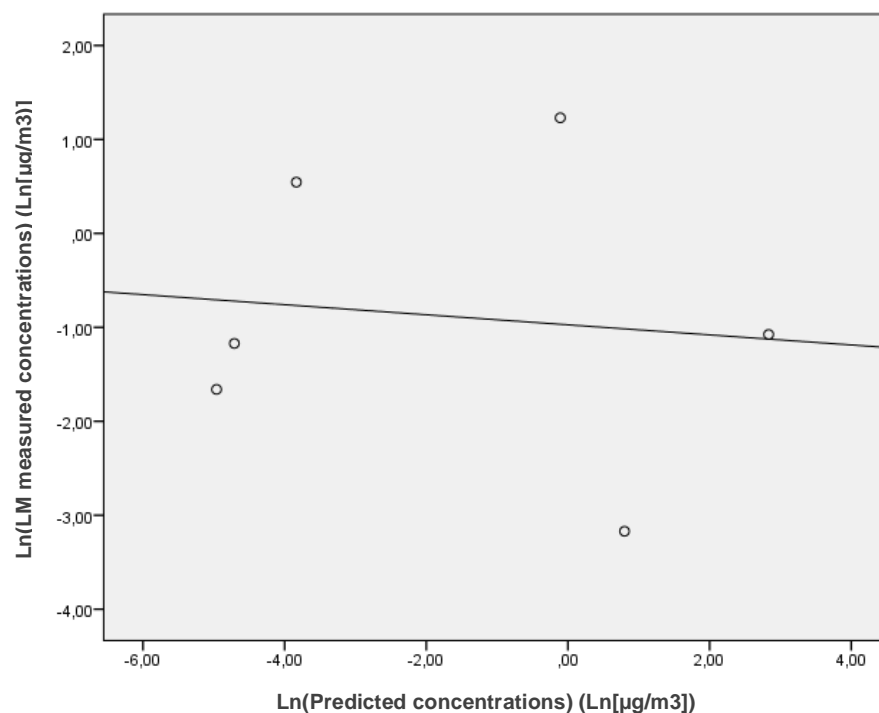
Figure 2.19: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of welding job tasks (combined exposure in P16)
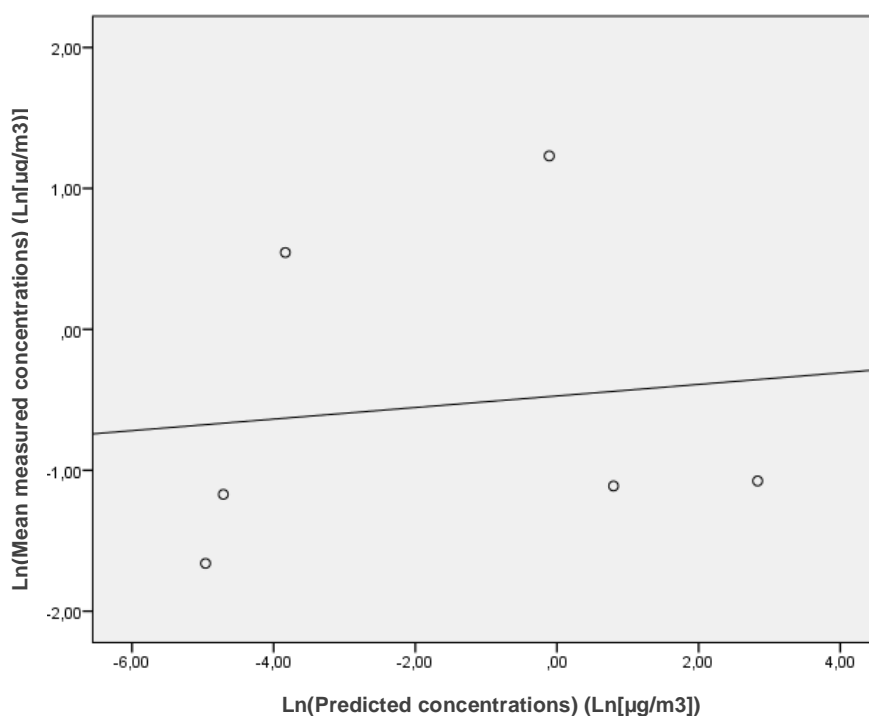
Figure 2.20: **Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of welding job tasks (combined exposure in P16)**

Table 2.13: Pearson's and Spearman's correlation coefficients and their corresponding p-values for welding job tasks (combined exposure in P16)

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Pearson's (r)	-0.11	0.12
Parametric Correlation significance: P-value	0.83	0.83
Spearman's (r)	0.14	0.54
Non-parametric Correlation significance: P-value	0.79	0.27

III.2.7. Comparing measured versus to NF-FF predicted concentrations in electroplating industry

III.2.7.1. Measured vs NF predicted concentrations in electroplating

a. Distributions

The NF predicted concentrations in electroplating include the System control of the Nickel-plating lines (P11) and the ABS plating (P13). In this case, the six replicates for the considered metals in both P11 and P13 were normally distributed, so, the *location measures* are the same as the Mean values.

Normality tests indicate that LM values are normally distributed. Hence, we will use the Pearson's correlation method and the Student's *t*-test.
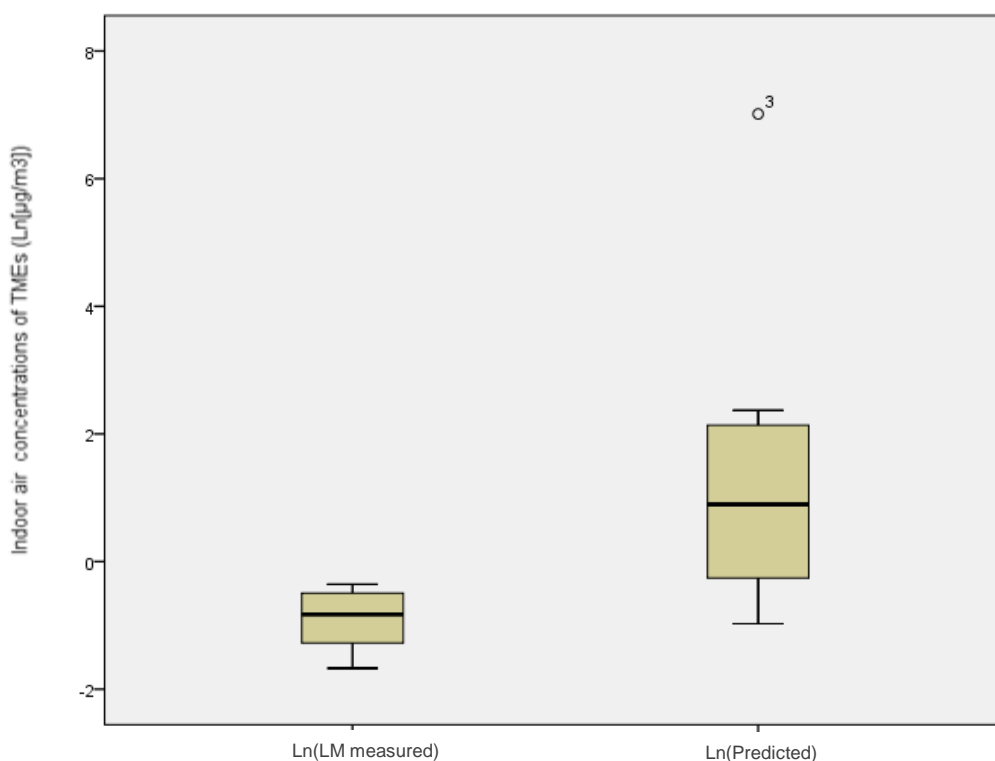

Figure 2.21: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) of electroplating job tasks (NF in P10 and P13)

An initial comparison is presented in figure 2.21 using boxplots of the distributions of the three variables; Ln(LM), Ln(Mean) and Ln(Predicted), for electroplating (NF) job tasks. The boxplot of Ln(Predicted) is larger and more elevated. It encompasses also an outlier that

corresponds to Cr prediction in P11 (System control of Ni-plating lines).This could show high uncertainty in concentration prediction in the electroplating industry.

       b.   Correlation

The scatter dot was plotted as showed in figure 2.22 in order to check the degree of association between LM measured concentrations and Predicted concentrations values.

The p-value of the Pearson's correlation coefficient (r) is high (table 2.14), suggesting absence of correlation between the Predicted values and measured LM/Mean values. Therefore, it is useless to conduct the *Student's* Test.

However, we tried the Spearman's correlation non-parametric method (Table 2.14); its p-value is also high confirming absence of correlation.
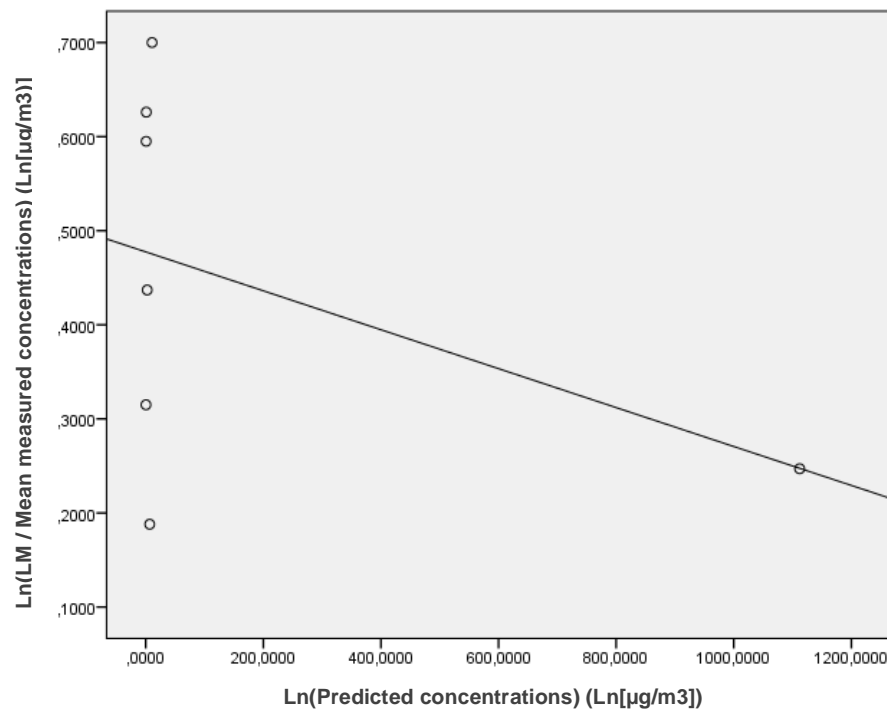
Figure 2.22: Linear regression of the Predicted TMEs concentrations against the LM/ Mean of the measured of the TMEs concentrations of electroplating job tasks (NF in P10 and P13)

Table 2.14: Pearson's and Spearman's correlation coefficients and their corresponding p-values for of electroplating job tasks (NF in P10 and P13)

	Measured LM / Mean *vs* Predicted
Pearson's (r)	-0.43
Parametric Correlation significance: P-value	0.33
Spearman's (r)	-0.14
Non-parametric Correlation significance: P-value	0.76

III.2.7.2.   Measured vs FF predicted concentrations in electroplating

a.   Distributions

The FF predicted concentrations in electroplating include the Zinc-plating (P10), Lifting hooks task job of the Nickel-plating lines (P12) and the Quality control in ABS plating workplace (P 14).
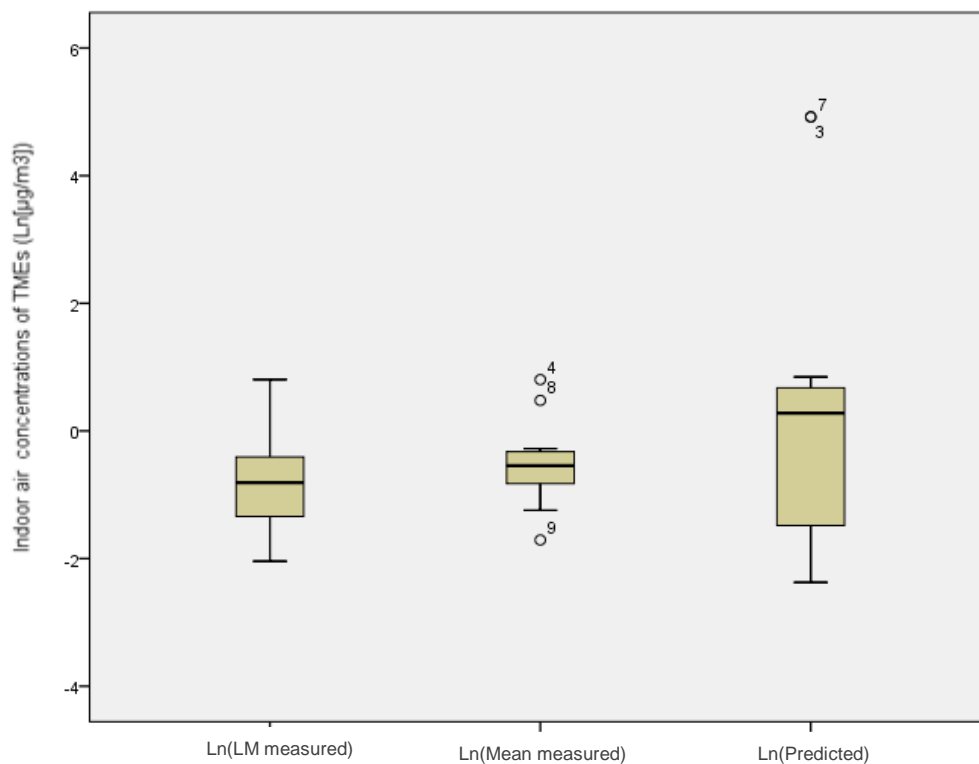
Figure 2.23: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) of electroplating job tasks (FF in P10, P12 and P14)

The log-transformed variable showed good normality. Thus, we can use the Pearson's correlation method and the Student's *t*-test.

This is probably due to the outliers in Cr concentrations. Contrarily to the other metals, these concentrations were predicted based on ready-to-use EFs. Results show that they are enormously overestimating the Cr concentrations compared to the measured ones.

The boxplots in figure 2.23 compare Ln(LM), Ln(Mean) and Ln(Predicted), electroplating industry (FF job tasks). The Ln(Predicted) distribution almost covers the same extend of the Ln(LM), Ln(Mean) distributions. However, it encompasses two outliers that correspond to Cr predictions in P10 and P12 (Zn-plating lines operator and lifting hooks of Ni-plating lines, respectively).

       b.   Correlation

Scatter dots were plotted as showed in figure 2.24 and 2.25 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively.
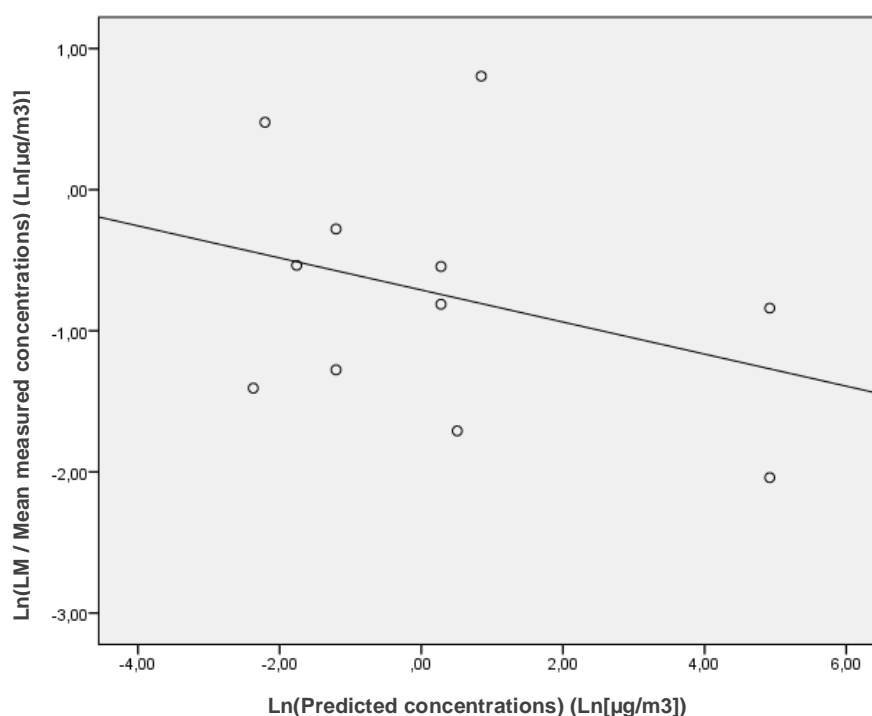
Figure 2.24: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(LM of the measured of the TMEs concentrations) of electroplating job tasks (FF in P10, P12 and P14)
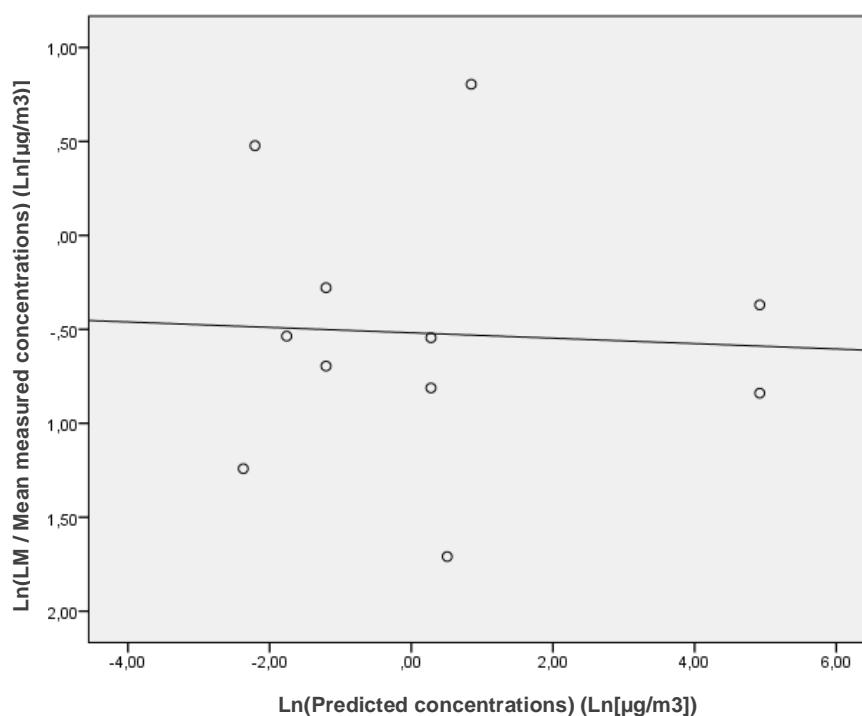
Figure 2.25: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of electroplating job tasks (FF in P10, P12 and P14)

The p-values of Pearson's correlation coefficients are high (table 2.15) for both Ln(measured LM) *vs* Ln(Predicted) and for Ln(measured Mean) *vs* Ln(Predicted), showing absence of correlations between the Predicted concentrations and both LM and the Mean of the measured concentrations. Therefore, it useless to conduct the *Student's* Test.

The Spearman's correlation on-parametric method did not alter this conclusion: there is no correlation between the Predicted values and measured LM and Mean values.

Table 2.15: Pearson's and Spearman's correlation coefficients and their corresponding p-values of electroplating job tasks (FF in P10, P12 and P14)

	Ln(measured LM) *vs* Ln(Predicted)	Ln(measured Mean) *vs* Ln(Predicted)
Pearson's (r)	-0.33	-0.05
Parametric Correlation significance: P-value	0.32	0.88
Spearman's (r)	-0.26	-0.02
Non-parametric Correlation significance: P-value	0.45	0.95

III.2.8. Comparing measured versus to FF predicted concentrations in the packaging job tasks

III.2.8.1. Distributions

The FF predicted concentrations in packaging job tasks is considered for P3 and P7 in steel cutting workplaces having several sources and P8 in the induction welding workplace.

After log-transformation, the normality tests showed that LM measured concentrations and Mean measured concentrations are log-normally distributed, not Ln(Predicted).

So, it is allowed to use parametric methods; the Pearson's correlation method and the Student's t-test.

We present an initial comparison using boxplots of the distributions of the three variables; Ln(LM), Ln(Mean) and Ln(Predicted), for packaging job tasks. Ln(Predicted) distribution is larger than both distributions of Ln(measured). Moreover, the top whisker of the Ln(Predicted) boxplot does not reach the same level as the top whiskers of the Ln(LM), Ln(Mean) measured boxplots.
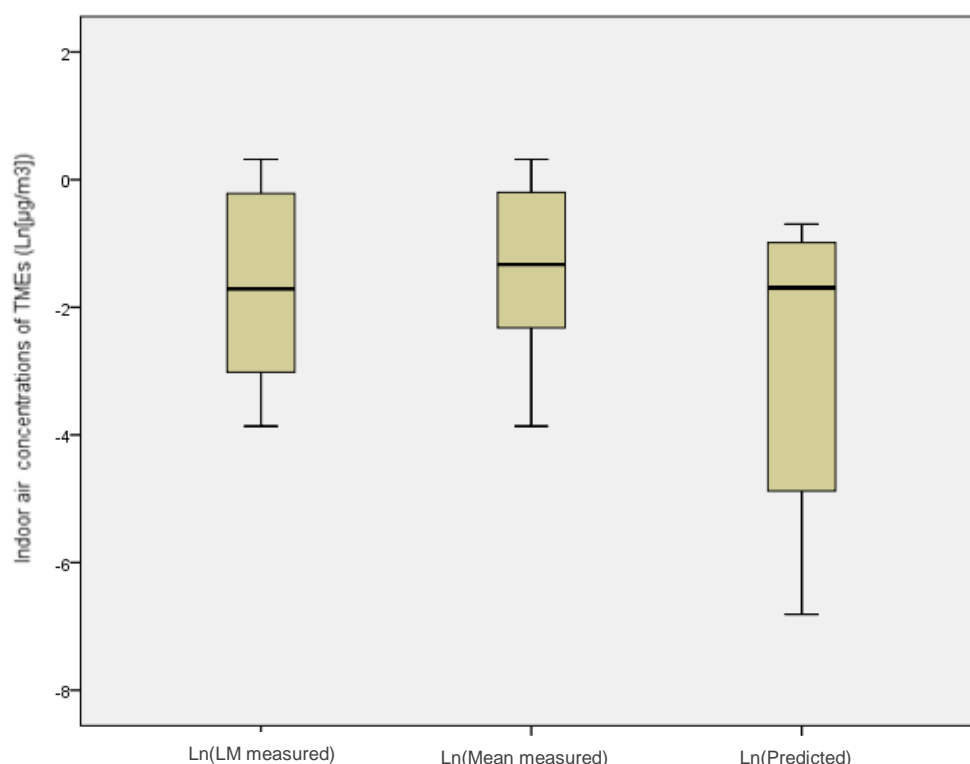


Figure 2.26: Distribution comparison of Ln(LM measured concentrations of the TMEs), Ln(Mean measured concentrations of the TMEs) and Ln(modeled TMEs concentrations) for packaging job tasks (FF for P3, P7 and P8)

III.2.8.2. Correlation

Scatter dots were plotted as showed in figure 2.27 and 2.28 in order to check the degree of association between Ln(LM) and Ln(Predicted), and Ln(Mean) and Ln(Predicted), respectively.

The p-values of the Pearson's correlation coefficients are high (table 2.16), showing absence of correlations between the Predicted concentrations and both LM of the measured concentrations and the Mean measured concentrations. Therefore, it useless to conduct the *Student's* Test.

Non-parametric methods did not alter this conclusion.
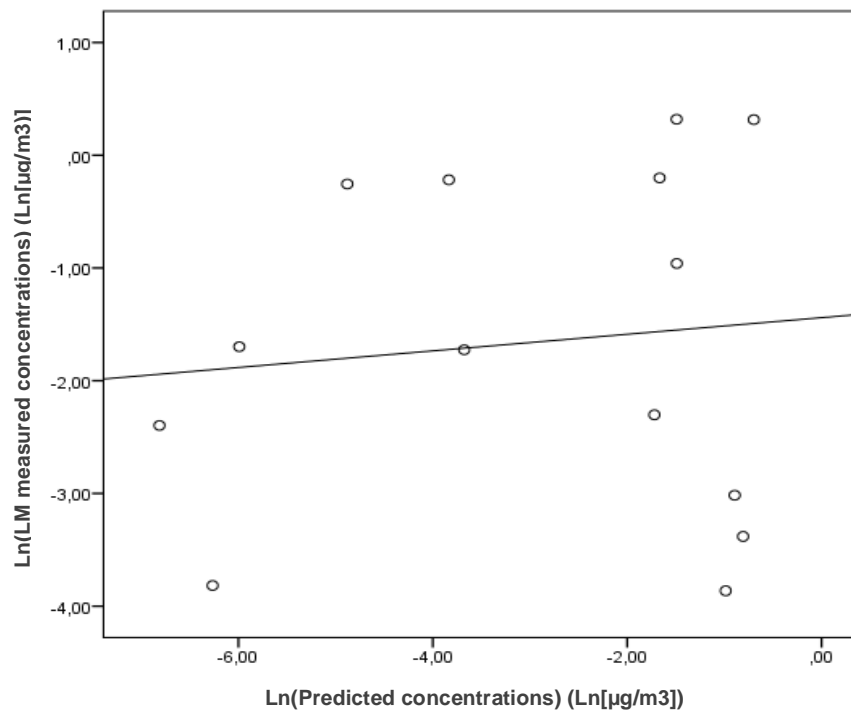
Figure 2.27: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(LM of the measured of the TMEs concentrations) of the packaging job tasks (FF for P3, P7 and P8)
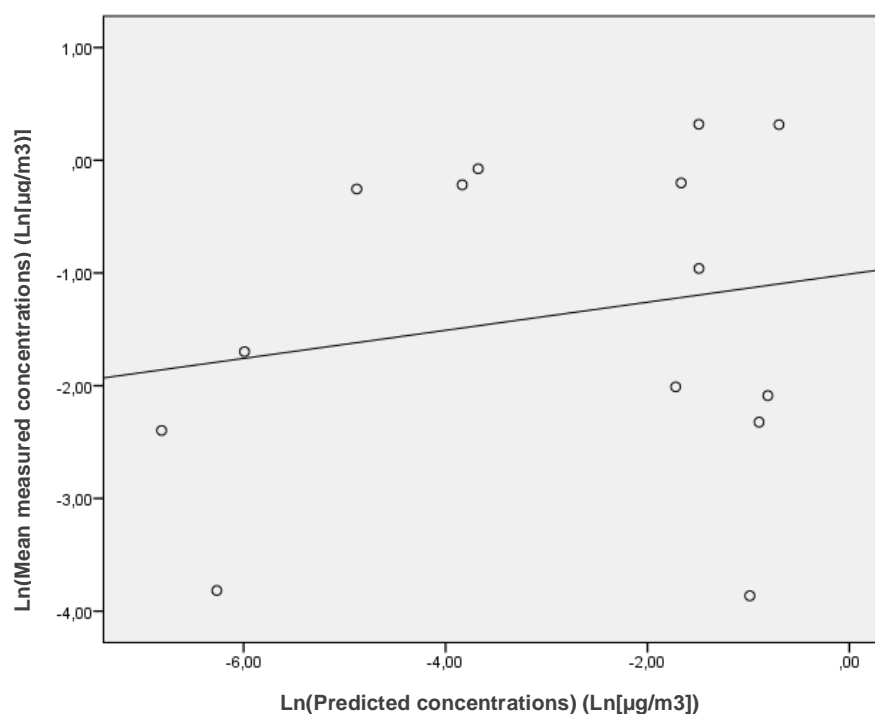
Figure 2.28: Linear regression of the Ln(Predicted TMEs concentrations) against the Ln(Mean of the measured of the TMEs concentrations) of the packaging job tasks (FF for P3, P7 and P8)

Table 2.16: Pearson's and Spearman's correlation coefficients and their corresponding p-values for the packaging job tasks (FF for P3, P7 and P8)

	Ln(Measured LM) vs Ln(Predicted)	Ln(Measured Mean) vs Ln(Predicted)
Pearson's (r)	0.109	0.195
Parametric Correlation significance: P-value	0.71	0.50
Spearman's (r)	0.073	0.178
Non-parametric Correlation significance: P-value	0.81	0.54

III.3. Correlation analysis between the internal and external doses

III.3.1. Biomonitoring results

Table 2.17 exhibits results of the biomonitoring data for every metal and every task job P. 61 workers provided urinary samples; 18 of them are considered to be non-occupationally exposed.

Table 2.17: Statistical analysis of urinary metal concentrations of the selected TMEs for each task job

Task jobs	Al			Cr			Ni		
	M (mg/L)	SD	Range	M (mg/L)	SD	Range	M (mg/L)	SD	Range
P1	9.232	0.430	8.617 to 9.847	0.300	0.0311	0.239 to 0.327	0.107	0.0233	0.056 to 0.124
P3	8.229	0.885	8.045 to 9.661	0.266	0.031	0.258 to 0.315	0.928	0.007	0.092 to 0.105
P4	8.997	0.782	8.44 to 9.550	0.290	0.015	0.279 to 0.301	0.101	0.005	0.098 to 0.105
P5	28.6811	-	-	0.2698	-	-	.1951	-	-
P6	9.524	10.357	9.203 to 32.077	0.293	0.015	0.279 to 0.319	0.107	0.0568	0.093 to 0.217
P7	17.565	12.165	8.964 to 26.167	0.312	0.0327	0.289 to 0.335	0.157	0.083	0.098 to 0.216
P8	19.415	14.841	8.922 to 29.910	0.322	0.075	0.269 to 0.375	0.179	0.118	0.096 to 0.262
P9	8.5817	-	-	0.2793	-	-	0.1008	-	-
P10 & P12	27.946	4.343	24.875 to 31.017	0.294	0.002	0.292 to 0.295	0.219	0.017	0.207 to 0.231
P11	30.216	-	-	0.2750	-	-	0.2105	-	-
P13	8.771	0.117	8.688 to 8.853	0.295	0.003	0.293 to 0.298	0.101	0.002	0.099 to 0.102
P14	26.668	8.458	8.598 to 29.197	0.329	0.040	0.272 to 0.364	0.215	0.059	0.101 to 0.258
P15	8.897	12.317	8.783 to 30.1740	0.284	0.049	0.282 to 0.368	0.098	0.096	0.095 to 0.263
P16	24.960	9.592	8.515 to 25.293	0.304	0.021	0.275 to 0.31	0.205	0.065	0.094 to 0.207
OE	**13.54**	**9.010**	**8.229 to 30.216**	**0.293**	**0.019**	**0.266 to 0.329**	**0.168**	**0.213**	**0.098 to 0.928**
NOE	**8.589**	**5.764**	**8.368 to 28.726**	**0.287**	**0.222**	**0.267 to 0.340**	**0.107**	**0.035**	**0.095 to 0.222**

Task jobs	Cu			Zn			Pb		
	M (mg/L)	SD	Range	M (mg/L)	SD	Range	M (mg/L)	SD	Range
P1	0.111	0.008	0.098 to 0.120	22.360	2.456	17.810 to 24.710	0.059	0.062	0.016 to 0.172
P3	0.106	0.002	0.105 to 0.109	17.722	3.981	16.915 to 24.179	0.052	0.116	0.0326 to 0.243
P4	0.183	0.0783	0.128 to 0.238	19.888	3.065	170720 to 22.056	0.128	0.136	0.032 to 0.224
P5	0.4458	-	-	5.0125	-	-	0.055	-	-
P6	0.249	0.116	0.079 to 0.355	20.787	7.814	7.453 to 25.096	0.051	0.036	0.021 to 0.127
P7	0.367	0.441	0.055 to 0.680	12.128	8.344	6.228 to 18.028	0.056	0.019	0.043 to 0.070
P8	0.151	0.110	0.073 to 0.228	13.249	8.520	7.224 to 19.274	0.101	0.097	0.032 to 0.169
P9	0.1134	-	-	16.8768	-	-	0.0283	-	-
P10 & P12	0.305	0.278	0.108 to 0.501	6.046	0.021	6.031 to 6.061	0.047	0.012	0.038 to 0.055
P11	0.0958	-	-	7.2487	-	-	0.062	-	-
P13	0.281	0.251	0.103 to 0.458	21.793	6.580	17.139 to 26.446	0.220	0.116	0.138 to 0.303
P14	0.460	0.283	0.121 to 0.804	7.189	4.560	5.152 to 16.657	0.051	0.010	0.035 to 0.062
P15	0.083	0.213	0.077 to 0.449	17.098	7.029	5.869 to 18.810	0.054	0.108	0.049 to 0.238
P16	0.097	0.175	0.022 to 0.374	6.307	6.79	6.085 to 17.963	0.038	0.003	0.036 to 0.042
OE	**0.167**	**0.018**	**0.083 to 0.460**	**15.063**	**6.457**	**5.013 to 22.3600**	**0.055**	**0.050**	**0.028 to 0.220**
NOE	**0.119**	**0.104**	**0.058 to 0.343**	**18.100**	**3.562**	**8.992 to 22.234**	**0.043**	**0.001**	**0.020 to 0.130**

OE: Occupationally exposed, NOE: Non-occupationally exposed

M: median

III.3.2. Correlation between urinary metals and indoor air measured concentrations

Correlations were investigated between urinary metals and indoor air measured concentrations.

Normality tests for the concentrations and for the log-transformed data, if needed, are presented in table 2.18 below. Correlation calculations were made for both parametric and non-parametric methods because sample sizes are relatively small. The samples sizes were 40 for Ni and Zn, 39 for Al and Cr, 37 for Pb, and 36 for Cu. The sizes are variable because we excluded the air measured concentrations that are blow than the detection limit.

Significant correlations are observed between urinary metals and indoor air measured concentrations for Al and Cu. Both correlations were medium, with a correlation coefficient r ~ 0.3.

Table 2.18: Normality tests and correlation coefficients of the urinary TME concentrations *vs* air measured concentrations

Metal	Normality test of the original data		Normality test of log-transformed data		Correlation coefficient (r)	Correlation significance: P-value
	M U (mg/L)	Air measured ($\mu g/m^3$)	Ln(M U) (mg/L)	Ln(Air measured) ($\mu g/m^3$)		
Al	0.00	0.00	0.00	0.03	0.33[b]	0.04*
Cr	0.05*	0.00	-	-	-0.11 [a]; -0.10 [b]	0.50; 0.56
Ni	0.00	0.00	0.00	0.27*	0.21 [a]; 0.15 [b]	0.19; 0.34
Cu	0.00	0.00	0.01	0.05	0.34[b]	0.04*
Zn	0.00	0.00	0.00	0.78*	0.00 [a]; 0.01[b]	0.98; 0.94
Pb	0.00	0.00	0.01	0.03	0.12[b]	0.50

MU: Metal in Urine
[a]: Pearson's coefficient, [b]: Spearman's coefficient
* p-value of the Shapiro Wilk is >0.05: normal distribution
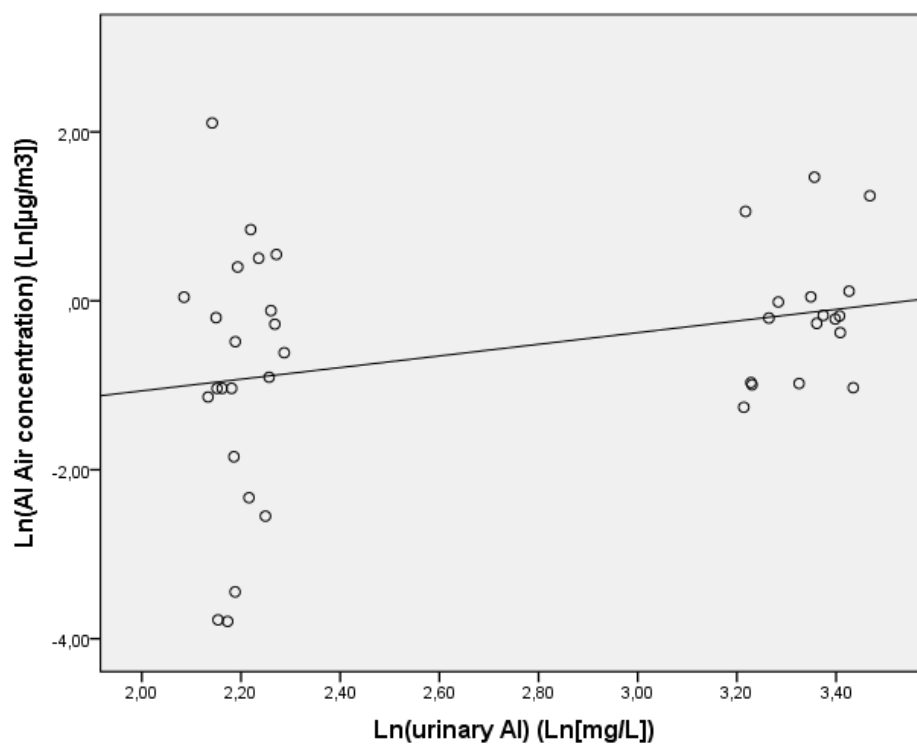
Figure 2.29: Linear regression of the Ln(urinary Al) against the Ln(Al air concentration) of 39 exposed workers
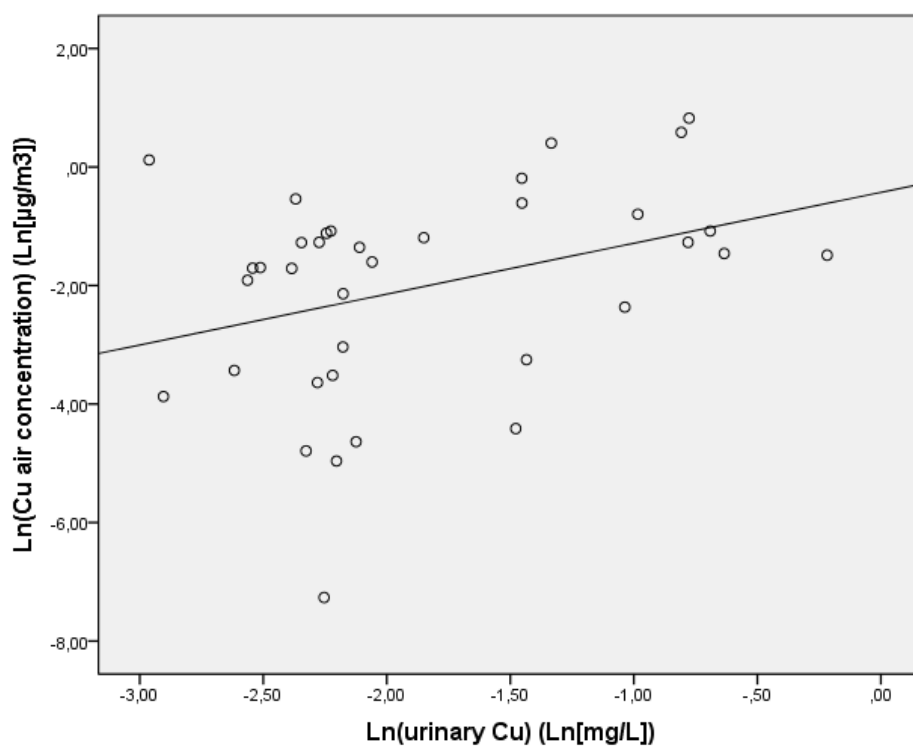
Figure 2.30: Linear regression of the Ln(urinary Cu) against the Ln(Cu air concentration) of 36 exposed workers

III.3.1. Correlation between urinary metals and models estimations

Correlations were also investigated between urinary metals and the predicted air concentrations (normality tests and correlation calculations are presented in table 2.19).

None of the TMEs showed significant correlations between urinary metals and the predicted air concentrations.

Table 2.19: Normality tests and correlation coefficients of the median urinary TME concentrations *vs* predicted air concentrations

Metal	Normality test of the original data		Normality test of log-transformed data		Correlation coefficient (r)	Correlation significance: P-value
	M U (mg/L)	Predicted (µg/m³)	Ln(M U) (mg/L)	Ln(predicted) (µg/m³)		
Al	0.009	0.000	0.014	0.897*	0.222 [a] 0.358 [b]	0.538 0.310
Cr	0.881*	0.000	-	-	-0.290 [a] -0.275 [b]	0.314 0.342
Ni	0.000	0.000	0.002	0.686*	0.015 [a] 0.216 [b]	0.960 0.459
Cu	0.030	0.000	0.107*	0.970*	0.129 [a] 0.121 [b]	0.660 0.681
Zn	0.374*	0.026	-	-	0.711 a	0.048
Pb	0.110*	0.858*	-	-	-0.017 [a] 0.500 [b]	0.989 0.667

MU: Metal in Urine
[a]: Pearson's coefficient, [b]: Spearman's coefficient
* p-value of the Shapiro-Wilk is >0.05: normal distribution

IV. Discussion

IV.1. Methodological choices

Although six replicates are recommended to characterize concentrations of workplace pollutants [1], they cannot fully determine the distribution because concentrations may vary depending on many factors such as the ventilation rate variability between days according to meteorology, the workers activity profile (e.g. number of tasks per day, which may also vary between workers and from day to day), etc. As illustrated in table 2.1, in many cases, the mean values were significantly higher than the LM values. For this reason, we considered a second comparison scenario with the mean values.

The log-transformation of air concentration samples was achieved to seek normal distribution. This operation decreases the variation range and brings the extreme values closer to the most common range.

It is well known that air pollutant measurements are frequently log-normally distributed [27–29]. So, extreme values are rather exceptional cases. Without this operation, extreme values have an overly high influence on the correlation calculations, which may decrease the correlation coefficients, leading to biases results and mislead conclusions. Consequently, we believe that the log-transformation does not only serve to adjust the samples into normal distribution, but also contributes to more accurate results.

The choice of two scenarios for correlations with the predicted concentrations was established when one or two extreme values were observed. Due to the small sizes of our samples (6 values), we decided to accommodate a statistically rigorous method by choosing the median of the distribution when normality was not met. On the other hand, it was worth to think about the effect of the extremes values by choosing a second scenario with the mean values.

According to our results, the global correlation for the modeling approach showed to be more significant (p-value <0.01) between the predicted concentrations vs measured Mean concentrations than vs the measured LM. This means that it is worth to establish comparisons with means of the measured concentrations because in some task jobs, the difference between the mean and the median is high.

However, in NF prediction for both steel cutting and welding, the significance was the same for the *location measures* and the Mean. This could be due to the small sizes of our samples, so that the extremes values did not have much influence. Thus, more replicates would be preferable, depending on the available resources.

On the other hand, the Pearson's coefficients (r) of the global correlation were relatively low, a finding that backs our methodology to stratify the global samples and check correlations for specific modeling methods.

IV.2.   Air monitoring

As a general observation, we already noticed that the highest TME concentrations of indoor air are generally found in the P5, P6, P16 and P10 job tasks. This is quite similar to our modeling estimations, if we disregard the plating task jobs that are suspected to be

overestimating the exposure due to Cr EFs. The job tasks with the highest exposure levels are also P5, P6 and P16.

Moreover, some other similarities were identified, such as for steel cutting job tasks and the packaging tasks related to them. Air monitoring results are in agreement with the magnitude of predicted exposure using the NF-FF models based on our cumulative approach.

The packaging workers P3 in workplace A1 are exposed to significantly higher concentrations for all TMEs (up to four folds, in figure 2.31.a). On the other hand, the packaging workers P6 in workplace A4 are exposed to lower concentrations for all TMEs (figure 2.31.b).

This is likely due to the number of machines in the workplace. The more emission sources, the higher the TME concentrations. Moreover, this could also be due to differences in ventilation rates between the workplaces. Although A1 is a large workplace, it is poorly ventilated according to our Q calculations (ACH = 0.85).

(a)   (b)
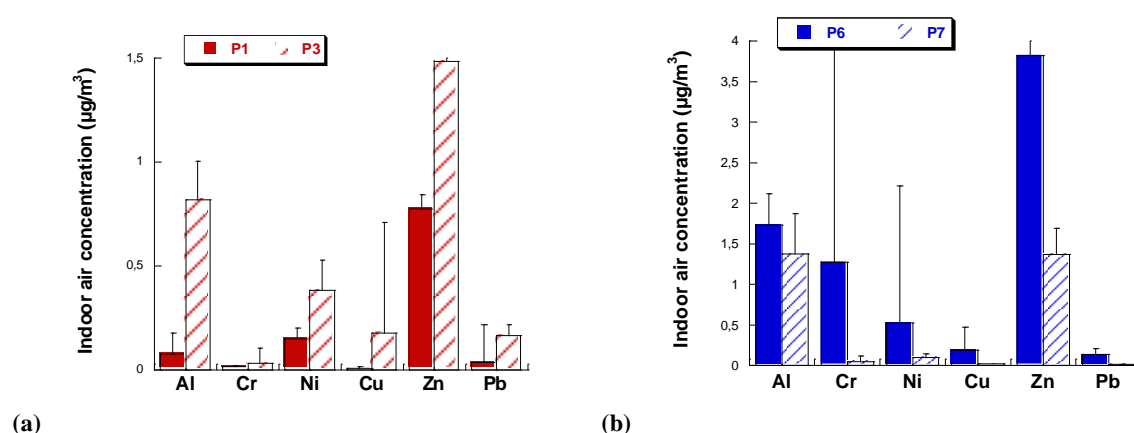
Figure 2.31: Indoor air monitoring concentrations (location measure values) of TMEs in steel cutting workplaces A1 (figure a: P1: stamping, P3: Packaging) and A4 (figure b: P6: slitting &shearing, P7: Packaging)

IV.3.   Predicted versus measured concentrations

Global correlation for our modeling approach showed to be significant to strongly significant between the predicted concentrations vs the measured LM, and the measured Mean concentrations, respectively. Although the Pearson's coefficient correlation is relatively low, this result is satisfying and shows that mathematical models for estimating occupational exposure can be used to predict indoor TMEs concentrations in metal working industry. Yet, some processes showed stronger correlations than others.

IV.3.1. Prediction effectiveness of the modeling approach

Strongly significant correlations were demonstrated for NF predictions in the steel cutting and welding jobs, and to a milder extent for plastic injection. Correlation with mean measured values showed to be approximately the same as LM values. Student's T test for paired samples showed also that the mean difference could reach zero.

IV.3.1.1. NF predictions in steel cutting processes

Besides the strong statistical significance, relatively high correlation coefficients (r ~0.85) were found between predicted and measured TMEs concentrations. This demonstrates the pertinence of our approach of the NF predictions for steel cutting processes.

The two basic inputs of indoor air monitoring are the generation rate G and the ventilation rate Q [30]. Their determination is considered to be decisive to the correctness and accuracy of the models' outputs [3]. Our findings suggest a good accuracy of our input characterization approach, notably of the G and the Q. We used the mass balance method to calculate the generation rates in the steel cutting processes via our modified formula (presented in part 1). Our results support that this approach is sufficiently effective to be used to similar processes where the chemical composition of the materials are available.

IV.3.1.2. NF predictions in welding processes

High correlations were also obtained for NF predictions for welding processes: Shielded Metal Arc Welding (SMAW) (P5) and Induction welding (P9). Two distinct methods were used to calculate their generation rates: the emission factor EF and the mass balance methods, respectively.

The EFs developed by US EPA for the SMAW process [31] conjointly used with a process-specific fume correction factor FCF developed by the SAN DIEGO Air Pollution Control District [32] showed efficient in emission predictions.

Contrarily to our approach, the unique study that used the NF-FF model in similar process have determined the G using prior air monitoring [2]. The authors have monitored exposure levels inside and outside the helmet, whereas in our case, the welder is not actually wearing such a PPE (personal protective equipment), but only holding it with his hand relatively away from his face (figure 1.12 in part I). This could explain the high exposure levels observed in P5.

We suspect that effective results can also be obtained for the Gas Metal Arc Welding (GMAW) process, because the EFs and the correction factor are constructed using the same methods. Unfortunately, we could not verify this in our study because the workers were simultaneously exposed to two kinds of emission source (P16) and, in this case, the resulting exposure levels were not correlated with the predicted ones.

Elsewhere, the Induction welding process is quite different from the SMAW, mainly because of the absence of consumable filler metal. Results showed good effectiveness of the mass balance method with such process, as long as all quantities and chemical compositions are known.

IV.3.1.3. NF predictions in plastic injection

As previously indicated, the plastic injection process does not involve metallic materials and TMEs are not considered as pollutants in such industry. However, air monitoring results showed TME concentrations in the same order of magnitude as in other job tasks for Al, Zn and Pb. Still, they showed the lowest concentrations for Cr and Ni, and Cu was under the limit of detection.

Surprisingly, our modeling predictions for plastic injection process showed effective results. One element was disregarded because it represented an outlier for the whole sample. Yet, this modeling method presented a significant correlation, with the highest coefficient (r=0.92). In this particular case, because we did not have an idea about the composition of the applied masterbatches, our calculations were based on literature and assumptions. These results confirmed that the mass balance method used with our approach of aggregate exposure from several emission sources is also effective in such processes.

Moreover, for both steel cutting and plastic injection, the volume-weighted averages of Q were calculated for the whole workplace, even though it was separated into two or three compartments (figure 1 and 26 of A1 and A8, respectively). This method was adopted because of lack of information about the quantity of material used in each compartment. Hence, our results showed that our method is sufficiently effective in both cases.

Finally, the determined G values for the 3 latter processes can also be re-used in the same workplaces under different conditions: after a deviation in the number of active machines, in other seasons when the Q are different, or when new material or equipment are introduced or

removed that may change the air volume (machines, stock, etc.), as long as the same amount and kind of material is used.

Nevertheless, it is worth to note that the 95% confidence intervals of the mean differences are rather wide. In similar findings for benzene vapor predictions [25], Nicas et al. stated that this was due to small size samples, with only 10 data pairs. In our study, we had 5, 9 and 10 data pairs for NF concentrations in plastic injection, steel cutting and welding. So, the increase of the size sample is likely to make the intervals shrink.

IV.3.2. Insufficient predict effectiveness of the modeling approach

Absence of correlation in the other job tasks could be due to many reasons we discuss hereafter.

IV.3.2.1. WMB predictions for RSW job task

No significant correlations were found for the Resistance Spot Welding (RSW) process. We believe that this is probably due to the G determination method. Both the emission factor and mass balance were not suitable for the RSW process (discussed in Part I). So we relied on a published study [33] that established an average emission rate calculated from several air monitoring trials in different circumstances. We suggest that the establishment of EFs for the RSW process would be useful.

WMB model was solely used for the RSW process. We believe that our model choice is not responsible for the discrepant results because it had been previously verified by calculating the inter-box air flow rate β near an emission source in case of the NF-FF model and the results showed (discussed in Part I) that the air is perfectly mixed.

IV.3.2.2. FF predictions in packaging job tasks

In the case of packaging job tasks in steel cutting workplaces, while our modeling approach of aggregate exposure from several emission sources effectively predicted the NF emissions, this was not the case for FF emissions. This could be probably due to the fact that air in both fields has to be homogeneously mixed. Now, this is probably not true, because the FF volume is considerably bigger than the NF in the workplaces.

In particular for the predictions in A1, the FF concentrations were higher than the NF concentrations, which violated one of the basics of the NF-FF model [1]. Still, our method

was able to detect the order of magnitude of the FF concentrations compared to the NF concentrations.

IV.3.2.3. Prediction for electroplating job tasks

Only few concentrations were correctly predicted and no correlations were found either for the NF or the FF concentrations.

Contrarily to the EFs used for SMAW process, the EFs were not effective in the generation rate determination especially for Cr. The ready-to-use EFs for Cr unreasonably overestimated the exposure levels in both workplaces with a single or multiple emission sources. This could be explained by the fact that these EFs depend basically on the kind of control system devices. This could be improved because control devices are more efficient nowadays compared to the ones used in the studies from which the EFs were derived decades ago [34].

For the other metals, the calculated EFs presented better results but good predictions were rare. Even when discarding the Cr predictions, no correlation was found. Despite that the calculated EFs are derived from field based information; the Cr EF is incorporated as the reference value, which can be the cause of the non-correlation.

Therefore, establishment of newer EFs that depend on specific field information is needed.

IV.4. Biomonitoring analysis

Biomonitoring results show higher Al, Ni and Cu values in the median urinary concentrations among the metalworking workers (all job tasks) than in non-occupationally exposed workers. In contrast, Cr and Pb concentrations are approximately similar while for Zn, a slightly higher value was observed.

These results for Al are in agreement with the literature. Al elimination depends on the exposure pathway and the metal chemical form. It was reported that contrarily to the oral route, 83% of the inhaled Al is eliminated through urines [14,35]. Since inhalation route is the main pathway in our study and in occupational exposure to Al in general [14,36], the elevated levels in the urines of workers are likely to be due to occupational exposure, in accord with other findings in the literature [36]. Moreover, urinary Al is considered to be a better indicator of occupational exposure than plasma [15,35].

Al accumulates in the human body, notably in the skeleton and the lung [14,36]. The half-life of Al urinary elimination increases with exposure duration and the redistribution of Al in

storage tissues. It is a three-phase process, starting with several hours (up to 40 hours), then some weeks, and a half-life of several months and even years [14].

In a recent study, a biological reference value for urinary Al in the general population was proposed, with a 90th percentile concentration lower than 11.5 µg/L [37].

Our results about Ni also agree with the published studies [17,38]. Urinary Ni does not depend on the exposure pathway and is considered as an indicator for occupational exposure [17].

The European Union Scientific Committee on Occupational Exposure Limits has established a Biological Guidance Values (BVG) for urinary Ni in the general population as 3 µg/L (last update in 2011) [17]. All our study workers, even the non-occupationally exposed ones, have higher urinary levels by 56 and 35 folds, respectively.

The half-life of Ni urinary elimination depends on the solubility of the compounds. For insoluble compounds, it is estimated as several months. For soluble compounds, it is a two phase-process beginning with 1 to 2 days, then it takes 1 to several months [17].

As for the urinary Cu, it is not considered as a good indicator for occupational exposure. This is mainly due to the fact that urinary excretion is low and because of high variations in urinary Cu in the general population [21]. A Belgian study established a biological reference value for urinary Cu in the general population, with the 90th percentile concentration lower than 20 µg/L [39]. In our study, both occupationally and non-occupationally exposed workers exceed this reference value, with the exposed workers presenting 41% higher urinary concentrations, a finding that this excess in urinary Cu could be due to occupational exposure. We do not have firm evidence since no correlation was demonstrated in the literature nor in our study between air monitoring levels and urinary concentrations [21].

The absorption of Cr through inhalation in occupational studies was reported to be more important for Cr(VI) compounds (may be found only in the plating processes in our study). However, Cr(VI) quantification in biological matrices is impossible, because of its rapid reduction to Cr(III). So, urinary Cr is considered as total chromium [20]. Total urinary Cr is considered as a good indicator for occupational exposure. However, it strongly depends on the solubility and the speciation of the metal. It is generally used for specific job tasks, notably electroplating and welding. Among all the six study metals, only Cr had biological limit values specifically established for the electroplating processes : the French agency ANSES

(*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*) has recently constructed a VLB (*Valeur Limite Biologique*) equal to 2.5 µg/L [20].

Cr excretion is mainly urinary and its half-life in urines has 3 phases; it begins with few hours (up to 7 hours), then few days (up to 30 days) and until 4 years.

In our study, median concentrations of urinary Cr, among exposed workers, is similar to that in non-occupationally exposed subjects. And, the concentrations of all job tasks are surprisingly close. This homogeneity suggests that Cr(VI) compounds are almost inexistent in our job tasks and that Cr(III) and metallic Cr are predominant.

Urinary Pb results show slightly higher values among exposed workers. Urinary Pb is not the preferable method to assess occupational exposure because external contamination could alter the results [18]. However, half of the total inhaled dose of inorganic Pb is excreted through urines [40]. An increase in urinary Pb is observed for big particle sizes, notably with metallic dust [40]. For the general population, a recent French study has set a biological reference value for urinary Pb, (3.76 µg/L) corresponding to the concentration of the 90th percentile in the population [37]. Both occupationally and non-occupationally exposed workers exceed this value by 15 and 11 folds, in our study population, respectively.

Finally, urinary Zn is preferred to plasmatic dosage in occupational biomonitring [16]. However, urinary excretion of Zn is partial, about 20%. There is little data about urinary Zn after inhalation in occupational settings but, a study demonstrated a correlation between airborne concentrations and urinary Zn [16].

Nisse et al. have also established a biological reference value for urinary Zn, with the 90th percentile concentration lower than 1.04 mg/L [37]. All our workers urinary Zn levels exceed this concentration by 5 to 22 folds.

In accord with other studies on Al [14], our results show medium correlations between urinary metals and indoor air measured concentrations at the workplace. In a study conducted on Al welders during 5 years [41], a similar average correlation coefficient of 0.367 was found in relationship between the total dust concentration and urinary Al.

As for Cu, it was reported that correlation studies between urinary metals and indoor air concentrations were not strong due to a high variability in urinary Cu in the general population because of many factors such as the pregnancy, estrogen treatments, oral contraceptives and some pathologies [21]. Still, in our study, we found a significant

correlation with a medium correlation coefficient (0.34). Because the majority of the variability factors are related to women, our correlation significance could be explained by the relatively small proportion of women in our sample (~ 23 %). Likewise, strong and significant correlations were reported in a Taiwanese study between Cu aerosols and urinary concentrations solely for the stamping process [42].

Still, the correlations significance were not strong (p-value = 0.04) which is probably due to lack of statistical power in relation with the limited sample size or with interference of the factors mentioned above.

Eventually, correlation results of Al and Cu support that a proportion of TMEs is coming from occupational exposure.

As for Zn, the Biotox report by INRS cited that a significant correlation was only found in the same Taiwanese study as for copper [16,42]. This was not the case in our study. This could be due to the fact that the correlation concerns only the stamping process and similar activities. Besides, it was reported that urinary Zn undergoes important daily variations [16]. So, it might be preferable to conduct several samples during a workweek as it was done in the Taiwanese study [42].

As for Ni and Pb, we found no significant correlation. Only soluble compounds of Ni and organic compounds of Pb were reported to induce correlations between urinary metals and airborne concentrations [17,18]. Thus, we believe that, the chemical form differences were the major reason for our findings.

Urinary concentrations of Al, Ni, Cu and to a lesser extent for Pb, values are greater among the exposed workers, suggesting an occupational origin for Ni and Pb and confirming that for Al and Cu.

Urinary levels of all occupationally or non-occupationally exposed workers exceed the available biological reference values. Now, the differences between exposure pathways (occupational and non-occupational) are less sharp then expected since the administration offices of the 5 companies – where non-exposed subjects were recruited - are either communicating with the metal workplaces through doors, or have doors or windows directly next to those of the metal working areas. This gives place to indirect exposure via ventilation and air flow.

Unfortunately, we did not measure metal particles in the office areas, mainly for time constraints reasons. This impaired our ability to include in our analysis data that are more spread, yielding limitations in statistical power. Moreover, it would be interesting to select other non-occupationally exposed persons outside the industrial field, such as students, in order to more firmly test our assumption.

Further, we cannot rule out other scenarios such as environmental pollutant sources or other specific sources in relation to population life-styles. For instance, the use of aluminum cooking vessels is very common in Tunisia. So, this could be a possible source of oral exposure. Finally, little is known about metals in food products in the study region, which could be another source of exposure variability. Inclusion of alternative non-occupationally exposed persons could help explore these confounding factors in future studies.

V. Conclusion of part 2

In this second part, our main objective was to compare airborne measured concentrations of TMEs with a number of modeling approaches in different task jobs in order to "validate" their usage.

We used correlation methods to assess the association between them and Student's *t*-test to have an exact idea about the mean differences and their confidence intervals. This step showed a significant to strongly significant global correlation. After stratification of the concentrations according to their job tasks and modeling method, NF concentrations predictions showed to be significant for steel cutting, welding and plastic injection. Moreover, their correlation coefficients are relatively high.

In a second step, we explored the correlations between urinary metals and indoor air measured concentrations. There were significant correlations only for Al and Cu, suggesting that they are due to occupational exposure. Still, we think that enlarging the size of our population and taking multiple samples for each worker might improve correlations.

Higher Al, Ni and Cu urinary levels were observed among metal working subjects, confirming the correlation findings for Al and Cu and also suggesting that they are due to occupational exposure. But, even non-occupationally exposed workers have high urinary metals for the six study metals. We believe these subjects were indirectly occupationally exposed through ventilation sources.

VI. Bibliography

1. Mark Nicas. Chapter 6: The Near Field/ Far Field (two box) Model with a constant contaminant emission rate. Math Models Estim Occup Expo Chem. USA: AIHA press; 2009. p. 47–52.

2. Boelter FW, Simmons CE, Berman L, Scheff P. Two-Zone Model Application to Breathing Zone and Area Welding Fume Concentration Data. J Occup Environ Hyg. 2009;6:298–306.

3. Arnold SF, Shao Y, Ramachandran G. Evaluation of the well mixed room and near-field far-field models in occupational settings. J Occup Environ Hyg. 2017;14:694–702.

4. Base de données MétroPol - Publications et outils - INRS [Internet]. [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/metropol.html

5. SKC Inc. SKC, Inc. [Internet]. SKC Inc. [cited 2018 Apr 5]. Available from: http://www.skcinc.com/catalog/index.php

6. Filter Cassettes, Blank, 37 mm, Clear Styrene, SKC, Inc. [Internet]. [cited 2016 Jun 13]. Available from: http://www.skcinc.com/catalog/product_info.php?products_id=343

7. INRS. Métaux et métalloïdes M-122 - MétroPol [Internet]. 2016 [cited 2016 Jun 13]. Available from: http://www.inrs.fr/publications/bdd/metropol/fiche.html?refINRS=METROPOL_122

8. Quartz Filters, 1.2 µm, 37 mm, Type R-100, SKC, Inc. [Internet]. [cited 2016 Jun 13]. Available from: https://www.skcinc.com/catalog/product_info.php?products_id=254

9. INRS. Prélèvement des aérosols par cassette fermée [Internet]. 2015. Available from: http://www.inrs.fr/dms/inrs/PDF/metropol-prelevement-principe.pdf

10. INRS. Préparation des dispositifs de prélèvement en vue d'une intervention en entreprise. 2015.

11. INRS. Principe général et mise en œuvre pratique du prélèvement [Internet]. 2015 [cited 2016 Sep 16]. Available from: http://www.inrs.fr/dms/inrs/PDF/metropol-prelevement-principe.pdf

12. OSHA Technical Center. METAL AND METALLOID PARTICULATES IN WORKPLACE ATMOS PHERES (ICP ANALYSIS) [Internet]. 2002 [cited 2014 Aug 18]. Available from: https://www.osha.gov/dts/sltc/methods/inorganic/id125g/id125g.pdf

13. INRS. Calcul de la concentration en polluants - Métropol. 2015.

14. INRS. Aluminium et composés (7429-90-5) / Aluminium urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_2

15. Riihimäki V, Aitio A. Occupational exposure to aluminum and its biomonitoring in perspective. Crit Rev Toxicol. 2012;42:827–53.

16. INRS. Zinc et composés (7440-66-6) / Zinc urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_73

17. INRS. Nickel et composés (7440-02-0) / Nickel urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_47

18. INRS. Plomb et composés (7439-92-1) / Plomb urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_53

19. Base de données Biotox - Publications et outils - INRS [Internet]. [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox.html

20. INRS. Chrome et chromates (7440-47-3) / Chrome urinaire - Biotox - INRS [Internet]. 2018 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_23

21. INRS. Cuivre et composés (7440-50-8) / Cuivre urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_27

22. Goullé J-P, Mahieu L, Castermant J, Neveu N, Bonneau L, Lainé G, et al. Metal and metalloid multi-elementary ICP-MS validation in whole blood, plasma, urine and hair. Forensic Sci Int. 2005;153:39–44.

23. Nicas M, Plisko MJ, Spencer JW. Estimating Benzene Exposure at a Solvent Parts Washer. J Occup Environ Hyg. 2006;3:284–91.

24. Plisko MJ, Spencer JW. Evaluation of a mathematical model for estimating solvent exposures in the workplace. J Chem Health Saf. 2008;15:14–21.

25. Nicas M, Neuhaus J. Predicting Benzene Vapor Concentrations with a Near Field/Far Field Model. J Occup Environ Hyg. 2008;5:599–608.

26. Spencer JW, Plisko MJ. A Comparison Study Using a Mathematical Model and Actual Exposure Monitoring for Estimating Solvent Exposures During the Disassembly of Metal Parts. J Occup Environ Hyg. 2007;4:253–9.

27. Kahn HD. Note On The Distribution of Air Pollutants. J Air Pollut Control Assoc. 1973;23:973–973.

28. KAN H-D, CHEN B-H. Statistical Distributions of Ambient Air Pollutants in Shanghai, China. :7.

29. Larsen RI. A New Mathematical Model of Air Pollutant Concentration Averaging Time and Frequency. J Air Pollut Control Assoc. 1969;19:24–30.

30. Charles B. Keil. Chapter 3: Modeling Pollutant Generation Rates. Math Models Estim Occup Expo Chem. USA; 2009.

31. US EPA Office of Air Quality Planning and Standards, US EPA. Chapter 12: Metallurgical Industry, section 19: Electric Arc Welding. AP 42 Compil Air Pollut Emiss

Factors [Internet]. Fifth Edition. 1995. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

32. SAN DIEGO Air Pollution Control District, editor. WELDING OPERATIONS [Internet]. 1998 [cited 2018 Jan 9]. Available from: http://www.sdapcd.org/content/dam/sdc/apcd/PDF/Toxics_Program/APCD_welding1.pdf

33. Gerhard Pohlmann, Charly Holzinger, Vilia Elena Spiegel-Ciobanu. Comparative investigations in order to characterise ultrafine particles in fumes in the case of welding and allied processes. Weldingand Cut [Internet]. 2013;12. Available from: https://www.bghm.de/fileadmin/user_upload/Arbeitsschuetzer/Fachinformationen/Schweissen/00_WC2_SpA_w20000014__.pdf

34. US EPA Office of Air Quality Planning and Standards. Chapter 12: Metallurgical Industry, section 20: Electroplating. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1996. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

35. Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, et al. HUMAN HEALTH RISK ASSESSMENT FOR ALUMINIUM, ALUMINIUM OXIDE, AND ALUMINIUM HYDROXIDE. J Toxicol Environ Health B Crit Rev. 2007;10:1–269.

36. ATSDR. Toxicological Profile: Aluminum [Internet]. 2008. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=191&tid=34

37. Nisse C, Tagne-Fotso R, Howsam M, Members of Health Examination Centres of the Nord − Pas-de-Calais region network, Richeval C, Labat L, et al. Blood and urinary levels of metals and metalloids in the general adult population of Northern France: The IMEPOGE study, 2008-2010. Int J Hyg Environ Health. 2017;220:341–63.

38. ATSDR. Toxicological Profile: Nickel [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=245&tid=44

39. Hoet P, Jacquerye C, Deumer G, Lison D, Haufroid V. Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium. Clin Chem Lab Med. 2013;51:839–49.

40. ATSDR. Toxicological Profile: Lead [Internet]. 2007. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22

41. Rossbach B, Buchta M, Csanády GA, Filser JG, Hilla W, Windorfer K, et al. Biological monitoring of welders exposed to aluminium. Toxicol Lett. 2006;162:239–45.

42. Wu C-C, Liu H-M. Determinants of Metals Exposure to Metalworking Fluid Among Metalworkers in Taiwan. Arch Environ Occup Health. 2014;69:131–8.

3rd PART:

Risk Characterization of Occupational Exposure to Trace Metallic Element Mixtures in Metalworking Industrial Indoor Air

3rd PART: Risk Characterization of Occupational Exposure to Trace Metallic Element Mixtures in Metalworking Industrial Indoor Air

I.   Introduction

In a Human Health Risk Assessment HHRA framework context, we have identified the used TMEs and quantified them in indoor air. Potential adverse effects on biological endpoints/ target organs were previously explored according to the inhalation exposure route. Then, in the dose-response step, reference values will be investigated. Finally, in the risk characterization final step, all information from the three previous steps will be gathered to associate and interpret the potential risk(s) for the exposed population.

The main objective of this part is to characterize the risk of the TME mixture in the metalworking industries. To do so, we selected threshold and non-threshold reference values.

Afterwards, we used a method that integrates the interactions between the mixtures' components for risk characterization by using the weight of evidence derived from the literature. In addition, a carcinogenic risk of the mixture was quantified.

II.   Materials and methods

II.1.   Hazard identification

Toxicological data were explored in the Toxicological Profiles documents from ATSDR [1–7], the IRIS (Integrated Risk Information System) from USEPA [8–16] and in the Toxicological Sheets from INRS [17–23].

II.2.   Reference values selection

II.2.1.   Toxicological reference values *vs* occupational exposure limit values

The toxicological reference values (TRV) generally correspond to quantitative theoretical estimations on which a population could be exposed to a particular substance without an observed adverse effect [24]. They are indicators of the dose-effect relationship [25]. TRVs are developed based on epidemiological and most commonly on toxicological available studies. These values are specific to the effect/ target organ, to the exposure pathway (inhalation, oral and dermal) and to exposure durations (acute, sub-chronic and chronic) [26]. There are two kinds of TRVs; (i) for threshold effects and (ii) for non-threshold (most commonly, carcinogenic) effects.

Whereas the occupational exposure limit values, called in French *Valeurs Limites d'Exposition Professionnelle* (*VLEP*), established for prevention purposes in order to protect the exposed workers from chemical substances that could induce occupational illnesses. They are currently constructed only for the inhalation route and only for threshold endpoints. They are also developed based on toxicological data, but preferably on occupational exposure studies [25]. Moreover, extrapolation method is different than for TRVs and less protective because it only considers occupationally-exposed populations and often stem from negotiations between the different stakeholders [26].

II.2.2.   Selection arguments

In a research context dealing with environmental health studies, TRVs are used or developed for the general population. As to occupational health studies, researchers can choose either TRVs or *VLEPs* according to their needs and objectives [24,25]. For the same pollutant, the *VLEP* threshold concentrations value is significantly higher than the TRV, due to less protective conversion and security factor [25]. *VLEPs* are established to prevent well established occupational illnesses, however, they do not necessarily protect workers from "non-severe" and reversible effects, such as irritations [26]; one may also question to what extent some effectively protect against known effects, given the magnitude of the difference with the corresponding TRVs.

In our study, in a context of HHRA, we decided to use the TRVs of the selected TMEs for the inhalation route and for chronic exposure, in order to reduce health risks.

TRVs of Al, Cr, Ni, Cu, Pb and Zn were explored within the World Health Organization data sets and browsing reports from numerous national and regional agencies that are constructing TRVs. We will highlight hereafter the most known and well-recognized Agencies from France, Netherlands, United States of America and Canada.

II.2.3.   Choice of critical toxic effects

In order to establish risk characterization of TMEs mixture, critical toxic effects are explored. Then, common toxic effects, by target organ, of TMEs' combination are identified.

II.3. Methods of health risk assessment for chemical mixtures

II.3.1. Addition hazard index

The hazard Index HI is simply calculated as below;

$$HI = \sum_{i=1}^{n} HQ_i = \sum_{i=1}^{n} \frac{Exposure_i}{TRV_i}$$

The main advantages of the HI method are: transparency, easiness to understand and direct relationship to TRVs [27,28].

However, it has many shortcomings such as the summation of individual uncertainty factors [28] and the total neglect of possible interactions between the components [29], which can lead to either over or under-estimation of the risk. It is recommended to be quite careful with the interpretation of HI results values [27].

II.3.2. Interaction-based hazard index

The interaction-based Hazard Index HI_{int} is a modified Hazard Index that takes into account binary interactions data between chemicals. It was initially introduced by the US-EPA [29] to improve the dose-additive hazard index, which underestimates cumulative risk.

The final following formula was introduced by US EPA [29]:

$$HI_{INT} = \sum_{j=1}^{n} HQ_j \cdot \left(\sum_{k \neq j}^{n} f_{jk} \cdot \left(M_{jk} \right)^{B_{jk} \cdot g_{jk}} \right)$$

Where;

M_{jk}: the magnitude of the interaction between the component j and k;

B_{jk}: the WOE (weight of evidence) score for the interaction of chemical j affecting toxicity of chemical k. These scores are fixed depending on a classification [29,30];

f: the exposure factor: it is the toxic hazard of the kth chemical relative to the total hazard from all components possibly interacting with chemical j (so k cannot equal j), and is expressed by the following formula; $f_{jk} = \frac{HQ_k}{HI - HQ_J}$

g: weighting factor for relative proportions of the components j and k and is expressed by the following formula; $g_{jk} = \dfrac{\sqrt{HQ_j HQ_k}}{(HQ_j + HQ_k)/2}$

The WOE scoring method was originally established by Mumtaz and Durkin [30,31]. Then, US EPA slightly modified the scores to derive a simpler classification [29].Score attribution depends on the available evidence of toxicological interactions in the literature. The B score is a number that varies from -1 to +1. We decided to use the original classifications and scores, because they are more detailed [30,31]. Moreover, they were also adopted in HI_{int} calculations for other combinations of metal mixtures [32,33].

Binary WOE scores are calculated as following:

$$B_{WOE} = Direction\ factor\ \times weighting\ factor$$

$$weighting\ factor = \prod weighting\ scores$$

The used factors and scores are summarized in the tables 3.1 [30].

The interaction magnitude M is defined as a proportionality factor of additivity deviation that varies from 0.2 to 5 according to US EPA. Moreover, it could be derived by dividing the observed ED_x by the predicted ED_x for dose addition [34]. ED_x is the Effective Dose of x % response rate in test animals [29]. In practice, studies frequently describe the magnitude of interaction qualitatively. Hence, a default value of 5 is recommended in case of lack of data [29]. Thus, depending on the available data, we are trying to determine M from studies conducted on animals. Otherwise, the default value of 5 is used.

HI_{int} can be calculated using RfCs for different effect/ target organ of interest. However, to be more specific and consistent, target organ specific HI_{int} is preferred. Risk estimate based on VTRs for a different effect can lead to an overestimation [27]. Indeed, Teuschler [35] recommends that the basic level of similarity between the mixture components required for chemical mixture risk assessment is a common toxic effect /target organ.

Thus, HI_{int} for a common toxic effect(s)/ target organ (s) will be calculated for the metalworking industry by selecting the 90th percentile concentrations of all measured data for each selected TME.

Table 3.1: (a) Classification and (b) scores of the WOE method:

(a)

Classification	Direction of Interaction	Direction factor
=	Additive	0
>	Greater than additive	+1
<	Less than additive	- 1
?	Indeterminate	0

(b)

Category	Quality of the Data	Weighting scores
Mechanistic Understanding		
I	Direct and Unambiguous Mechanistic Data: The mechanism(s) by which the interactions could occur has been well characterized and leads to an unambiguous interpretation of the direction of the interaction.	1.0
II	Mechanistic Data on Related Compounds: The mechanism(s) by which the interactions could occur have not been well characterized for the chemicals of concern but structure-activity relationships, either quantitative or informal, can be used to infer the likely mechanisms(s) and the direction of the interaction.	0.71
III	Inadequate or Ambiguous Mechanistic Data: The mechanism(s) by which the interactions could occur has not been well characterized or information on the mechanism(s) does not clearly indicate the direction that the interaction will have.	0.32
Toxicological Significance		
A	The toxicological significance of the interaction has been directly demonstrated.	1.0
B	The toxicological significance of the interaction can be inferred or has been demonstrated for related chemicals.	0.71
C	The toxicological significance of the interaction is unclear.	0.32
Modifiers		
1	Anticipated exposure duration and sequence	1.0
2	Different exposure duration or sequence	0.79
a	In vivo data	1.0
b	In vitro data	0.79
i	Anticipated route of exposure	1.0
ii	Different route of exposure	0.79

II.3.3. Total cancer risk

It was previously named as "excess or incremental risk" by the US EPA [36]. The total cancer risk is a response–addition method for carcinogenic pollutants [30]. It assumes that

carcinogens could have independent actions. It can also be calculated for different types of cancers [37].

It is calculated by summing the individual cancer risks [30]:

$$Total\ cancer\ risk = \sum_i cancer\ risk\ _i \sum_i UR_i \times C_{exp,i}$$

Where:

UR_i: is the slope factor (carcinogenic potency) for carcinogenic i

$C_{exp,\ i}$: is the exposure concentration of carcinogenic i.

III.   Results

III.1.   Occupational exposure limit values

Table 3.2 exhibits occupational exposure limit values constructed by official institutions from France, Germany and the United States of America.

The indoor air concentrations of the majority of the TMEs in our study plants are under these regulatory values.

However, concentrations exceed these values for the job posts P10 and P11 where Cr(VI) compounds are used. When compared to the most protective limit value -the PEL constructed by NIOSH [38] - the Cr airborne concentrations exceed the PEL for P11 (0.000247 mg Cr/ m^3), and by twofold for P10 (0.000432 mg Cr/ m^3).

Table 3.2: Occupational exposure limit values from different institutions to TMEs of concern

DATA BASE	Al (mg.m^{-3})		Cr (mg.m^{-3})			Ni (mg.m^{-3})		Cu (mg.m^{-3})		Pb (mg.m^{-3})	Zn (mg.m^{-3})	
	Metal *	Fumes**	Metal *	Cr III	Cr(VI) compounds as Cr	Dust *	Fumes/ mist **	Dust	Fumes		Dust*	fumes
VLEP [a] (France) [17]	10 [22]	5 [22]	-	-	0.001*** [23]	1	-	1 [21]	0.2 [21]	0.1[19]	10 [20]	5 [20]
TLV®[b] by ACGIH®[c] 2017 (USA) [38]	1	-	0.01	0.5	0.05*** [23]	0.2	0.1	1	0.2	0.05	2	2
MAK[d] (Germany) [17]	4 [22]	-	-	-	-	-	-	0.1 [21]	-	-	2 [20]	2 [20]
PEL[e] by OSHA[f] (USA) [38]	5	-	1	0.5	-	1	1	1	0.1	-	5	5
PEL[e] by Cal/ OSHA[g] (USA)[38]	5	-	0.5	0.5	0.005***	0.1	0.05	1	0.1	0.05	5	5
PEL[e] by NIOSH[h] (USA) [38]	5	5	0.5	0.5	0.0002***	0.015	0.015	1	0.1	0.05	5	5

[a] *Valeurs Limites d'Expositions Professionnelles*

[b] Threshold Limit Value

[c] American Conference of Governmental Industrial Hygienists

[d] *Maximum Permissible Concentration*

[e] Permissible Exposure Limit

[f] Occupational Safety and Health Administration

[g] Division of Occupational Safety and Health in California

[h] National Institute for Occupational Safety and Health

*Metal/ insoluble inorganic compounds** Soluble inorganic compounds*** as chromium

III.2. Toxicological reference values for selected trace metallic elements

III.2.1. Data availability

TRVs of the selected TMEs (Al, Cr, Ni, Cu, Pb and Zn) were explored. We gave precedence to the most known and well-recognized Agencies: Agency for Toxic Substances and Disease Registry (ATSDR) [6], IRIS (Integrated Risk Information System) by US EPA [39], the French *Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail* (ANSES) [40], Health Canada [41], California Office of Environmental Health Hazard Assessment (OEHHA) [42], Texas Commission on Environmental Quality (TCEQ) [43] and Netherlands National Institute for Public Health and the Environment (RIVM) [44] (in Table 3. 3 and 3.4).

A target-organ toxicity dose TTD or TTC ('concentration', for inhalation [29]) can be used as a TRV if the latter is constructed for a different target organ [29,45]. The ATSDR endorsed the TTD concept [30] and derived target-organ toxicity values for some TMEs but only for oral exposure in the interaction profiles intended for metals [30,46].

Sometimes, we have more than one VRT for the same substance. We decided to choose the most protective one. TRVs for Cu, Cr, chromic acid, Ni, NiSO$_4$and Pb are listed in the two tables below. Table 3.3 contains threshold TRVs from different agencies for chronic inhalation exposure, and the second one, 3.4, includes non-threshold unit risks.

Table 3.3: Threshold TRVs from different Agencies of chronic inhalation exposure to MHs of concern

DATA BASE	Al	Cr metal & CrIII insoluble compounds	Ni Metal & dust	Cu	Pb	Zn
ATSDR	*NM* [5]	MRL[a] = 5 µg.m^{-3} [7]	*NM* [3]	*NM* [1]	*NM* [4]	*NM* [2]
USEPA	*NM*	*NM* [15]	*NM* [8–10]	*NM* [11]	*NM* [13]	*NM* [14,47]
ANSES [40]	*NM*	*NM*	*NM*	*NM*	*NM*	*NM*
Health Canada [41]	*NM*	*NM*	TC[b] = 0.018 µg. m^{-3}	*NM*	*NM*	*NM*
OEHHA	*NM*	*NM* [48]	REL[c] = 0.014Ni µg. m^{-3} [49]	*NM* [50]	*NM* [51]	*NM*
WHO [52]	*NM*	*NM*	*NM*	*NM*	*NM*	*NM*
TCEQ [43]	*NM*	Chronic ReV[d] = 0.14 µg. m^{-3} [53]	Chronic ReV[d] = 0.23 µg. m^{-3} [54]	*NM*	*NM*	*NM*
RIVM [44]	*NM*	TCA[b] = 60 µg.m^{-3}	TCA[b]= 0.05 µg. m^{-3}	TCA[b] = 1 µg.m^{-3}	*NM*	*NM*

Table 3.4:Non-threshold unit risks from different Agencies of chronic inhalation exposure to MHs of concern

DATA BASE	Al	Cr metal & CrIII insoluble compounds	Ni Metal& dust	Cu	Pb	Zn
ATSDR	*NM* [5]	*NM* [7]	*NM* [3]	*NM* [1]	*NM* [4]	*NM* [2]
USEPA	*NM*	*NM*	UR^e = 1.8 .10^{-4} per µg. m^{-3}	*NM*	*NM*	*NM*
ANSES	*NM*	*NM*	*NM*	*NM*	*NM*	*NM*
Health Canada [41]	*NM*	*NM*	*NM*	*NM*	*NM*	*NM*
OEHHA	*NM*	*NM*	*NM*	*NM*	UR^e= 1.2 10^{-5} per µg. m^{-3}	*NM*
WHO [52]	*NM*	*NM*	UR^e = 3.8.10^{-4} per µg. m^{-3}	*NM*	*NM*	*NM*
TCEQ [43]	*NM*	*NM* [53]	URF^e =1.7 10^{-4} per µg. m^{-3} [54]	*NM*	*NM*	*NM*
RIVM [44]	*NM*	*NM*	*NM*	*NM*	*NM*	*NM*

NM: Not Mentioned,

[a]: Minimal Risk Levels

[b]: Tolerable Concentration in Air

[c]: Chronic Reference Exposure

[d]:Level Reference Value

[e]: inhalation Unit Risk or Unit Risk Factor: increased cancer risk from inhalation exposure to a of 1 µg.m^{-3} for a lifetime

[f]:The Tumorigenic Concentration 05: concentration in air associated with a 5% increase in incidence or mortality due to tumors (is used to calculate a unit risk)

III.2.2. TRVs selection

Table 3.5 and 3.6 show the selected, most protective, TRVs for threshold and carcinogenic critical effects /target organs.

Table 3.5: Non-carcinogenic critical effects /target organs and most protective TRVs for chronic inhalation exposure to MHs of concern

Metal	Target organ	Most protective TRVs	Agency
• Al	-	-	-
Cr: Metal	lung and respiratory tract effects	Chronic ReV = 0.14 μg. m^{-3}	**TCEQ** [53]
• Ni: metal & dust	Lung damage & inflammation	REL = 0.014 Ni μg. m^{-3}	**OEHHA** [49]
• Cu	Respiratory tract effects	TCA = 1 μg.m^{-3}	**RIVM** [44]
• Pb	-	-	-
• Zn	-	-	-

Table 3.6: Carcinogenic critical effects and most protective TRVs for chronic inhalation exposure to MHs of concern

Metal	Carcinogenic critical effect	Most protective TRVs	Agency
• Al	-	-	-
• Cr	-	-	-
• Ni: metal & dust	Lung cancer	UR = 3.8.10^{-4} per μg. m^{-3}	**WHO** [52]
• Cu	-	-	-
• Pb	Kidney cancer	UR= 1.2 10^{-5} per μg. m^{-3}	**OEHHA** [55]
• Zn	-	-	-

III.3. Critical effects

III.3.1. Effects with thresholds

The respiratory tract is the common target organ of chronic exposure to Cu, Cr, Ni (table 3.5). Both the upper and the lower respiratory tract are involved. Several adverse effects were identified. They include active lung inflammation (Ni [3] and Cr [7]), up to pathological changes in lungs (Ni [49] and Cr [53]) and morphological and functional changes in alveolar cells (Ni [41,56]) such as septal cell hyperplasia (Cr [7]).

III.3.2. No-threshold effects

Lung cancer is confirmed to be the non-threshold critical effect of chronic inhalation exposure to Ni. As to Pb, the non-Threshold effect is kidney cancer.

III.4. Risk characterization of trace metallic element mixtures in metalworking industries

III.4.1. Threshold risk characterization

III.4.1.1. Weight of evidence for binary toxic interactions

Binary toxic interactions were explored for the 3 metals Cr, Ni and Cu.

A study showed that CrIII has a synergetic effect on Ni by enhancing severe respiratory effects. It was conducted on rabbits exposed by the inhalation route over 4 months [3].

Two in vitro studies [57,58] showed an antagonistic effect of non-toxic concentrations of Ni on Cr cytotoxicity. However, cytotoxic concentrations of Ni showed a synergetic effect on Cr [59]. Other synergistic effects of Ni on Cr were demonstrated in DNA damage and oxidative stress [57]. Since we are adopting a protective scenario, the synergetic effect is adopted in the WOE scoring.

A study on rats exposed by ingestion observed an increase in copper deficiency when Ni was added to the diet [60]. The mechanism of interaction between Ni and Cu was not well characterized.

In vitro study showed a strong synergetic effect of small concentrations of Cu on the cytotoxicity of Ni towards alveolar macrophages extracted from rabbits [61]. However, when

the Cu concentrations were increased, the interaction was hardly noticeable. Since we are adopting a protective scenario, an indeterminate effect is adopted in WOE scoring.

An in vitro study assessed and showed and antagonistic effect of Cu on the mutagenic health effects of Cr [7].

Table 3.7: Binary WOE scoring (see table 3.1 for the scores of the WOE method)

Effect of	On the toxicity of		
	Cr	Ni	Cu
Cr		>II A 1 a i (+0.71) [3]	? (0)
Ni	> I A 2 b ii (+0.493) [57,58]		< II A 2 a ii (-0.443) [60]
Cu	< I A 2 b ii (-0.493) [7]	? II A 2 b ii (0) [61]	

NB: In reference to table 3.1, the case for the effect of Cr on the toxicity of Ni should be read as>**II A 1 a i (+0.71)**; >**(corresponding to +1):** Direction of Interaction is Greater than additive, **II(score = 0.71):** Mechanistic data have not been well characterized for the chemicals of concern, **A(score = 1):** The toxicological significance of the interaction has been directly demonstrated, **1(score = 1):** Anticipated exposure duration and sequence, **a (score =1):** In vivo data, **i(score =1):** Anticipated route of exposure.

III.4.1.2. Health risk of TMEs mixture in metalworking industries

We began with individual hazard quotient HQ calculations of the 90th percentile concentrations of the metalworking industry for the three metals that yield respiratory effects, Cr, Ni and Cu. Then, the addition HI was calculated in order to compare it with the interaction-based HI_{int} for respiratory adverse effects (Table 3.8).

We can clearly note that even individual HQs exceed one, up to 67.9 for Ni.

Then, after the combination of all WOE data that span from antagonistic to synergetic effects, the value of HI_{int} showed a value greater than the addition HI_{add}, suggesting that a global interaction between Cr, Ni and Cu leads to more than additive effect.

Table 3.8: HQs of Cr, Ni and Cu and addition HI and interaction-based HI$_{int}$ for respiratory / lung effects

	Cr	Ni	Cu
90th-percentile concentrations (μg/m^3)	0.58	0.95	1.80
HQ $_{90P}$	4.1	67.9	1.8
HI$_{add}$	73.8		
HI$_{int}$	93.6		

III.4.2. Non-threshold risk characterization

The total cancer risk is calculated using the 90th percentile concentrations for Ni and Pb for two different kinds of cancers. The resulting value in table 3.9 means that more than 3 additional cases of cancer are expected to occur during a lifetime in a population of 10000 persons.

Table 3.9: Lifetime cancer risks of Ni and Pb and total cancer risk

	Ni	Pb
90-percentile concentration (μg/m^3)	0.950	0.400
Cancer Risk $_{90P}$	Lung cancer: 3.6×10^{-4}	Kidney cancer: 4.8×10^{-6}
Total Cancer Risk	3.7×10^{-4}	

IV. Discussion

IV.1. Limitations in the literature data

IV.1.1. Toxicological reference values

TRVs of chronic exposure by inhalation have been explored by several agencies. However, among the six selected TMEs, Al, Zn and Pb do not currently have published TRVs for threshold effects, nor Al, Cr, Cu and Zn for non-threshold effects. This is principally due to

lack of quantitative exposure data to establish an appropriate dose-response relationship. ATSDR indicates that additional toxicological studies are needed to establish chronic-duration TRVs [1,2,62].

Yet, it is worth to note that other forms of Ni and Cr did have threshold and non-threshold TRVs. These chemical compounds are nickel sulfate $NiSO_4$ and the chromic acid CrH_2O_4 that we can usually be used in electroplating processes.

The respiratory tract is also the target organ of chronic exposure to CrH_2O_4 and $NiSO_4$. Both the upper and the lower respiratory tract are involved. The identified adverse effects vary from nasal irritations (CrH_2O_4 [7]), active lung inflammation ($NiSO_4$ [41,56], and hypergenesis of dust cells ($NiSO_4$ [41,56]).Thus, threshold TRVs were established for Ni sulfate by ATSDR [3] and Health Canada [41]; MRL = 0.09 µg Ni/m^3 and TC = 0.0035 µg Ni/m^3 respectively. As for chromic acid, only OEHHA has established a REL (reference exposure level) equal to 0.002 µg Cr/m^3 that could be used with total Cr concentrations [48].

Moreover, CrH_2O_4 is considered to be a Cr(VI) compound. Hence, both CrH_2O_4 and $NiSO_4$ are also considered to induce lung cancer. A unit risk was established by USEPA [15] UR= 1.2 $.10^{-2}$ per $µg.m^{-3}$. And Health Canada [41], has constructed a Tumorigenic Concentration 05 TC_{05}= 0.07 mg. m^{-3}.As previously mentioned, it is not a carcinogenic TRV, but a unit risk can be derived from this value.

Threshold TRVs of $NiSO_4$ and CrH_2O_4 are considered for total metal exposure. If we compare them with the formerly adopted threshold TRVs of elemental metal, we can notice that the most protective threshold TRV of $NiSO_4$ proposed by Health Canada [41] is 4 times lower than the TRV adopted for Ni. And the threshold TRV of CrH_2O_4 is 70 times lower than the TRV adopted for Cr. If we had the possibility to use exposure data on $NiSO_4$ and CrH_2O_4 to compute specific HI_{int} for electroplating process, the result would most probably show a high value. Unfortunately, this was not possible because both Ni and Cr are released within complex mixtures where other substances are present in the plating baths besides $NiSO_4$ and CrH_2O_4, and we cannot know how much Ni or Cr are released as $NiSO_4$ and CrH_2O_4, respectively.

As a perspective, for future analyses or studies, an electroplating specific HI_{int} can be calculated by $NiSO_4$ and CrH_2O_4 quantifications, either by monitoring or by modeling if

possible. There are methods to calculate the evaporation amount from open surfaces [63]. However these methods were established and used for single chemical substances and not for complex mixtures, mainly because they use physico-chemical properties of the liquid.

IV.1.2.   Weight of evidence of binary toxic interactions

Toxicological interactions between TMEs are mainly accommodated by ATSDR in their two interaction profiles [46,64]. However, binary combinations for Cr, Ni and Cu have not been investigated in these profiles. Elemental toxicological profiles of the study metals were explored for interaction data. Two by two interactions were mostly characterized according to in vitro and in vivo published data. Yet, the interaction effect of Cr on the toxicity Cu could not be determined because of lack of data, according to the best of our knowledge. Additional toxicological and mechanistic studies on mores TMEs combinations would be of a great use to implement the WOE method.

IV.2.   Toxicological Reference Values

IV.2.1.   Choice of TRVs for risk characterization

As previously mentioned, in the HHRA research context of occupational exposure, one may not only *VLEPs* (the French version), but also TRVs. Hence, in our study, the TRVs were chose over the occupational exposure limit values *VLEP* for the reasons we comment hereafter.

VLEP are especially developed to manage risks to occupational populations. They incorporate small uncertainty factors, compared to TRVs, because the occupational settings are considered to be principally controlled by the implementation of collective protective equipment [26]. Indeed, in occupational settings, compliance with these values also encompasses usage of these protective tools [25]. However, the presence, and effectiveness of such equipment is variable from a company to another, especially in Tunisia where industrial surveillance of exposure levels is not obligatory.

Moreover, even in countries where the collective protective equipments are more effective than in Tunisia, compliance with *VLEP* is not always a guarantee to prevent adverse effects on human health. In many cases, *VLEP* values are quite high because they are negotiated values. Indeed, throughout the construction of *VLEPs,* other inputs than scientific data are

used. Stakeholders such as governmental departments, workers unions, industrial corporations, etc. contribute also in the establishment of the *VLEPs* by considering their applicability and economic costs [26].

On the other hand, TRVs are strictly constructed based on a scientific basis and evidence from toxicological and epidemiological studies throughout rigorous construction methods. In our case, based on animal exposure studies and uncompromising quality construction approaches, TRVs derived from BMD approach "Benchmark Dose" (for Cr [53] and Ni [49]) or from the NOAEL approach "No-Observed-Adverse-Effect Level" (for Cu [44]) are considered to provide a high level of protection against respiratory adverse effects, when not exceeded, whereas one cannot guaranty a high protection level of *VLEPs*.

Elsewhere, when it comes to exposure to mixtures, research studies are increasingly demonstrating that the exposure limit values, even in some cases including the most protective ones such as TRVs, are not absolutely protective [65] because these values were established based on single exposure studies where the pollutant is considered individually, not taking account of interactions.

Therefore, we believe that the use of TRVs is more prudent to study health impacts, especially when dealing with mixtures. Unlike *VLEPs*, TRVs also allow to explore the interaction implications on the risk level.

Of relevance for the purpose of our study, there is a decision support tool named "Mixie" that can be used for risk characterization using the *VLEP*. It calculates an "*Indice d'exposition des effets Additionnels* " noted IAE (or Rm in the Canadian version) that is similar to the addition the HI we used, but applied to *VLEPs* data instead of TRVs. Mixie was developed by Montreal University and the "*Institut de recherche Robert-Sauvé en santé et sécurité au travail*" [66], and revised by the INRS in the French version [67]. This tool is designed to help assess multi-exposure to chemicals in occupational settings. However, it integrates all *VLEPs*, irrespective of specific critical effects or target organs. Now, in order to aggregate the effects of a mixture, it is considered to be more rigorous to use TRVs that are established for the same endpoint [35].

Moreover, analogously to the addition HI, this tool does not take into account interactions between the components. Thus, we believe that Mixie could be an alternative in cases when no TRV is available but should be used with caution in such circumstances.

Finally, we believe that our findings support the relevance of our choice because even though the *VLEPs* were exceeded only in two job posts, the HI_{int} calculated for the 90th percentile concentrations in our study population tremendously exceeded unity (93.6).

IV.2.2.   TRVs selection

The most protective TRVs were chosen. However, we are aware that they may not always be the most well grounded ones. That is why; we only relied on the best known agencies that are known to conduct high quality evaluations and reports. Moreover, we checked the critical studies, the critical effect/ target organ, the duration and route of exposure in the critical study, the tested species or population, the derivation methodology and the uncertainty factors that had been used.

Since all the critical effects were about the respiratory tract for threshold TRVs and lung cancer for Ni, we considered them as comparable values and decided to choose the most protective ones.

IV.3.   Strengths and weaknesses of interaction-based hazard index

As to exposure to TME mixtures, to the best of our knowledge, the HI_{int} method based on WOE approach was used for very few studies. One assessed risks associated with ingestion of a mixture of As, Cu and Zn from milkfish [32]. Lin et al. used the classic dose–additive HI, HI_{int} for different critical effects for the whole mixture and then target-organ-specific interaction-based hazard indexes for gastrointestinal and hematological effects. They found a lower risk when they considered binary interactions using HI_{int}. The same approach was conducted to assess As, Mn and Cd in drinking water [33]. The older version of HI_{int} [29,31] was used to evaluate Cr, Cu, Zn, Cd, Hg and Pb in Food Crops [68].

All these studies deal with the oral exposure to TME mixtures. Inhalation exposure of TME mixtures has not been explored using this approach to date.

IV.3.1.   Interaction magnitude

Besides the WOE scores, the interaction magnitude M_{ij} could also have an impact in the HI_{int} calculations. Ryker &Small have showed that even if a maximum value of M_{ij} is considered, when the B_{ij} score is too low, the HI_{int} is close to the addition HI. But when B_{ij} is close to 1, the M_{ij} has a strong impact on the results [33].

The default value recommended by USEPA for the interaction magnitude M_{ij} is 5 [29]. However, it has been showed that M_{ij} could even reach 10 [33]. Thus, a M_{ij} is recommended if data are available.

IV.3.2.   Health risks from inhalation of TMEs mixture

Table 3.8 shows that the $HQ_{90P}$for Cr, Ni and Cu, respectively are 4.1, 67.9 and 1.8, all above 1. Thus, even exposure to only one of these metals is associated with a possible risk, and adverse non-cancer respiratory effects cannot be ruled out. Now, as it is well established, HQ cannot be considered as scaling a probability, but it indicates the magnitude of exceedance of the highest exposures considered as harmless.

HQs of different chemicals are not always comparable, but since they affect the same target organ, the calculation of HI and especially HI_{int} makes sense.

Given all the B_{ij} scores for each binary combination, the HI_{int} is 93.6for chronic-duration respiratory and lung effects. It showed a 26% increase compared to the addition HI. So, the resulting global effect between these 3 metals showed synergetic.

HI_{int} is not proportional to the risk but there is a higher concern of respiratory toxic effects when workers are exposed to such levels of Cr, Ni and Cu.

As to total cancer risk, we only had two unit risk values for different types of cancers from lifetime exposure to Ni and Pb. So, we could not calculate a tumor-specific cancer risk. Thus, we aggregated the cancer effect, which is also allowed [30,37]. We found that over a lifetime inhalation exposure, more than 3 extra workers might experience a lung or kidney cancer in a population of 10000 workers.

We do not have an exact idea of the size of the occupationally exposed population in the metalworking industry in Tunisia. However, lifetime cancer risk is generally compared to a

population of 10^5. So, a total cancer risk equal to 3.7 10^{-4} is considered to represent a high risk in the metalworking workers population.

IV.3.3. Other possible interactions

Due to the absence of TRVs for all the six considered TMEs, other possible interactions could not be considered in the HI_{int} calculations. For instance, in the ATSDR interaction profile, antagonistic interactions between Cu-Zn and Zn-Cu were demonstrated [64]. Incorporation of such interaction data could change the HI_{int} value. Therefore, we believe that the establishment of TRVs is necessary to help consider more binary interactions in larger TME mixtures.

IV.3.4. Methodological choice

The global risk characterization calculations were based on the 90th percentile of the exposure distribution of all job tasks. Thus, the HI_{int} and total cancer risk results involve 10% of the most highly exposed job posts and notably from the most polluted job tasks (P5, P6, P10 and P16) that were identified in Part 2. Indeed, some indoor air concentrations of the considered metals have exceeded the 90th percentile concentrations in P5 and P6.

It is also worth to note that even smaller job-specific HI_{int} can present concerns about respiratory toxic effects when substantially higher than 1, say above 5 given the security factors often included in derivation of the TRVs. According to our indoor air monitoring result, this is the case of the majority of the job tasks because all mean and LM measured concentrations of Ni and more than the half of Cr concentrations are above 5 folds of their corresponding TRVs.

V. Conclusion of part 3

In the third part, our main objective was to conduct a risk characterization of the occupational inhalation exposure to mixture of TMEs in the metalworking industry. To do so, we used the HI_{int} approach based on the relevant TRVs, binary interaction scores and the level for the 90th percentile of the exposure distribution we observed after our workplace measurements. Metal-specific HQs of Cr, Ni and Cu are exceeding one, which indicates possible toxic risks. Then, HI_{int} showed higher risks than the HI, suggesting more than additive respiratory effects from inhalation exposure to the study metals.

We discussed some limitations of our results that are essentially due to lack of information in the literature, such as the non-availability of all the VTRs for chronic inhalation of Al, Pb and Zn. We believe that despite all these limitations, our study shows that there are real concerns about potential risks to workers exposed to TME mixtures by inhalation in the metal working industry, especially in relation to the synergetic effect between Cr, Ni and Cu.

VI.   Bibliography

1. ATSDR. Toxicological Profile: Copper [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=206&tid=37

2. ATSDR. Toxicological Profile: Zinc [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=302&tid=54

3. ATSDR. Toxicological Profile: Nickel [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=245&tid=44

4. ATSDR. Toxicological Profile: Lead [Internet]. 2007. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22

5. ATSDR. Toxicological Profile: Aluminum [Internet]. 2008. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=191&tid=34

6. ATSDR. Toxicological Profiles. Agency for Toxic Substances and Disease Registry (US); 2009.

7. ATSDR. TOXICOLOGICAL PROFILE FOR CHROMIUM [Internet]. 2012. Available from: https://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=17

8. US EPA. Nickel subsulfide CASRN 12035-72-2 | IRIS | US EPA, ORD [Internet]. 1687 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=273

9. US EPA. Nickel carbonyl CASRN 13463-39-3 | IRIS | US EPA, ORD [Internet]. 1986 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=274

10. US EPA. Nickel refinery dust CASRN NA | IRIS | US EPA, ORD [Internet]. 1987 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=272

11. US EPA. Copper (CASRN 7440-50-8) | IRIS | US EPA - 0368_summary.pdf [Internet]. 1988 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0368_summary.pdf

12. US EPA. Nickel, soluble salts CASRN NA | IRIS | US EPA, ORD [Internet]. 1994 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=271

13. US EPA. Lead and compounds (inorganic) CASRN 7439-92-1 | IRIS | US EPA, ORD [Internet]. 2004 [cited 2016 Jun 17]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=277

14. US EPA. Zinc and Compounds CASRN 7440-66-6 | IRIS | US EPA, ORD [Internet]. 2005 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=426

15. US EPA O. Chromium(III), insoluble salts CASRN 16065-83-1 | IRIS | US EPA, ORD [Internet]. 1998 [cited 2017 Dec 8]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=28

16. US EPA O. Chromium(VI) CASRN 18540-29-9 | IRIS | US EPA, ORD [Internet]. 1998 [cited 2017 Dec 8]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=144

17. Fiches toxicologiques - Publications et outils - INRS [Internet]. [cited 2016 May 25]. Available from: http://www.inrs.fr/publications/bdd/fichetox.html

18. INRS. Nickel et ses oxydes - Fiche toxicologique [Internet]. 2009 [cited 2016 Jun 8]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_68

19. INRS. Plomb et composés minéraux - Fiche toxicologique [Internet]. 2006 [cited 2016 Jun 8]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_59

20. INRS. Zinc et composés minéraux (FT 75) - Fiche toxicologique [Internet]. 2012 [cited 2016 Jun 1]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_75

21. INRS. Cuivre et composés (FT 294) - Fiche toxicologique [Internet]. 2013 [cited 2016 May 31]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_294

22. INRS. Aluminium et ses composés minéraux (FT 306) - Fiche toxicologique [Internet]. 2014 [cited 2016 May 25]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_306

23. INRS. Trioxyde de chrome (FT 1) - Fiche toxicologique - INRS [Internet]. 2017 [cited 2018 Jan 17]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_1&section=pathologieToxicologie

24. Bonvallot N, Péry A, Lafon D, Boulanger G, Karg F, Mosqueron L, et al. Chemical risk assessment in occupational and environmental health: Objectives and methods. Environ Risques Santé. 2013;434–441.

25. Péry A, Bonvallot N, Yamani ME, Boulanger G, Karg F, Mosqueron L, et al. Valeurs limites d'exposition professionnelles (VLEP), valeurs toxicologiques de référence (VTR) : objectifs et méthodes. Environ Risques Santé. 2013;12:442–9.

26. Unité cancer environnement. Valeurs de référence | Cancer et environnement [Internet]. 2016 [cited 2016 May 25]. Available from: http://www.cancer-environnement.fr/232-Valeurs-de-reference.ce.aspx

27. Nordberg GF, Gerhardsson L, Mumtaz MM, Ruiz P, Fowler BA. Chapter 11: Interactions and Mixtures in Metal Toxicology. Handb Toxicol Met [Internet]. Elsevier; 2015 [cited 2017

Dec 22]. p. 213–38. Available from: http://linkinghub.elsevier.com/retrieve/pii/B9780444594532000111

28. Wilkinson CF, Christoph GR, Julien E, Kelley JM, Kronenberg J, McCarthy J, et al. Assessing the risks of exposures to multiple chemicals with a common mechanism of toxicity: how to cumulate? Regul Toxicol Pharmacol RTP. 2000;31:30–43.

29. US EPA. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures [Internet]. 2000 [cited 2015 Dec 24]. Available from: http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486

30. ATSDR. Framework for Assessing Health Impacts of Multiple Chemicals and Other Stressors [Internet]. 2018 Feb. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip-ga/ipga.pdf

31. Mumtaz MM, Durkin PR. A weight-of-evidence approach for assessing interactions in chemical mixtures. Toxicol Ind Health. 1992;8:377–406.

32. Lin Y-J, Ling M-P, Chen S-C, Chen W-Y, Hsieh N-H, Cheng Y-H, et al. Mixture risk assessment due to ingestion of arsenic, copper, and zinc from milkfish farmed in contaminated coastal areas. Environ Sci Pollut Res. 2017;24:14616–26.

33. Ryker SJ, Small MJ. Combining Occurrence and Toxicity Information to Identify Priorities for Drinking-Water Mixture Research. Risk Anal. 2008;28:653–66.

34. Hertzberg RC, Teuschler LK. Evaluating quantitative formulas for dose-response assessment of chemical mixtures. Environ Health Perspect. 2002;110:965–70.

35. Teuschler LK. Deciding which chemical mixtures risk assessment methods work best for what mixtures. Toxicol Appl Pharmacol. 2007;223:139–47.

36. US EPA O. Guidelines for the Health Risk Assessment of Chemical Mixtures [Internet]. 1986 [cited 2018 Jan 22]. Available from: https://www.epa.gov/risk/guidelines-health-risk-assessment-chemical-mixtures

37. Williams PRD, Dotson GS, Maier A. Cumulative Risk Assessment (CRA): Transforming the Way We Assess Health Risks. Environ Sci Technol. 2012;46:10868–74.

38. OSHA. OSHA Annotated PELs [Internet]. 2017 [cited 2017 Dec 6]. Available from: https://www.osha.gov/dsg/annotated-pels/tablez-1.html

39. US EPA. IRIS Assessments; Integrated Risk Information System [Internet]. [cited 2016 May 25]. Available from: https://cfpub.epa.gov/ncea/iris2/atoz.cfm

40. ANSES. Liste des Valeurs Toxicologiques de Référence (VTR) construites par l'Anses [Internet]. [cited 2018 Apr 10]. Available from: https://www.anses.fr/fr/content/liste-des-valeurs-toxicologiques-de-r%C3%A9f%C3%A9rence-vtr-construites-par-l%E2%80%99anses

41. Health Canada. ARCHIVED - Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/Concentrations for Priority Substances [Internet]. 2013 [cited 2016 May

25]. Available from: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/hbct-jact/index-eng.php#TC

42. Office of Environmental Health Hazard Assessment. Air Chemicals | OEHHA [Internet]. [cited 2016 May 25]. Available from: http://oehha.ca.gov/air/chemicals

43. TCEQ. Final Development Support Documents (DSDs) [Internet]. TCEQ. [cited 2017 Dec 8]. Available from: https://www.tceq.texas.gov/toxicology/dsd/final.html

44. A.J. Baars, R.M.C. Theelen, P.J.C.M. Janssen, J.M. Hesse, M.E. van Apeldoorn, M.C.M. Meijerink, et al. Re-evaluation of human-toxicological maximum permissible risk levels [Internet]. RIVM National Institute for Public Health and the Environment; 2001 Mar. Available from: http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

45. Mumtaz M, Poirier KA, Colman J. Risk assessment for chemical mixtures: Fine-tuning the hazard index approach. 1997;6:189–204.

46. ATSDR. Interaction Profile: Arsenic, Cadmium, Chromium and Lead [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/interactionprofiles/ip04.html

47. US EPA. Zinc cyanide CASRN 557-21-1 | IRIS | US EPA, ORD [Internet]. 1987 [cited 2016 Jun 1]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=127

48. OEHHA. Air Chemicals | Chromic Trioxide [Internet]. OEHHA. 2015 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/air/chemicals/chromic-trioxide

49. OEHHA. Air Chemicals | Nickel and Nickel Compounds | OEHHA [Internet]. 2012 [cited 2016 Jun 2]. Available from: http://oehha.ca.gov/air/chemicals/nickel-and-nickel-compounds

50. OEHHA. Air Chemicals | Copper OEHHA [Internet]. 1999 [cited 2016 May 31]. Available from: http://oehha.ca.gov/air/chemicals/copper

51. OEHHA. Chemicals | Lead and Lead Compounds [Internet]. OEHHA. 2015 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/chemicals/lead-and-lead-compounds

52. Regional Office for Europe Copenhagen, Frank Theakston, editors. Air quality guidelines for Europe. 2nd edition. Copenhagen: World Health Organization, Regional Office for Europe; 2000.

53. Michael S. Aplin, Toxicology Division. Chromium All Compounds except Hexavalent Chromium [Internet]. TCEQ; 2009 Oct. Available from: https://www.tceq.texas.gov/assets/public/implementation/tox/dsd/final/october09/chromium3_16065-83-1.pdf

54. Darrell D. McCant, Joseph T. Haney, Roberta L. Grant, Toxicology Division. Nickel and Inorganic Nickel Compounds [Internet]. TCEQ; 2017 Jul. Available from: https://www.tceq.texas.gov/assets/public/implementation/tox/dsd/final/june11/nickel_&_compounds.pdf

55. OEHHA. Air Chemicals | Lead and Lead Compounds [Internet]. OEHHA. 2016 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/air/chemicals/lead-and-lead-compounds

56. Canadian Environmental Protection Act. Priority Substances List Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances [Internet]. Health Canada; 1996 [cited 2016 Jun 2]. Available from: http://www.tera.org/iter/HCPSL1supportdoc.pdf

57. Lou J, Jin L, Wu N, Tan Y, Song Y, Gao M, et al. DNA damage and oxidative stress in human B lymphoblastoid cells after combined exposure to hexavalent chromium and nickel compounds. Food Chem Toxicol. 2013;55:533–40.

58. Rudolf E, Cervinka M. Nickel modifies the cytotoxicity of hexavalent chromium in human dermal fibroblasts. Toxicol Lett. 2010;197:143–50.

59. Ge Y, Bruno M, Wallace K, Leavitt S, Andrews D, Spassova MA, et al. Systematic Proteomic Approach to Characterize the Impacts of Chemical Interactions on Protein and Cytotoxicity Responses to Metal Mixture Exposures. J Proteome Res. 2015;14:183–92.

60. Samal L, Mishra C. Significance of Nickel in Livestock Health and Production. Int J Agro Vet Med Sci. 2011;5:349.

61. Geertz R, Gulyas H, Gercken G. Cytotoxicity of dust constituents towards alveolar macrophages: Interactions of heavy metal compounds. Toxicology. 1994;86:13–27.

62. ATSDR. Toxicological Profile for Aluminum - tp22.pdf [Internet]. 2008 [cited 2016 May 24]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp22.pdf

63. Charles B. Keil. Chapter 3: Modeling Pollutant Generation Rates. Math Models Estim Occup Expo Chem. USA; 2009.

64. ATSDR. ATSDR - Interaction Profile: Lead, Manganese, Zinc, and Copper [Internet]. 2004 [cited 2018 Jan 21]. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip06.html

65. Kostoff RN. Effects of Toxic Stimuli Combinations on Determination of Exposure Limits [Internet]. Georgia Institute of Technology; 2018 [cited 2018 Jun 6]. Available from: https://smartech.gatech.edu/handle/1853/59719

66. IRSST. Mixie: Mixtures of substances in the workplace: computer-based tool for evaluating the chemical risk [Internet]. 2014 [cited 2014 Mar 31]. Available from: https://www.irsst.qc.ca/en/-tool-mixie-mixtures-of-substances-in-the-workplace-computer-based-tool-for-evaluating-the-chemical-risk-calculation-of-the-rm.html

67. INRS. MiXie - Interactions toxicologiques [Internet]. [cited 2014 Aug 25]. Available from: http://www.inrs-mixie.fr/

68. Cao H, Zhu H, Jia Y, Chen J, Zhang H, Qiao L. Heavy Metals in Food Crops and the Associated Potential for Combined Health Risk due to Interactions between Metals. Hum Ecol Risk Assess Int J. 2011;17:700–11.

GENERAL DISCUSSION

The health risk assessment process in relation to occupational exposure to chemicals is dedicated to inform risk prevention and industrial hygiene, like its counterpart for environmental hazards [1]. Companies' managers should be more aware of such procedures in order to improve the working environment and to ensure control of risks in the workplaces.

In the Tunisian regulatory framework, there are two sections about the prevention of occupational risks in the chapter VI of law number 94-28 of February 21th, 1994 [2] and in chapter V of the law number 95-56 of June 28th, 1995 [3] for the private and public sectors, respectively. These two texts require from the managers to implement a prevention strategy to avoid work accidents and occupational illnesses by taking all appropriate preventive actions relative to their activity. Yet, they are general and vague; no specific rules and actions are required. For instance, no indoor air quality standards and regulations are available. Thus, the managers do not feel obliged to conduct exposure assessment if there is no accident or a problematic situation. However, we believe that it is necessary to conduct exposure assessment and surveillance for preventive reasons in order to recognize the appropriate measures and invest in equipment that regulates the pollutants' levels. Depending on the airborne concentrations, the quality, quantity and the strength of the prevention systems can vary substantially. So, in order to effectively comply with these laws; a new culture of periodic risk assessment has to be set up.

In the particular setting of our study, the implementation of such a culture will reduce the high risk of respiratory conditions in the metalworking industry, which would in turn result in better health and productivity of workers and less medical leaves. Such measures might also contribute to higher confidence from workers and professional involvement.

Still, we acknowledge that air sampling and the corresponding analyses are not always accessible because of their high price. Therefore, mathematical models for estimating occupational exposure to chemical can be useful and represent an alternative tool that is both time-saving and cost-effective in comparison with direct air monitoring approaches. Moreover, occupational hygienists are also interested in such models because one cannot monitor everything, so they could be used as a quantitative and scientifically explicit method to support expert judgment [4]. Such models can be used in exposure assessment purposes in workplaces or even in the planning step before the implementation of a new workplace. Thus, in our study we assessed the models prediction abilities for TMEs in

several job tasks and demonstrated the effectiveness of the NF-FF model to predict indoor air concentrations in different types of steel cutting and welding and plastic injection.

We seek to cooperate with governmental institutions and bodies such as the Tunisian Occupational Health and Safety Institute ISST (*Institut de Santé et de Sécurité au* Travail) in order to take advantage of this modeling approach at a national scale and apply these models in exposure assessment in other industrial settings. In this intention, and in order to test this approach to more diverse settings and other industrial branches, we solicit their support, especially to establish contacts and recruitment of companies.

As we previously mentioned, the exactitude of technical information to establish the models parameters yields better results. So, it is important that the companies' managers are convinced of all the benefits of the risk assessment procedure. In this respect, the dialogue between all stakeholders is necessary and beneficial for everyone.

We also address the Ministry of Vocational Training and Employment and highlight the high risk encountered in the metalworking industry; an awareness program geared to the managers and the workers would be useful to expose the multiple advantages of the exposure assessment approach and to introduce this tool, which is new in the Tunisian context.

It is worth to note that this work was conducted thanks to reasonableness, awareness and the good will of the managers of the five participating companies. As previously mentioned, many others have refused to be involved. The participating volunteers are, obviously, conscious of the issues and are likely to be more careful about occupational risks in their workplaces, which is probably not the case of all metalworking companies in Sfax. That is why we call for caution about the general situation in Sfax. Hence, risk levels described in this study are definitely underestimated regarding the whole metalworking industry in the Sfax Metropolis.

Bibliography

1. National Research Council. Science and Decisions: Advancing Risk Assessment [Internet]. Washington, DC: The National AcademiesPress; 2009. Available from: https://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment

2. République Tunisienne. Loi n°94-28 du 21 Février 1994 [Internet]. Journal Officiel du 22 Février 1994. Available from: https://www.ilo.org/dyn/natlex/docs/SERIAL/38574/33476/F2145285572/TUN-38574.pdf

3. République Tunisienne. Loi n°95-56 du 28 juin 1995 [Internet]. Journal Officiel du 4 Juillet 1995. Available from: http://www.legislation.tn/sites/default/files/journal-officiel/1995/1995F/Jo05395.pdf

4. Jayjock MA, Chaisson CF, Arnold S, Dederick EJ. Modeling framework for human exposure assessment. J Expo Sci Environ Epidemiol. 2007;17:S81–9.

GENERAL CONCLUSION & PERSPECTIVES

At the end of this study, we brought to light, via the human health risk assessment – HHRA - approach, that workers in the metalworking industry in Sfax Metropolis are exposed to trace metallic elements mixtures through inhalation of dust and aerosols at levels that may elicit respiratory illnesses; the risk levels may even be enhanced by synergetic effects. Now the measured airborne concentrations do not exceed the *VLEPs* published in the literature or in effect in other countries, except for two job posts in metal electroplating.

During the HHRA, for exposure assessment purposes, we used mathematical models for estimating occupational exposure to TMEs in several metalworking processes and real-life exposure scenarios using available field–related information, literature and inexpensive measurements (temperature, air velocity, etc.). The models efficiencies were assessed by comparing direct measured airborne concentrations of TMEs with the predicted concentrations in order to "validate" their usage. Associations were checked using correlation methods together with Student's *t*-test to have an exact idea about the mean differences.

Results showed a strongly significant global correlation. When we further conducted comparisons, depending on the process and the modeling methods, the NF predictions of TME concentrations showed to be applicable for three kinds of steel cutting, two kinds of welding and in the plastic injection process.

We also tried to investigate the correlations between urinary metals and the measured airborne concentrations; however, no significant correlation for all the considered TMEs was determined. We assume that this is mainly due to lack of statistical power, due to the rather small size of our population but we cannot rule out interference with uncontrolled confounders.

Urinary Al, Ni and Cu were higher among the exposed workers, which suggest that they are due to occupational exposure. Now, non-occupationally exposed workers have also high urinary metals for the six study metals, compared to the biological reference value in the general population. We explain this by the fact that these workers were indirectly occupationally exposed through ventilation sources.

Finally, for risk characterization purposes, we used the interaction-based Hazard Index approach by means of the WOE approach and the corresponding Threshold Reference Values to calculate a global HI_{int} hazard index based on the 90th percentile of the exposure

distribution of all job tasks. Results are of great concerns about non-carcinogenic respiratory toxic effects, especially for the Shielded metal arc welding and the slitting and metal shearing and slitting task jobs. This risk is also likely to be enhanced because of the more than additive interaction resulting from the combination of the Cr, Ni and Cu.

For the non-threshold effects, a total cancer risk was calculated that recognized high risks of lung and kidney cancers (the predicted life-long total cancer risk for exposed workers is 3.7×10^{-4}).

The results derived from the HHRA procedure, either for predictive models for risk characterization of mixtures, are interesting and useful for the different stakeholders in the occupational field such as companies' managers, workers' union and public institutions responsible for risk control and industrial hygiene.

Along this doctoral thesis, we also identified limitations in applying modeling approaches to predict exposures and risks in face of multiple chemical exposures. This represents serious challenges for research. We have suggested some topics for a research agenda, such as;

- uncertainty analysis by Monte Carlo in order to determine the output distribution and interval,
- air monitoring in office areas to verify the exposure levels,
- urinary sampling for other non-occupationally exposed persons outside the industrial field to have background levels and confirmation about the occupational proportion of TMEs in urines
- Specific monitoring of nickel sulfate and chromic acid for the electroplating process so as to provide more accurate information about the risk, because their TRVs are considerably lower than for the elemental metals.
- Construction of a Unit Risk for total Cr based on the Tumorigenic Concentration 05 established by Health Canadian order to improve the total cancer risk estimation, especially because the total Cr is related to lung cancer like the Ni.
- Derivation of generation rates from our air monitoring results (in the breathing zones) for the job processes where our modeling approach was not applicable, and assessment of their prediction ability.
- Establishment of HI_{int} for every job task in order to allow comparisons between specific risks depending on the process.

We think these topics offer new opportunities for national and international collaboration, with the support of the ministry of higher education and scientific research.

BIBLIOGRAPHY

A.J. Baars, R.M.C. Theelen, P.J.C.M. Janssen, J.M. Hesse, M.E. van Apeldoorn, M.C.M. Meijerink, et al. Re-evaluation of human-toxicological maximum permissible risk levels [Internet]. RIVM National Institute for Public Health and the Environment; 2001 Mar. Available from: http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

Abrams R, Ali M, Denton P, Igualada J, Groen M, Gschwind E. Colouring plastics: fundamentals and trends. Plast Addit Compd. 2001;3:18–25.

AIHA, Charles B. Keil, Cathrine E. Simmons, T. Renée Anthony. Mathematical Models for Estimating Occupational Exposure to Chemicals. 2nd edition. AIHA press; 2009.

AIHA. Exposure Assessment Strategies Committee [Internet]. [cited 2016 Nov 14]. Available from: https://www.aiha.org/get-involved/VolunteerGroups/Pages/Exposure-Assessment-Strategies-Committee.aspx

Akkas N, Varol F, Ferik E, Ilhan E, Ozsarac U, Aslanlar S. Effect of Welding Current on Mechanical Properties of Welding Joints in S235JR(Cu) Steel Sheets in Resistance Spot Welding. Acta Phys Pol A. 2014;125:500–2.

Annabi A, Said K, Messaoudi I. Heavy metal levels in gonad and liver tissues—effects on the reproductive parameters of natural populations of Aphanius facsiatus. Environ Sci Pollut Res. 2013;20:7309–19.

ANSES. Liste des Valeurs Toxicologiques de Référence (VTR) construites par l'Anses [Internet]. [cited 2018 Apr 10]. Available from: https://www.anses.fr/fr/content/liste-des-valeurs-toxicologiques-de-r%C3%A9f%C3%A9rence-vtr-construites-par-l%E2%80%99anses

Antonini JM. Health Effects of Welding. Crit Rev Toxicol. 2003;33:61–103.

Armstrong T. IH Mod "Mathematical Modeling to Estimate Exposures" User's Blog [Internet]. Welcome IH Mod Math. Model. Estim. Expo. Users Blog. [cited 2018 Jan 3]. Available from: http://ihmod.org/about-this-site-and-ih-mod.html

Arnold SF, Shao Y, Ramachandran G. Evaluating well-mixed room and near-field–far-field model performance under highly controlled conditions. J Occup Environ Hyg. 2017;14:427–37.

Arnold SF, Shao Y, Ramachandran G. Evaluation of the well mixed room and near-field far-field models in occupational settings. J Occup Environ Hyg. 2017;14:694–702.

ATSDR. ATSDR - Interaction Profile: Lead, Manganese, Zinc, and Copper [Internet]. 2004 [cited 2018 Jan 21]. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip06.html

ATSDR. Detailed data table for the 2011 priority list of hazardous substances that will be the subject of toxicological profiles [Internet]. 2011 [cited 2014 Feb 7]. Available from: http://www.atsdr.cdc.gov/spl/resources/ATSDR_2011_SPL_Detailed_Data_Table.pdf

ATSDR. Framework for Assessing Health Impacts of Multiple Chemicals and Other Stressors [Internet]. 2018 Feb. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip-ga/ipga.pdf

ATSDR. Interaction Profile: Arsenic, Cadmium, Chromium and Lead [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/interactionprofiles/ip04.html

ATSDR. Toxicological Profile for Aluminum - tp22.pdf [Internet]. 2008 [cited 2016 May 24]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp22.pdf

ATSDR. TOXICOLOGICAL PROFILE FOR CHROMIUM [Internet]. 2012. Available from: https://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=17

ATSDR. Toxicological Profile: Aluminum [Internet]. 2008. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=191&tid=34

ATSDR. Toxicological Profile: Copper [Internet]. 2004. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=206&tid=37

ATSDR. Toxicological Profile: Lead [Internet]. 2007. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22

ATSDR. Toxicological Profile: Nickel [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=245&tid=44

ATSDR. Toxicological Profile: Zinc [Internet]. 2005. Available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=302&tid=54

ATSDR. Toxicological Profiles. Agency for Toxic Substances and Disease Registry (US); 2009.

AWS E6013 Welding Electrode [Internet]. [cited 2016 Oct 12]. Available from: http://www.tenweld.com/aws-e6013-welding-electrode.html

Banni M, Bouraoui Z, Ghedira J, Clearandeau C, Jebali J, Boussetta H. Seasonal variation of oxidative stress biomarkers in clams Ruditapes decussatus sampled from Tunisian coastal areas. Environ Monit Assess. 2008;155:119–28.

Banni M, Jebali J, Daubeze M, Clerandau C, Guerbej H, Narbonne JF, et al. Monitoring pollution in Tunisian coasts: application of a classification scale based on biochemical markers. Biomarkers. 2005;10:105–16.

Barhoumi S, Messaoudi I, Deli T, Saïd K, Kerkeni A. Cadmium bioaccumulation in three benthic fish species, Salaria basilisca, Zosterisessor ophiocephalus and Solea vulgaris collected from the Gulf of Gabes in Tunisia. J Environ Sci. 2009;21:980–4.

Base de données Biotox - Publications et outils - INRS [Internet]. [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox.html

Base de données MétroPol - Publications et outils - INRS [Internet]. [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/metropol.html

Ben Fredj F, Wali A, Khadhraoui M, Han J, Funamizu N, Ksibi M, et al. Risk assessment of heavy metal toxicity of soil irrigated with treated wastewater using heat shock proteins stress responses: case of El Hajeb, Sfax, Tunisia. Environ Sci Pollut Res [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s11356-013-2411-5

Bertrand N, Vincent R. Modélisation des expositions professionnelles aux agents chimiques. Bilan et perspectives. Hygiène Sécurité Trav ND [Internet]. 2010 [cited 2014 Feb 9];2333. Available from: http://www.hst.fr/inrs-pub/inrs01.nsf/IntranetObject-accesParIntranetID/OM:Document:6DD39CCF247C5DBDC12577B5002C6497/$FILE/Visu.html

Boelter FW, Simmons CE, Berman L, Scheff P. Two-Zone Model Application to Breathing Zone and Area Welding Fume Concentration Data. J Occup Environ Hyg. 2009;6:298–306.

Bolgar M, Hubball J, Groeger J, Meronek S. Handbook for the Chemical Analysis of Plastic and Polymer Additives, Second Edition. CRC Press; 2015.

Bonvallot N, Péry A, Lafon D, Boulanger G, Karg F, Mosqueron L, et al. Chemical risk assessment in occupational and environmental health: Objectives and methods. Environ Risques Santé. 2013;434–441.

Canadian Environmental Protection Act. Priority Substances List Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances [Internet]. Health Canada; 1996 [cited 2016 Jun 2]. Available from: http://www.tera.org/iter/HCPSL1supportdoc.pdf

Cao H, Zhu H, Jia Y, Chen J, Zhang H, Qiao L. Heavy Metals in Food Crops and the Associated Potential for Combined Health Risk due to Interactions between Metals. Hum Ecol Risk Assess Int J. 2011;17:700–11.

Chambre de commerce et d'industrie de Sfax, Tunisie. Guide des exportateurs de Sfax. Tunisie; 2010.

Charles B. Keil. chapter 2: General principals of physical-chemical models. Math Models Estim Occup Expo Chem. USA; 2009.

Charles B. Keil. Chapter 3: Modeling Pollutant Generation Rates. Math Models Estim Occup Expo Chem. USA; 2009.

ChemTRAC - Environmental Health - Toronto Public Health | [Internet]. [cited 2016 May 11]. Available from: http://www1.toronto.ca/wps/portal/contentonly?vgnextoid=8e00ebfc2bb31410VgnVCM10000071d60f89RCRD

Committee on the Institutional Means for Assessment of Risks to Public Health, National Research Council, Division on Earth and Life Studies, Commission on Life Sciences. Risk Assessment in the Federal Government:: Managing the Process. National Academies Press; 1983.

Darrell D. McCant, Joseph T. Haney, Roberta L. Grant, Toxicology Division. Nickel and Inorganic Nickel Compounds [Internet]. TCEQ; 2017 Jul. Available from: https://www.tceq.texas.gov/assets/public/implementation/tox/dsd/final/june11/nickel_&_compounds.pdf

de Santana IJ, Paulo B, Modenesi PJ. High frequency induction welding simulating on ferritic stainless steels. J Mater Process Technol. 2006;179:225–30.

DigitalCavalry. Firstinox : acier inoxydableFirstinox, acier inoxydable, aluminium damier. Inox : 304, 304L,316L, 4307 [Internet]. [cited 2016 Jun 20]. Available from: http://www.firstinox.fr/inox-composition-chimique-acier-inoxydable/

Ebrahimnia M, Goodarzi M, Nouri M, Sheikhi M. Study of the effect of shielding gas composition on the mechanical weld properties of steel ST 37-2 in gas metal arc welding. Mater Des. 2009;30:3891–5.

El Ati-Hellal M, Hedhili A, Hellal F, Boujlel K, Dachraoui M, Bousnina M, et al. Lead and cadmium concentrations in seawater and algae of the Tunisian coast. Arch Inst Pasteur Tunis. 2005;82:75–82.

En_S235JR.pdf [Internet]. [cited 2016 Apr 21]. Available from: http://www.atrspa.eu/allegati/prodotti/en/en_S235JR.pdf

EnerPlastics. EnerPlastics – Masters in the art of colouring [Internet]. [cited 2018 Feb 16]. Available from: http://www.enerplastics.com/

Environmental Protection Agency Johnstown Castle Estate Wexford, Ireland. Emissions Monitoring Guidance Note (AG2) [Internet]. 2017 Sep. Available from: http://www.epa.ie/pubs/advice/air/emissions/AG2%20Air%20Emissions%20Monitoring%20 Guidance%20Note_rev3.pdf

ER70S-6 [Internet]. WeldWire. [cited 2017 Nov 21]. Available from: http://www.weldwire.net/weld_products/ww70s-6/

Euromaster Spa. Euromaster Spa Masterbatches and compounds [Internet]. Euromaster Spa. [cited 2018 Feb 16]. Available from: https://www.euromasterspa.com/en/

Fairbrother A, Wenstel R, Sappington K, Wood W. Framework for Metals Risk Assessment. Ecotoxicol Environ Saf. 2007;68:145–227.

Feki-Tounsi M, Olmedo P, Gil F, Khlifi R, Mhiri M-N, Rebai A, et al. Cadmium in blood of Tunisian men and risk of bladder cancer: interactions with arsenic exposure and smoking. Environ Sci Pollut Res. 2013;20:7204–13.

Fiches toxicologiques - Publications et outils - INRS [Internet]. [cited 2016 May 25]. Available from: http://www.inrs.fr/publications/bdd/fichetox.html

Filter Cassettes, Blank, 37 mm, Clear Styrene, SKC, Inc. [Internet]. [cited 2016 Jun 13]. Available from: http://www.skcinc.com/catalog/product_info.php?products_id=343

Fournier K, Glorennec P, Bonvallot N. Derivation of toxicological reference values for taking mixtures into account in health risk assessment: Existing methods and recent applications. Environ Risques Santé. 2014;203–221.

Gargouri D, Azri C, Serbaji MM, Jedoui Y, Montacer M. Heavy metal concentrations in the surface marine sediments of Sfax Coast, Tunisia. Environ Monit Assess. 2010;175:519–30.

Gargouri I, Rebaï A, Khadhraoui M, Kallel M, Jmal-Hammami K, Medhioub K, et al. Impact sanitaire des variations quotidiennes de la pollution atmosphérique urbaine: étude de faisabilité dans la ville de Sfax (Tunisie). Environ Risques Santé. 2006;5:467–75.

Garnier R. Toxicité du plomb et de ses dérivés. Pathol Prof Environ EMC. 2006;1:1–15.

Ge Y, Bruno M, Wallace K, Leavitt S, Andrews D, Spassova MA, et al. Systematic Proteomic Approach to Characterize the Impacts of Chemical Interactions on Protein and Cytotoxicity Responses to Metal Mixture Exposures. J Proteome Res. 2015;14:183–92.

Geertz R, Gulyas H, Gercken G. Cytotoxicity of dust constituents towards alveolar macrophages: Interactions of heavy metal compounds. Toxicology. 1994;86:13–27.

Gerhard Pohlmann, Charly Holzinger, Vilia Elena Spiegel-Ciobanu. Comparative investigations in order to characterise ultrafine particles in fumes in the case of welding and allied processes. Weldingand Cut [Internet]. 2013;12. Available from: https://www.bghm.de/fileadmin/user_upload/Arbeitsschuetzer/Fachinformationen/Schweissen /00_WC2_SpA_w20000014__.pdf

Golbabaei F, Khadem M. Chapter 2: Air Pollution in Welding Processes — Assessment and Control Methods. In: Nejadkoorki F, editor. Curr Air Qual Issues [Internet]. InTech; 2015 [cited 2016 May 12]. Available from: http://www.intechopen.com/books/current-air-quality-issues/air-pollution-in-welding-processes-assessment-and-control-methods

Goullé J-P, Mahieu L, Castermant J, Neveu N, Bonneau L, Lainé G, et al. Metal and metalloid multi-elementary ICP-MS validation in whole blood, plasma, urine and hair. Forensic Sci Int. 2005;153:39–44.

Hamza-Chaffai A, Cosson RP, Amiard-Triquet C, El Abed A. Physico-chemical forms of storage of metals (Cd, Cu and Zn) and metallothionein-like proteins in gills and liver of marine fish from the Tunisian coast: ecotoxicological consequences. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol. 1995;111:329–41.

Hamza-Chaffai A, Roméo M, el Abed A. Heavy metals in different fishes from the middle eastern coast of Tunisia. Bull Environ Contam Toxicol. 1996;56:766–73.

Health Canada. ARCHIVED - Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/Concentrations for Priority Substances [Internet]. 2013 [cited 2016 May 25]. Available from: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/hbct-jact/index-eng.php#TC

Hentati O, Chaker S, Wali A, Ayoub T, Ksibi M. Effects of long-term irrigation with treated wastewater on soil quality, soil-borne pathogens, and living organisms: case study of the vicinity of El Hajeb (Tunisia). Environ Monit Assess [Internet]. 2013 [cited 2014 Feb 7]; Available from: http://link.springer.com/10.1007/s10661-013-3570-z

Hertzberg RC, Teuschler LK. Evaluating quantitative formulas for dose-response assessment of chemical mixtures. Environ Health Perspect. 2002;110:965–70.

Hoet P, Jacquerye C, Deumer G, Lison D, Haufroid V. Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium. Clin Chem Lab Med. 2013;51:839–49.

IHMod - Outil - INRS [Internet]. [cited 2016 Nov 14]. Available from: http://www.inrs.fr/media.html?refINRS=outil27

INOX 304-316-FT-FINAL.pdf [Internet]. [cited 2016 Jun 12]. Available from: http://docs.indigo-group.be/catalogs/cat01/INOX%20304-316-FT-FINAL.pdf

INRS. Aluminium et composés (7429-90-5) / Aluminium urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_2

INRS. Aluminium et ses composés minéraux (FT 306) - Fiche toxicologique [Internet]. 2014 [cited 2016 May 25]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_306

INRS. Calcul de la concentration en polluants - Métropol. 2015.

INRS. Chrome et chromates (7440-47-3) / Chrome urinaire - Biotox - INRS [Internet]. 2018 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_23

INRS. Cuivre et composés (7440-50-8) / Cuivre urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_27

INRS. Cuivre et composés (FT 294) - Fiche toxicologique [Internet]. 2013 [cited 2016 May 31]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_294

INRS. Métaux et métalloïdes M-122 - MétroPol [Internet]. 2016 [cited 2016 Jun 13]. Available from: http://www.inrs.fr/publications/bdd/metropol/fiche.html?refINRS=METROPOL_122

INRS. MiXie - Interactions toxicologiques [Internet]. [cited 2014 Aug 25]. Available from: http://www.inrs-mixie.fr/

INRS. Nickel et composés (7440-02-0) / Nickel urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_47

INRS. Nickel et ses oxydes - Fiche toxicologique [Internet]. 2009 [cited 2016 Jun 8]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_68

INRS. Plomb et composés (7439-92-1) / Plomb urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_53

INRS. Plomb et composés minéraux - Fiche toxicologique [Internet]. 2006 [cited 2016 Jun 8]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_59

INRS. Prélèvement des aérosols par cassette fermée [Internet]. 2015. Available from: http://www.inrs.fr/dms/inrs/PDF/metropol-prelevement-principe.pdf

INRS. Préparation des dispositifs de prélèvement en vue d'une intervention en entreprise. 2015.

INRS. Principe général et mise en œuvre pratique du prélèvement [Internet]. 2015 [cited 2016 Sep 16]. Available from: http://www.inrs.fr/dms/inrs/PDF/metropol-prelevement-principe.pdf

INRS. Trioxyde de chrome (FT 1) - Fiche toxicologique - INRS [Internet]. 2017 [cited 2018 Jan 17]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_1&section=pathologieToxicologie

INRS. Zinc et composés (7440-66-6) / Zinc urinaire - Biotox - INRS [Internet]. 2017 [cited 2018 Apr 5]. Available from: http://www.inrs.fr/publications/bdd/biotox/dosage.html?refINRS=Dosage_73

INRS. Zinc et composés minéraux (FT 75) - Fiche toxicologique [Internet]. 2012 [cited 2016 Jun 1]. Available from: http://www.inrs.fr/publications/bdd/fichetox/fiche.html?refINRS=FICHETOX_75

InVS, Afsset. Estimation de l'impact sanitaire d'une pollution environnementale et évaluation quantitative des risques sanitaires [Internet]. 2007. Available from: http://www.invs.sante.fr/publications/2008/pollution_invs_afsset/rap_pollution_invs_afsset_nov_2007.pdf

IRSST. Mixie: Mixtures of substances in the workplace: computer-based tool for evaluating the chemical risk [Internet]. 2014 [cited 2014 Mar 31]. Available from: https://www.irsst.qc.ca/en/-tool-mixie-mixtures-of-substances-in-the-workplace-computer-based-tool-for-evaluating-the-chemical-risk-calculation-of-the-rm.html

Jayjock MA, Armstrong T, Taylor M. The Daubert Standard as Applied to Exposure Assessment Modeling Using the Two-Zone (NF/FF) Model Estimation of Indoor Air Breathing Zone Concentration as an Example. J Occup Environ Hyg. 2011;8:D114–22.

Jayjock MA, Chaisson CF, Arnold S, Dederick EJ. Modeling framework for human exposure assessment. J Expo Sci Environ Epidemiol. 2007;17:S81–9.

Jayjock MA. Uncertainty Analysis in the Estimation of Exposure. Am Ind Hyg Assoc J. 1997;58:380–2.

Kahn HD. Note On The Distribution of Air Pollutants. J Air Pollut Control Assoc. 1973;23:973–973.

KAN H-D, CHEN B-H. Statistical Distributions of Ambient Air Pollutants in Shanghai, China. :7.

Kaščák Ľ, Viňáš J, Spišák E. Deltaspot as an innovative method of resistance spot welding. Sci Lett Rzesz Univ Technol - Mech. 2012;84:43–53.

Keil CB, Nicas M. Predicting Room Vapor Concentrations Due to Spills of Organic Solvents. AIHA J. 2003;64:445–54.

Kessabi K, Annabi A, Hassine AIH, Bazin I, Mnif W, Said K, et al. Possible chemical causes of skeletal deformities in natural populations of Aphanius fasciatus collected from the Tunisian coast. Chemosphere. 2013;90:2683–9.

Kessabi K, Kerkeni A, Saïd K, Messaoudi I. Involvement of Cd Bioaccumulation in Spinal Deformities Occurrence in Natural Populations of Mediterranean Killifish. Biol Trace Elem Res. 2008;128:72–81.

Kessabi K, Navarro A, Casado M, Saïd K, Messaoudi I, Piña B. Evaluation of environmental impact on natural populations of the Mediterranean killifish Aphanius fasciatus by quantitative RNA biomarkers. Mar Environ Res. 2010;70:327–33.

Ketata I, Smaoui-Damak W, Guermazi F, Rebai T, Hamza-Chaffai A. In situ endocrine disrupting effects of cadmium on the reproduction of Ruditapes decussatus. Comp Biochem Physiol Part C Toxicol Pharmacol. 2007;146:415–30.

Khlifi R, Hamza-Chaffai A. Head and neck cancer due to heavy metal exposure via tobacco smoking and professional exposure: A review. Toxicol Appl Pharmacol. 2010;248:71–88.

Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Chakroun A, Rebai A, et al. Blood nickel and chromium levels in association with smoking and occupational exposure among head and neck cancer patients in Tunisia. Environ Sci Pollut Res. 2013;20:8282–94.

Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Hammami B, Rebai A, et al. Biomonitoring of cadmium, chromium, nickel and arsenic in general population living near mining and active industrial areas in Southern Tunisia. Environ Monit Assess. 2014;186:761–79.

Khlifi R, Olmedo P, Gil F, Feki-Tounsi M, Hammami B, Rebai A, et al. Risk of laryngeal and nasopharyngeal cancer associated with arsenic and cadmium in the Tunisian population. Environ Sci Pollut Res. 2013;21:2032–42.

Khlifi R, Olmedo P, Gil F, Hammami B, Chakroun A, Rebai A, et al. Arsenic, cadmium, chromium and nickel in cancerous and healthy tissues from patients with head and neck cancer. Sci Total Environ. 2013;452–453:58–67.

Kong IC. Joint effects of heavy metal binary mixtures on seed germination, root and shoot growth, bacterial bioluminescence, and gene mutation. J Environ Sci. 2013;25:889–94.

Kostoff RN. Effects of Toxic Stimuli Combinations on Determination of Exposure Limits [Internet]. Georgia Institute of Technology; 2018 [cited 2018 Jun 6]. Available from: https://smartech.gatech.edu/handle/1853/59719

Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, et al. HUMAN HEALTH RISK ASSESSMENT FOR ALUMINIUM, ALUMINIUM OXIDE, AND ALUMINIUM HYDROXIDE. J Toxicol Environ Health B Crit Rev. 2007;10:1–269.

Laboratory Ventilation ACH Rates Standards and Guidelines [Internet]. 2012 Jan. Available from: http://www.aircuity.com/wp-content/uploads/Aircuity-White-Paper_Lab-Ventilation-ACH-Rates_Standards-Guidelines_ACHWP_20120103-2.pdf

Lahbib Y, Mleiki A, Marigomez I, Trigui El Menif N. Copper, zinc, and cadmium body concentrations in Hexaplex trunculus collected from the Tunisian coast. Environ Monit Assess. 2013;185:8967–75.

Larry F. Jeffus. Chapter 6: related processes and technology. Weld Princ Appl. USA: Cengage Learning; 2004.

Larsen RI. A New Mathematical Model of Air Pollutant Concentration Averaging Time and Frequency. J Air Pollut Control Assoc. 1969;19:24–30.

Lauwerys R. Toxicologie industrielle et intoxications professionnelles. 3 éme édition. Paris: Masson; 1990.

Lin Y-J, Ling M-P, Chen S-C, Chen W-Y, Hsieh N-H, Cheng Y-H, et al. Mixture risk assessment due to ingestion of arsenic, copper, and zinc from milkfish farmed in contaminated coastal areas. Environ Sci Pollut Res. 2017;24:14616–26.

Løkke H, Ragas AMJ, Holmstrup M. Tools and perspectives for assessing chemical mixtures and multiple stressors. Toxicology. 2013;313:73–82.

Lou J, Jin L, Wu N, Tan Y, Song Y, Gao M, et al. DNA damage and oxidative stress in human B lymphoblastoid cells after combined exposure to hexavalent chromium and nickel compounds. Food Chem Toxicol. 2013;55:533–40.

MacIntosh DL, International Programme on Chemical Safety, editors. Human exposure assessment. Geneva: World Health Organization; 2000.

Mark Nicas. Chapter 6: The Near Field/ Far Field (two box) Model with a constant contaminant emission rate. Math Models Estim Occup Expo Chem. USA: AIHA press; 2009. p. 47–52.

Martínez-Pacheco M, Hidalgo-Miranda A, Romero-Córdoba S, Valverde M, Rojas E. mRNA and miRNA expression patterns associated to pathways linked to metal mixture health effects. Gene. 2014;533:508–14.

Mezghani-Chaari S, Hamza A, Hamza-Chaffai A. Mercury contamination in human hair and some marine species from Sfax coasts of Tunisia: levels and risk assessment. Environ Monit Assess. 2011;180:477–87.

Michael Jayjock, Gumurthy Ramachandran, Susan F. Arnold. Chapter 10: Uncertainty. Math Models Estim Occup Expo Chem. USA; 2009.

Michael S. Aplin, Toxicology Division. Chromium All Compounds except Hexavalent Chromium [Internet]. TCEQ; 2009 Oct. Available from: https://www.tceq.texas.gov/assets/public/implementation/tox/dsd/final/october09/chromium3_16065-83-1.pdf

MSMildSteel.pdf [Internet]. [cited 2017 Nov 22]. Available from: https://www.mathesongas.com/industrialgas/pdfs/MSMildSteel.pdf

Mucha J, Witkowski W. The clinching joints strength analysis in the aspects of changes in the forming technology and load conditions. Thin-Walled Struct. 2014;82:55–66.

Mumtaz M, Fisher J, Blount B, Ruiz P. Application of Physiologically Based Pharmacokinetic Models in Chemical Risk Assessment. J Toxicol. 2012;2012:1–11.

Mumtaz M, Poirier KA, Colman J. Risk assessment for chemical mixtures: Fine-tuning the hazard index approach. 1997;6:189–204.

Mumtaz MM, Durkin PR. A weight-of-evidence approach for assessing interactions in chemical mixtures. Toxicol Ind Health. 1992;8:377–406.

Murphy J. Additives for Plastics Handbook. Elsevier; 2001.

National Research Council. Science and Decisions: Advancing Risk Assessment [Internet]. Washington, DC: The National Academies Press; 2009. Available from: https://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment

Nicas M, Boelter FW, Simmons CE, Scheff P, Berman L. Letter to the Editor. J Occup Environ Hyg. 2009;6:D69–71.

Nicas M, Jayjock M. Uncertainty in Exposure Estimates Made by Modeling Versus Monitoring. AIHA J. 2002;63:275–83.

Nicas M, Neuhaus J. Predicting Benzene Vapor Concentrations with a Near Field/Far Field Model. J Occup Environ Hyg. 2008;5:599–608.

Nicas M, Plisko MJ, Spencer JW. Estimating Benzene Exposure at a Solvent Parts Washer. J Occup Environ Hyg. 2006;3:284–91.

Nicas M. Estimating Methyl Bromide Exposure Due to Offgassing from Fumigated Commodities. Appl Occup Environ Hyg. 2003;18:200–10.

Nicas M. The near field/far field model with constant application of chemical mass and exponentially decreasing emission of the mass applied. J Occup Environ Hyg. 2016;13:519–28.

Nisse C, Tagne-Fotso R, Howsam M, Members of Health Examination Centres of the Nord − Pas-de-Calais region network, Richeval C, Labat L, et al. Blood and urinary levels of metals and metalloids in the general adult population of Northern France: The IMEPOGE study, 2008-2010. Int J Hyg Environ Health. 2017;220:341–63.

Nordberg GF, Gerhardsson L, Mumtaz MM, Ruiz P, Fowler BA. Chapter 11: Interactions and Mixtures in Metal Toxicology. Handb Toxicol Met [Internet]. Elsevier; 2015 [cited 2017 Dec 22]. p. 213–38. Available from: http://linkinghub.elsevier.com/retrieve/pii/B9780444594532000111

OEHHA. Air Chemicals | Chromic Trioxide [Internet]. OEHHA. 2015 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/air/chemicals/chromic-trioxide

OEHHA. Air Chemicals | Copper OEHHA [Internet]. 1999 [cited 2016 May 31]. Available from: http://oehha.ca.gov/air/chemicals/copper

OEHHA. Air Chemicals | Lead and Lead Compounds [Internet]. OEHHA. 2016 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/air/chemicals/lead-and-lead-compounds

OEHHA. Air Chemicals | Nickel and Nickel Compounds | OEHHA [Internet]. 2012 [cited 2016 Jun 2]. Available from: http://oehha.ca.gov/air/chemicals/nickel-and-nickel-compounds

OEHHA. Chemicals | Lead and Lead Compounds [Internet]. OEHHA. 2015 [cited 2017 Dec 8]. Available from: https://oehha.ca.gov/chemicals/lead-and-lead-compounds

Office of Environmental Health Hazard Assessment. Air Chemicals | OEHHA [Internet]. [cited 2016 May 25]. Available from: http://oehha.ca.gov/air/chemicals

OK With ESAB [Internet]. [cited 2016 May 18]. Available from: http://www.esab.fr/france-benelux/fr/okwithesab/

OSHA Technical Center. METAL AND METALLOID PARTICULATES IN WORKPLACE ATMOS PHERES (ICP ANALYSIS) [Internet]. 2002 [cited 2014 Aug 18]. Available from: https://www.osha.gov/dts/sltc/methods/inorganic/id125g/id125g.pdf

OSHA. OSHA Annotated PELs [Internet]. 2017 [cited 2017 Dec 6]. Available from: https://www.osha.gov/dsg/annotated-pels/tablez-1.html

Patricia H. Reinke, Charles B. Keil. Chapter 4: Well-Mixed Box Model. Math Models Estim Occup Expo Chem. USA; 2009.

Péry A, Bonvallot N, Yamani ME, Boulanger G, Karg F, Mosqueron L, et al. Valeurs limites d'exposition professionnelles (VLEP), valeurs toxicologiques de référence (VTR) : objectifs et méthodes. Environ Risques Santé. 2013;12:442–9.

Plisko MJ, Spencer JW. Evaluation of a mathematical model for estimating solvent exposures in the workplace. J Chem Health Saf. 2008;15:14–21.

Product List: | ICC Chemical Corporation [Internet]. [cited 2018 Feb 16]. Available from: https://www.iccchem.com/products

Quartz Filters, 1.2 μm, 37 mm, Type R-100, SKC, Inc. [Internet]. [cited 2016 Jun 13]. Available from: https://www.skcinc.com/catalog/product_info.php?products_id=254

Ramirez JE. Characterization of high-strength steel weld metals: chemical composition, microstructure, and nonmetallic inclusions. Weld J-N Y-. 2008;87:65.

Regional Office for Europe Copenhagen, Frank Theakston, editors. Air quality guidelines for Europe. 2nd edition. Copenhagen: World Health Organization, Regional Office for Europe; 2000.

République Tunisienne. Loi n°94-28 du 21 Février 1994 [Internet]. Journal Officiel du 22 Février 1994. Available from: https://www.ilo.org/dyn/natlex/docs/SERIAL/38574/33476/F2145285572/TUN-38574.pdf

République Tunisienne. Loi n°95-56 du 28 juin 1995 [Internet]. Journal Officiel du 4 Juillet 1995. Available from: http://www.legislation.tn/sites/default/files/journal-officiel/1995/1995F/Jo05395.pdf

Riihimäki V, Aitio A. Occupational exposure to aluminum and its biomonitoring in perspective. Crit Rev Toxicol. 2012;42:827–53.

Robbins CA, Krause MW, Atallah RH, Plisko MJ. Comparison of exposure measurements to near field–far field modeled results for benzene and base solvents during a cleaning process using plain or 0.1% benzene spiked toluene and xylene. J Chem Health Saf. 2012;19:3–11.

Rossbach B, Buchta M, Csanády GA, Filser JG, Hilla W, Windorfer K, et al. Biological monitoring of welders exposed to aluminium. Toxicol Lett. 2006;162:239–45.

Rudolf E, Cervinka M. Nickel modifies the cytotoxicity of hexavalent chromium in human dermal fibroblasts. Toxicol Lett. 2010;197:143–50.

Ryker SJ, Small MJ. Combining Occurrence and Toxicity Information to Identify Priorities for Drinking-Water Mixture Research. Risk Anal. 2008;28:653–66.

S235JR Chemical Composition, S235JR Mechanical Properties, S235JR Heat Treatment [Internet]. Longhai Spec. Steel. [cited 2016 May 1]. Available from: http://www.steelgr.com

S235JR Steel Grade, Mechanical Properties, Chemical Composition, Grade Equivalent [Internet]. [cited 2016 May 1]. Available from: http://www.b2bmetal.eu/en/pages/index/index/id/141/

S235JR.pdf [Internet]. [cited 2016 Apr 21]. Available from: https://www.metaldata.info/reports/S235JR.pdf

s235jren42.pdf [Internet]. [cited 2016 Apr 21]. Available from: http://www.lucefin.com/wp-content/files_mf/s235jren42.pdf

Saïdi SA, Azaza MS, Windmolders P, van Pelt J, El-Feki A. Cytotoxicity evaluation and antioxidant enzyme expression related to heavy metals found in tuna by-products meal: An in vitro study in human and rat liver cell lines. Exp Toxicol Pathol. 2013;65:1025–33.

Samal L, Mishra C. Significance of Nickel in Livestock Health and Production. Int J Agro Vet Med Sci. 2011;5:349.

SAN DIEGO Air Pollution Control District, editor. WELDING OPERATIONS [Internet]. 1998 [cited 2018 Jan 9]. Available from: http://www.sdapcd.org/content/dam/sdc/apcd/PDF/Toxics_Program/APCD_welding1.pdf

Sasso AF, Isukapalli SS, Georgopoulos PG. A generalized physiologically-based toxicokinetic modeling system for chemical mixtures containing metals. Theor Biol Med Model. 2010;7:17.

Schneider T, Kildes J, Breum NO. A two compartment model for determining the contribution of sources, surface deposition and resuspension to air and surface dust concentration levels in occupied rooms. Build Environ. 1999;34:583–95.

Serbaji MM, Azri C, Medhioub K. Anthropogenic Contributions to Heavy Metal Distributions in the Surface and Sub-surface Sediments of the Northern Coast of Sfax, Tunisia. Int J Environ Res. 2012;6:613–26.

SKC Inc. SKC, Inc. [Internet]. SKC Inc. [cited 2018 Apr 5]. Available from: http://www.skcinc.com/catalog/index.php

Smaoui-Damak W, Berthet B, Hamza-Chaffai A. In situ potential use of metallothionein as a biomarker of cadmium contamination in Ruditapes decussatus. Ecotoxicol Environ Saf. 2009;72:1489–98.

Smaoui-Damak W, Berthet B, Rebai T, Hamza-Chaffai A. Effets de la pollution par les metaux sur le potentiel reproducteur de la palourde Ruditapes decussatus (L.) issue du Golfe de Gabes (Tunisie). Bull Société Zool Fr. 2008;133:131–139.

Smaoui-Damak W, Rebai T, Berthet B, Hamza-Chaffai A. Does cadmium pollution affect reproduction in the clam Ruditapes decussatus? A one-year case study. Comp Biochem Physiol Part C Toxicol Pharmacol. 2006;143:252–61.

Spencer JW, Plisko MJ. A Comparison Study Using a Mathematical Model and Actual Exposure Monitoring for Estimating Solvent Exposures During the Disassembly of Metal Parts. J Occup Environ Hyg. 2007;4:253–9.

TCEQ. Final Development Support Documents (DSDs) [Internet]. TCEQ. [cited 2017 Dec 8]. Available from: https://www.tceq.texas.gov/toxicology/dsd/final.html

Teuschler LK. Deciding which chemical mixtures risk assessment methods work best for what mixtures. Toxicol Appl Pharmacol. 2007;223:139–47.

Total Materia - La Base de Données sur les Matériels la Plus Complète au Monde [Internet]. [cited 2016 Mar 24]. Available from: http://www.totalmateria.com/page.aspx?ID=Home&LN=FR

U.S. Department of Health and Human Services Public Health Service, ATSDR. INTERACTION PROFILE FOR: LEAD, MANGANESE, ZINC, AND COPPER [Internet]. 2004 May. Available from: https://www.atsdr.cdc.gov/interactionprofiles/ip-metals2/ip06.pdf

U.S. DEPARTMENT OF THE NAVY CARDEROCK DIVISION. Characterizing Shipyard Welding Emissions and Associated Control Options. NSRP 0457 [Internet]. 1995. Available from: http://www.dtic.mil/dtic/tr/fulltext/u2/a455525.pdf

Unité cancer environnement. Valeurs de référence | Cancer et environnement [Internet]. 2016 [cited 2016 May 25]. Available from: http://www.cancer-environnement.fr/232-Valeurs-de-reference.ce.aspx

US EPA O. AP-42: Compilation of Air Emission Factors [Internet]. 1995 [cited 2018 Jan 12]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

US EPA O. Chromium(III), insoluble salts CASRN 16065-83-1 | IRIS | US EPA, ORD [Internet]. 1998 [cited 2017 Dec 8]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=28

US EPA O. Chromium(VI) CASRN 18540-29-9 | IRIS | US EPA, ORD [Internet]. 1998 [cited 2017 Dec 8]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=144

US EPA O. Guidelines for the Health Risk Assessment of Chemical Mixtures [Internet]. 1986 [cited 2018 Jan 22]. Available from: https://www.epa.gov/risk/guidelines-health-risk-assessment-chemical-mixtures

US EPA Office of Air Quality Planning and Standards, US EPA. Chapter 12: Metallurgical Industry, section 19: Electric Arc Welding. AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1995. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

US EPA Office of Air Quality Planning and Standards. Chapter 12: Metallurgical Industry, section 20: Electroplating. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. 1996. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/index.html

US EPA Office of Air Quality Planning and Standards. Intoduction. Emiss Factors AP 42 Compil Air Pollut Emiss Factors [Internet]. Fifth Edition. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emission-factors

US EPA, Office of the Science Advisor. Framework for Metals Risk Assessment [Internet]. 2007 Mar. Available from: https://www.epa.gov/risk/framework-metals-risk-assessment

US EPA. AP-42: Compilation of Air Emissions Factors [Internet]. US EPA. 2016 [cited 2018 Mar 26]. Available from: https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emissions-factors

US EPA. Copper (CASRN 7440-50-8) | IRIS | US EPA - 0368_summary.pdf [Internet]. 1988 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0368_summary.pdf

US EPA. Emission Factor Documentation for AP-42 Section 12.20 Electroplating Final Report [Internet]. 1996 Jul. Available from: https://www3.epa.gov/ttn/chief/ap42/ch12/bgdocs/b12s20.pdf

US EPA. IRIS Assessments; Integrated Risk Information System [Internet]. [cited 2016 May 25]. Available from: https://cfpub.epa.gov/ncea/iris2/atoz.cfm

US EPA. Lead and compounds (inorganic) CASRN 7439-92-1 | IRIS | US EPA, ORD [Internet]. 2004 [cited 2016 Jun 17]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=277

US EPA. Lead and compounds (inorganic) CASRN 7439-92-1 | IRIS | US EPA, ORD [Internet]. 2004 [cited 2016 Jun 17]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=277

US EPA. Nickel carbonyl CASRN 13463-39-3 | IRIS | US EPA, ORD [Internet]. 1986 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=274

US EPA. Nickel refinery dust CASRN NA | IRIS | US EPA, ORD [Internet]. 1987 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=272

US EPA. Nickel subsulfide CASRN 12035-72-2 | IRIS | US EPA, ORD [Internet]. 1687 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=273

US EPA. Nickel, soluble salts CASRN NA | IRIS | US EPA, ORD [Internet]. 1994 [cited 2016 Jun 2]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=271

US EPA. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures [Internet]. 2000 [cited 2015 Dec 24]. Available from: http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486

US EPA. Zinc and Compounds CASRN 7440-66-6 | IRIS | US EPA, ORD [Internet]. 2005 [cited 2016 May 31]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=426

US EPA. Zinc cyanide CASRN 557-21-1 | IRIS | US EPA, ORD [Internet]. 1987 [cited 2016 Jun 1]. Available from: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=127

von Stackelberg K, Guzy E, Chu T, Henn BC. Mixtures, Metals, Genes and Pathways: A Systematic Review. 2013 [cited 2014 Feb 10]; Available from: http://www.hsph.harvard.edu/hcra/files/2013/09/von-Stackelberg-et-al.-Sept-2013.pdf

Weman K. Chapter 8 - Pressure welding methods. Weld Process Handb [Internet]. Woodhead Publishing; 2003 [cited 2018 Mar 16]. p. 80–92. Available from: https://www.sciencedirect.com/science/article/pii/B9781855736894500114

WHO World Health Organization. IARC Monographs- Classifications [Internet]. [cited 2018 Jan 16]. Available from: http://monographs.iarc.fr/ENG/Classification/latest_classif.php

Wilkinson CF, Christoph GR, Julien E, Kelley JM, Kronenberg J, McCarthy J, et al. Assessing the risks of exposures to multiple chemicals with a common mechanism of toxicity: how to cumulate? Regul Toxicol Pharmacol RTP. 2000;31:30–43.

Williams PRD, Dotson GS, Maier A. Cumulative Risk Assessment (CRA): Transforming the Way We Assess Health Risks. Environ Sci Technol. 2012;46:10868–74.

Wu C-C, Liu H-M. Determinants of Metals Exposure to Metalworking Fluid Among Metalworkers in Taiwan. Arch Environ Occup Health. 2014;69:131–8.

SCIENTIFIC VALORIZATION

Publications

I.1. Article:

Omrane F, Gargouri I, Khadhraoui M, Elleuch B, Zmirou-Navier D. Risk assessment of occupational exposure to heavy metal mixtures: a study protocol. BMC Public Health. 2018;18:314.

I.2. Communication:

Omrane F, Gargouri I, Khadhraoui M, Elleuch B, Zmirou-Navier D. Identification and modeling of occupational exposure to heavy metals in sfax metropolis (Tunisia). Toxicol Lett. 2016;258, Supplement:S229.

Communications in scientific events

Rencontres scientifique du réseau doctoral en santé publique: March 22 and 23, 2016**, *Ecole des Hautes Etudes en Santé Publique (EHESP) Paris, France*.

F. Omrane, I. Gargouri, M. Khadhraoui, B. Elleuch, D. Zmirou-Navier. **Identification and modeling of occupational exposure to heavy metals in Sfax metropolis (Tunisia).** Poster communication.

4th European Doctoral College on Environment and Health (EDCEH 2016): June 6-8, 2016,*Ecole des Hautes Etudes en Santé Publique (EHESP), Rennes, France.*

F. Omrane, I. Gargouri, M. Khadhraoui, B. Elleuch, D. Zmirou-Navier. **Mathemathical modeling of occupational exposure to heavy metals in Sfax metropolis.** Poster communication.

International Conference in Integrated Management of Environment (ICIEM 2016): October 27-30, 2016, *Sousse –Tunisia.*

F. Omrane, I. Gargouri, M. Khadhraoui, B. Elleuch, D. Zmirou-Navier. **Modeling of occupational exposure to heavy metals in companies from Sfax metropolis.** Oral communication.

Rencontres scientifique du réseau doctoral en santé publique: March 14 and 15, 2017**, *Ecole des Hautes Etudes en Santé Publique (EHESP) Paris, France*.

<u>F. Omrane</u>, I. Gargouri, M. Khadhraoui, B. Elleuch, D. Zmirou-Navier. **Application of mathematical models to estimate indoor air concentration of heavy metals.** Oral communication.

International Conference in Integrated Management of Environment (ICIEM 2018): May 2-5, 2018, *Sousse –Tunisia.*

<u>F. Omrane</u>, I. Gargouri, M. Khadhraoui, B. Elleuch, D. Zmirou-Navier. **Predicting heavy metal concentrations with Near Field-Far Field models for Occupational Exposure Assessment Purposes in steel cutting industry.** Oral communication.

APPENDICES

APPENDICES

Enquête Environnement et Santé

EVALUATION DES IMPACTS SANITAIRES DES EXPOSITIONS PROFESSIONNELLES
A DES MELANGES DE METAUX LOURDS
DANS LA METROPOLE DE SFAX

Sfax, le 26/07/2018

Entreprise ....

Monsieur ....,

Nous vous remercions d'avoir accepté de participer à notre projet.

Après avoir fixé un rendez-vous, afin de réaliser la première étape de l'étude, nous allons réaliser un questionnaire dit de repérage qui consiste à recueillir un certain nombre d'informations tel que les compositions et les quantités des produits et des matériaux utilisés, le nombre des salariés, leurs emplois du temps de travail au sein de l'entreprise et l'architecture et les dimensions des ateliers.

Veillez agréé, Monsieur ...., nos salutations les meilleures.

Mlle Fatma OMRANE   Dr Imed GARGOURI   Dr Moncef KHADRAOUI   Pr Boubaker ELLEUCH

Enquête Environnement et Santé

EVALUATION DES IMPACTS SANITAIRES DES EXPOSITIONS PROFESSIONNELLES A DES MELANGES DE METAUX LOURDS
DANS LA METROPOLE DE SFAX

N° de saisie I_I_I_I
Date: .../.../201...

Questionnaire de Repérage des Entreprises

« Ce questionnaire est strictement confidentiel »

Codage (ne pas remplir SVP)

➔ **L'ENTREPRISE**

Entreprise : ………………………………………………………………………………..……….

Adresse : ………………………………………………………………………………...

Téléphone : ……………………...

♦ Code Entreprise : I_I_I_I_I_I_I   I_I_I_I_I_I

♦ **Secteur d'activité : Industrie**

- Métallurgique/ d'alliages $\square_1$
- De traitement de surface $\square_2$
- D'engrais phosphatés $\square_3$
- Electrique $\square_4$
- De verre $\square_5$
- De vernis $\square_6$
- De plastique $\square_7$

CONTACTS DES SALARIES AVEC LES METAUX LOURDS (ML)

♦ Nombre total de salariés dans l'entreprise :

I_I_I_I_I   I_I_I_I_I

♦ Nombre total de **salariés actuellement en contact avec** les ML :

I_I_I_I   I_I_I_I
➔ salariés utilisateurs (Manipulateurs)

I_I_I   I_I_I
➔ salariés non manipulateurs

I_I_I   I_I_I

Nombre de **salariés utilisateurs** ayant une **durée cumulée d'exposition** aux ML
au sein de l'entreprise (que cette exposition persiste ou non actuellement), de :

➜ < 5 ans |_|_|_| |_|_|_|

➜ ≥ 5 et < 10 ans |_|_|_| |_|_|_|

➜ ≥ 10 et < 15 ans |_|_|_| |_|_|_|

➜ ≥ 15 ans |_|_|_| |_|_|_|

L'ACTIVITE EXPOSANT AUX METAUX LOURDS DE L'ENTREPRISE

♦ **Quels sont les métaux lourds utilisés pour ces activités ?**
Précisez le **nom** des substances (commercial et/ou d'usage courant)

Nom
1.
2.
3.
4.
5.
6.
7.
8.

♦ **Les salariés utilisateurs des substances contenant des métaux lourds portent-ils :**

➜ des **vêtements de travail** différents de leurs vêtements de ville ?

Oui ☐1   Non ☐2

↳ **Si Oui**, précisez le **%** de salariés |_|_| |_|

|_|_|

➜ des **masques de protection** lors du travail ?

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Oui ☐$_1$ Non ☐$_2$

↳ **Si Oui**, précisez le **%** de salariés   I_I_I   I_I

I_I_I

L'ATELIER DE REALISATION DES TRAVAUX EXPOSANT
➔ **AUX METAUX LOURDS**

Atelier 1 :

♦ **Quelle est la superficie de l'atelier ?**   I_I_I_I_I_I m^2 I_I_I_I_I

♦ **Quelle est l'architecture de l'atelier ?**

➔ Nombre de pièces   I_I_I   I_I_I

➔ Faites un schéma de l'atelier en précisant :

Longueur = …… m, largeur = ….. m, Hauteur = ….. m

➔ Faites un descriptif de l'ambiance générale de l'atelier :

	OUI$_1$	NON$_2$	
▪ le bâtiment est une nouvelle construction	☐	☐	I_I
▪ les locaux sont bien entretenus	☐	☐	I_I
▪ il existe des vestiaires et une cantine	☐	☐	I_I
▪ il est situé dans des locaux d'habitation	☐	☐	I_I

♦ **Comment est assurée la ventilation dans l'atelier ?**

➔ Aucune aération (espace confiné)   ☐$_1$ I_I

➔ Aération naturelle (portes et fenêtres)   ☐$_2$

➔ Ventilation mécanique générale (extraction d'air) : ☐$_3$

➔ Extraction à la source d'utilisation des ML   ☐$_4$

➔ Autre   ☐$_5$

Si autre, veuillez préciser : ……………………………..……

Quels sont les métaux lourds utilisés pour ces activités dans l'atelier 1 ?

Précisez le **nom** des substances (commercial et/ou d'usage courant)
et **l'entreprise productrice**

METAUX LOURDS			
Nom	Entreprise productrice	Quantité utilisée/an	Nbre de Salariés directement exposés
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

AUTRES PRODUITS			
Nom	Entreprise productrice	Quantité utilisée/an	Nbre de Salariés directement exposés
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

Atelier 2 :

♦ **Quelle est la superficie de l'atelier ?**   I_I_I_I_I_I m²

♦ **Quelle est l'architecture de l'atelier ?**
   ➔ Nombre de pièces   I_I_I

   ➔ Faites un schéma de l'atelier en précisant :

Longueur = …… m, largeur = ….. m, Hauteur = ….. m

   ➔ Faites un descriptif de l'ambiance générale de l'atelier :

	OUI₁	NON₂
▪ le bâtiment est une nouvelle construction	☐	☐
▪ les locaux sont bien entretenus	☐	☐
▪ il existe des vestiaires et une cantine	☐	☐
▪ il est situé dans des locaux d'habitation	☐	☐

♦ **Comment est assurée la ventilation dans l'atelier ?**
   ➔ Aucune aération (espace confiné)   ☐₁   I_I
   ➔ Aération naturelle (portes et fenêtres)   ☐₂
   ➔ Ventilation mécanique générale (extraction d'air) :   ☐₃
   ➔ Extraction à la source d'utilisation des ML   ☐₄
   ➔ Autre   ☐₅

   Si autre, veuillez préciser : …………………………..……

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Quels sont les métaux lourds utilisés pour ces activités dans l'atelier 2 ?

Précisez le **nom** des substances (commercial et/ou d'usage courant)
et **l'entreprise productrice**

METAUX LOURDS			
Nom	Entreprise productrice	Quantité utilisée/an	Nbre de Salariés directement exposés
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

AUTRES PRODUITS			
Nom	Entreprise productrice	Quantité utilisée/an	Nbre de Salariés directement exposés
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

Atelier 3 :

♦ **Quelle est la superficie de l'atelier ?** |_|_|_|_|_| m^2 |_|_|_|_|

♦ **Quelle est l'architecture de l'atelier ?**
➔ Nombre de pièces |_|_| |_|_|
➔ Faites un schéma de l'atelier en précisant :

Longueur = ... m, largeur = ... m, Hauteur = ... m

➔ Faites un descriptif de l'ambiance générale de l'atelier :

	OUI$_1$	NON$_2$	
▪ le bâtiment est une nouvelle construction	☐	☐	|_|
▪ les locaux sont bien entretenus	☐	☐	|_|
▪ il existe des vestiaires et une cantine	☐	☐	|_|
▪ il est situé dans des locaux d'habitation	☐	☐	|_|

♦ **Comment est assurée la ventilation dans l'atelier ?**
➔ Aucune aération (espace confiné) ☐$_1$ |_|
➔ Aération naturelle (portes et fenêtres) ☐$_2$
➔ Ventilation mécanique générale (extraction d'air) : ☐$_3$
➔ Extraction à la source d'utilisation des ML ☐$_4$
➔ Autre ☐$_5$

Si autre, veuillez préciser : ……………………………..……

Quels sont les métaux lourds utilisés pour ces activités dans l'atelier 3 ?

Précisez le **nom** des substances (commercial et/ou d'usage courant)
et **l'entreprise productrice**

METAUX LOURDS			
Nom	**Entreprise productrice**	**Quantité utilisée/an**	**Nbre de Salariés directement exposés**
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

AUTRES PRODUITS			
Nom	**Entreprise productrice**	**Quantité utilisée/an**	**Nbre de Salariés directement exposés**
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

**Vérifiez que vous avez bien répondu à toutes les questions.
Pour toute question concernant le questionnaire, vous pouvez contacter
Fatma OMRANE au 21552700 ou omrannefatma@gmail.com**

Enquête Environnement et Santé

EVALUATION DES IMPACTS SANITAIRES DES EXPOSITIONS PROFESSIONNELLES A DES MELANGES DE METAUX LOURDS

DANS LA METROPOLE DE SFAX

N° de saisie ☐☐☐

FICHE DESCRIPTIVE DES TACHES (ETUDE DE POSTE)

Date : …../……./ 201......

Codage

Entreprise : « ………………………………………………. »   ☐☐

Dénomination de l'atelier : « …………………….………..………………… »   ☐☐

Dénomination du(s) poste(s) : « …………………….………..………………
…………………….………..…………………»   ☐☐

Nombre d'agents :   ☐☐   ☐☐
      Hommes   ☐☐   ☐☐
      Femmes   ☐☐   ☐☐

Produit(s) manipulé(s) :   nombre ☐☐   ☐☐
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….
    ▶ …………………………………………….

Métaux manipulés / étudiés   ☐

    ZINC ☐   NICKEL ☐
    CHROME ☐   PLOMB ☐
    CUIVRE ☐   CADMIUM ☐
    ALUMINIUM ☐   FER ☐

Conditions de travail :
    ◆ Travail à l'intérieur (les 3 derniers jours): Non $\square_0$ Oui $\square_1$ ☐
        Si non, % temps à l'extérieur ☐☐   ☐☐
    ◆ Température :
        ➢ de l'atelier : ……………...°C
        ➢ à l'extérieur de l'atelier : ……………...°C

◆ Pression Atmosphérique :
   ➢ de l'atelier : ……………..hPa ou mmHg ou Bar
   ➢ à l'extérieur de l'atelier : …………..hPa ou mmHg ou Bar

◆ Humidité : …………………………..%

◆ Atelier :
   Ventilation avec extraction   Non $\square_0$ Oui $\square_1$ $\square$
   Atmosphère confinée   Non $\square_0$ Oui $\square_1$ $\square$
   Ventilation naturelle   Non $\square_0$ Oui $\square_1$ $\square$
   Climatisation centrale   Non $\square_0$ Oui $\square_1$ $\square$
   Ventilateur (au plafond,…)   Non $\square_0$ Oui $\square_1$ $\square$

Indiquer l'emplacement
   ◆ du(s) travailleur(s) (la(s) poste(s))
   ◆ des machines
   ◆ des source(s) d'émission des métaux
   ◆ des sources des ventilations

Longueur = …… m, largeur = ….. m, Hauteur = ….. m

Volume / superficie
   ◆ de l'atelier : …………
   ◆ des contenus de la pièce

   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………

   ◆ Surfaces des points de ventilations :
   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………
   …………………………………   …………………………………

Mode de la génération des contaminants :

◆ Continu ☐
◆ Discontinu ☐
(Préciser les durées) …………………………………………………

◆ Cyclique ☐
(Préciser les durées) …………………………………………………

◆ Croissant ☐
(Préciser les durées/ les débits (V/t)) …………………………………
………………………………

◆ Décroissant ☐
(Préciser les durées/ les débits (V/t)) …………………………………
………………………………

Source d'émission des métaux :

◆ Ponctuelle ☐

◆ Une zone : limitée ☐
: Étendue ☐
(Préciser la superficie : ………………………………)

Les matériaux :
◆ Masses des matières premières utilisées dans le processus :
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J
………………………/ an, sem., J

◆ Masse des produits : ………………………/ an, sem., J
◆ Masse des déchets recueillis du processus …………………/ an, sem., J

Mesures des vitesses de l'air : (dans chaque point de ventilation)+ (à proximité de la source d'emission)

Enterprise : …….……… : Semaine ……...
Atelier : ………………
Jour 1 : …/…/17

Time (15 min)	8h	8h15	8h30	8h45	9h	9h15	9h30	9h45	10h	10h15	10h30	10h45	11h	11h15	11h30	11h45	12h
Temp (°C)																	
Air velocity (1min average) m/s																	

Time (15 min)	13h	13h15	13h30	13h45	14h	14h15	14h30	14h45	15h	15h15	15h30	15h45	16h	16h15	16h30	16h45	17h
Temp (°C)																	
Air velocity (1min average) m/s																	

Enterprise : ……….……. : Semaine ……..
Atelier : ………………
Jour 2 : …/…/17

Time (15 min)	8h	8h15	8h30	8h45	9h	9h15	9h30	9h45	10h	10h15	10h30	10h45	11h	11h15	11h30	11h45	12h
Temp (°C)																	
Air velocity (1min average) m/s																	

Time (15 min)	13h	13h15	13h30	13h45	14h	14h15	14h30	14h45	15h	15h15	15h30	15h45	16h	16h15	16h30	16h45	17h
Temp (°C)																	
Air velocity (1min average) m/s																	

Enterprise : ……….…… : Semaine ……...
Atelier : ………………
Jour 3 : …/…/17

Time (15 min)	8h	8h15	8h30	8h45	9h	9h15	9h30	9h45	10h	10h15	10h30	10h45	11h	11h15	11h30	11h45	12h
Temp (°C)																	
Air velocity (1min average) m/s																	

Time (15 min)	13h	13h15	13h30	13h45	14h	14h15	14h30	14h45	15h	15h15	15h30	15h45	16h	16h15	16h30	16h45	17h
Temp (°C)																	
Air velocity (1min average) m/s																	

République Tunisienne
Ministère de la Santé

MINISTERE DE LA SANTE

COMITE DE PROTECTION DES PERSONNES SUD

« C.P.P.SUD »

Le Comité de Protection des Personnes Sud « CPP Sud», à été saisi, le Mardi 02 Mai 2017, Le Groupe de recherche mixte Tuniso-Français entre le laboratoire GEET à l'Ecole Nationale d'Ingénieurs de Sfax (ENIS), de l'Université de Sfax et l'Eole des Hautes Etudes de Santé Publique (EHESP) de France en vue d'une publication dans une revue scientifique.

D'un travail intitulé :

L'évaluation du risque d'exposition professionnelle à des mélanges de métaux

Les auteurs sont : (Fatma Omrane, Imed Gargouri, Moncef Khadhraoui, Boubaker Elleuch et Denis Zmirou-Navier)

Références CPP Sud : ....**0034/2017**..................................

Après discussion avec les auteurs de ce travail, les membres du Comité « CPP Sud », attestent que ce travail obéit aux règles d'éthiques de notre pays. Ils ont vérifié la véracité des documents d'informations et les consentements éclairés.

Un avis **favorable** a été émis par le Comité.

Sfax le.02/05/2017

Signature du Président

Comité de Protection des Personnes
CPP SUD
Le Président
Professeur Zouhir Bahloul

CONVENTION : Lab GEET – [REDACTED]

« Evaluation du risque chimique »
(Semi-quantitative et Quantitative)

ENTRE :

LE LABORATOIRE « GENIE DE L'ENVIRONEMENT ET ECOTECHNOLOGIE à l'ENIS,
représenté par Monsieur le Professeur Boubaker ELLEUCH, Directeur

ci-après désigné par « **Labo GEET** »

d'une part,

ET :

L'ETABLISSEMENT [REDACTED], représenté par Monsieur [REDACTED]
Directeur Général

ci-après désignée par « [REDACTED] »

d'autre part,

désignés comme les Parties.

Etant préalablement exposé que :

Le « **Lab GEET : LR16ES19** » de l'ENIS, dirigé par le Professeur Boubaker **ELLEUCH**, conduit un programme de recherche en vue d'évaluer les impacts sanitaires à court et à long terme des expositions aux métaux utilisés en milieu professionnel dans la région de Sfax (Tunisie), travaux dirigés par **les Docteurs Imed GARGOURI et Moncef KHADHRAOUI**

Et que

La [REDACTED] conduit un programme de prévention en santé et sécurité au travail au profit de ses employés, travaux dirigés par **Monsieur** [REDACTED]

Il a été convenu et arrêté ce qui suit :

ARTICLE 1 - OBJET

La présente convention définit les conditions de la collaboration scientifique entre le Lab GEET de l'ENIS et l'EHK en vue de réaliser (i) une évaluation du risque chimique par modélisation (semi-quantitative) ; (ii) Une évaluation Bio-toxicologique (Quantitative), suite à la première phase : des prélèvements atmosphériques et urinaires, et de les analyser suite à des expositions aux métaux utilisés dans l'entreprise (iii) proposer des solutions et des alternatives si nécessaire.

ARTICLE 2 - DUREE

La présente convention prend effet à compter de sa date de signature pour une période de 3 ans. Si des retards dans le déroulement du programme apparaissaient, la modification de la durée de la présente convention ferait l'objet d'un avenant.

ARTICLE 3 - CONDITIONS D'EXECUTION

Les travaux, objet de la présente convention, seront exécutés conformément à la description incluse dans l'**annexe scientifique** (*les modes d'intervention*).
Les correspondants désignés du **Lab GEET** pour la conduite de cette collaboration scientifique sont **messieurs Imed GARGOURI**, MD-PhD en évaluation du risque professionnel et environnemental et **Moncef KHADHRAOUI**, PhD en chimie analytique.

Le correspondant désigné de l'[ ] cet effet est **Monsieur** [   ] Directeur de l'usine.

ARTICLE 4 – ACTIVITES DES PARTENAIRES PREVUES AU TITRE DE LA COLLABORATION

[   ] est à l'initiative des analyses et en assure la coordination. Elle engagera toutes les démarches en vue d'obtenir la collaboration des employés, ainsi que les démarches administratives nécessaires au déroulement des analyses.

Le Lab GEET assure les explorations visant à apprécier et mesurer les expositions des personnels aux métaux. Le Lab GEET met à la disposition des partenaires de [   ] pour la réalisation des analyses des métaux et des urines, un matériel lourd ainsi que de compétences humaines perfectionnées pour l'analyse et l'expertise.

ARTICLE 5 - CONFIDENTIALITE

Les analyses des métaux et des urines sont la propriété de « [   ] ». Le partenaire « Labo GEET » est tenu par le secret professionnel.

Aucune utilisation de ces analyses n'est possible sans l'autorisation écrite de « [   ] ».

ARTICLE 6 - PUBLICATIONS - COMMUNICATIONS

Les publications et communications résultant de l'exécution de la présente convention associeront, d'un commun accord, les scientifiques ayant contribués significativement aux travaux, et feront mention des apports des deux parties, à moins que l'une ou l'autre ne souhaite pas figurer parmi les co-auteurs.

ARTICLE 7 – CALENDRIER PREVISIONNEL

Les deux volets du programme d'intervention (article1) se dérouleront dans les périodes d'Août 2015 et Août- Septembre 2017. L'exploitation des données, les échanges scientifiques et la rédaction des articles scientifiques en découlant pourront se poursuivre jusqu'au terme de la présente convention. Des réunions d'échanges scientifiques, pourront avoir lieu pendant cette période, par décision conjointe des partenaires.

ARTICLE 8 - DISPOSITIONS FINANCIERES

Pour chaque action un avenant précisant la modalité du payement sera élaboré.

ARTICLE 9 - MODIFICATIONS OU ADJONCTIONS A LA CONVENTION

Les stipulations de la présente convention pourront être modifiées ou complétées par voie d'avenant signé par les deux parties.

Cette convention sera reconduite par tacite reconduction.

ARTICLE 10 - ENREGISTREMENT

La présente convention est exemptée de la formalité de l'enregistrement et du timbrage.

Fait à Sfax, le .... 20......
en quatre exemplaires originaux

Pour le Lab GEET à l'ENIS

Le Directeur,

Monsieur le Professeur Boubaker ELLECH

Pr.Boubaker ELLEUCH

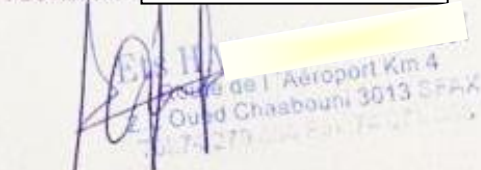Le responsable scientifique des recherches sur les expositions aux métaux

Monsieur le Docteur Imed GARGOURI

Docteur Imed GARGOURI
M.C.A. Hospitalo-Universitaire
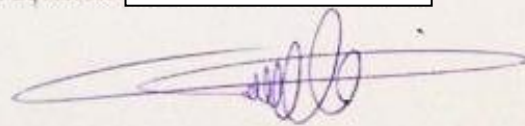en Médecine du Travail
Faculté de Médecine de Sfax

Pour la [redacted]

Le Président Directeur Général

Monsieur [redacted]

Le Directeur de l'usine

Monsieur [redacted]

Abstract:

Trace metallic elements (TMEs) are pollutants of great concern even in trace amounts because of their toxicity and cumulative property. Some of them can be carcinogenic. The Sfax metropolis, located in the southern region of Tunisia, has been affected by releases of TMEs for decades. Several studies confirmed that this pollution is predominantly originated from anthropogenic sources, mainly from industrial activities. It represents a threat to the health of residents, particularly for those also exposed during occupational activities in industrial processes.

The present study aims to assess health risks associated with occupational exposure in industries handling TMEs in their production processes, following the human health risk assessment approach.

To this end, five companies using raw material containing TMEs to produce a variety of metallic products accepted to participate to the study. The metals that were investigated are Al, Cr, Ni, Cu, Zn and Pb.

Mathematical models for estimating occupational exposure to chemicals were used to predict indoor air TME exposure levels in 15 different job tasks. Air monitoring was conducted in order to compare the predicted workplace air concentrations versus the direct measured ones, using both workplace-fixed monitors and personal samplers. And finally, urine samples were collected from 61 workers to assess whether TMEs excretion correlate with job exposure levels.

Globally, the predicted air estimates relate well with measured concentrations over the whole set of job tasks. Better predictions were found for certain activities, in particular for steel cutting and welding processes.

The values that correspond to the 90th percentile of the exposure distribution were then used in the interaction-based hazard index HI_{int} to assess health risks associated with the mixtures of TMEs. Total cancer risk was also investigated.

Results showed high exposures for metals that may elicit respiratory conditions, with a HI_{int} reaching 93.6, the highest levels being for the shielded metal arc welding and metal shearing and slitting tasks. The risk is enhanced by a synergetic effect between Cr, Ni and Cu. High risks of lung and kidney cancers were demonstrated (the predicted life-long total cancer risk for exposed workers is 3.7×10^{-4}).

This work shows that mathematical models can be accurate in predicting TME airborne exposure levels for several processes in the metallurgic industry, a result that is of interest to help the different stakeholders to monitor efficiently exposure surveillance and abatement. Progress in industrial hygiene is needed in this industrial sector to reduce the high level of health risks currently experienced by the metalworking workers.

Key words: Occupational exposure, trace metallic elements, human health risk assessment, mathematical models, air monitoring, biomonitoring.

Résumé:

Les éléments trace métalliques (ETM) sont des polluants qui sont sources de préoccupations majeures à cause de leurs toxicités et de leurs propriétés cumulatives. Certains d'eux peuvent être cancérogènes. La métropole de Sfax, située au sud de la Tunisie, a été touchée par des rejets et émissions d'ETM depuis des décennies. Plusieurs études ont confirmé que la pollution métallique est principalement d'origine anthropique, liée en particulier aux activités industrielles. Cela présente un risque sur la santé des habitants, particulièrement pour ceux qui sont également exposés par leur métier dans des procédés industriels.

L'objectif de cette étude est d'évaluer les risques sanitaires associés à l'exposition professionnelle dans les industries qui manipulent des ETM dans leurs processus de production, en suivant l'approche de l'évaluation des risques sanitaires.

Dans ce but, cinq entreprises qui utilisent des métaux comme matière première pour produire une variété de produits métalliques, ont accepté d'adhérer à notre étude. Les métaux qui étaient explorés sont Al, Cr, Ni, Cu, Zn and Pb.

Des modèles mathématiques de prédiction des expositions professionnelles aux agents chimiques ont été utilisés pour estimer les concentrations des ETM dans l'air intérieur pour 15 postes différents. Des prélèvements atmosphériques ont été effectués afin de comparer les concentrations prédites à celles mesurées, en utilisant des prélèvements individuels ou sur postes fixes. Finalement, des prélèvements urinaires ont été collectés chez 61 travailleurs afin d'évaluer le lien entre l'excrétion des ETM et les niveaux atmosphériques.

Globalement, les estimations des concentrations atmosphériques avaient une bonne concordance avec les valeurs mesurées sur l'ensemble des postes de travail. Des meilleures prédictions ont été trouvées pour certaines activités, en particulier pour des processus de découpage des tôles et de soudures. Les valeurs qui correspondent au 90ème percentile de la distribution de l'exposition ont été utilisées pour le calcul du « *interaction-based hazard index HI_{int}* » pour évaluer les risques associés aux mélanges d'ETM. Un excès de risque total de cancer a été aussi calculé.

Les résultats ont montré des expositions élevées qui peuvent provoquer des pathologies respiratoires, avec un HI_{int} allant jusqu'à 93,6. Les niveaux les plus élevés sont attribués à la soudure à l'arc à l'électrode enrobée et au débitage et cisaillage des tôles. Ces risques augmentent à cause de l'effet synergique qui existe entre Cr, Ni et Cu. Des risques élevés de cancer du poumon et du rein ont été encore démontrés (risque total vie entière de cancer pour les ouvriers exposés : 3.7×10^{-4}).

Ce travail montre que les modèles mathématiques peuvent prédire correctement les niveaux d'exposition des ETM dans l'air intérieur pour plusieurs processus de la métallurgie. Ce résultat est intéressant pour aider les différents acteurs pour piloter de manière efficiente les systèmes de surveillance et la réduction des expositions dans ce secteur économique. Des progrès en matière d'hygiène industrielle sont nécessaires dans ce secteur industriel pour minimiser le risque sanitaire élevé auquel sont actuellement exposés les travailleurs concernés.

Mots clés: exposition professionnelle, éléments trace métalliques, évaluation des risques sanitaires, modèles mathématiques, prélèvements atmosphériques, biométrologie.