# A retrospective analysis of nickel exposure data at a South African base metal refinery

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**BSc, BSc Hons.**

Mini dissertation submitted in *partial* fulfillment of the requirements for the degree *Magister Scientiae* in Occupational Hygiene at the Potchefstroom Campus of the North-West University

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It all starts here ™

# Preface

This mini-dissertation is submitted in partial fulfillment of the degree *Master of Science in Occupational Hygiene* at the North-West University (NWU), and adheres to the requirements of the NWU manual for postgraduate studies.  This mini-dissertation is written according to UK English spelling and presented in the form of an article. References are for uniformity purposes written according to the guidelines of the accredited journal *Annals of Occupational Hygiene*.

Chapter One includes a general introduction to the nickel industry and the necessity of retrospective analyses of occupational exposure data within the industry. The research aim, objectives and hypothesis are also included in Chapter One. Chapter Two is a comprehensive literature study containing discussions on nickel's properties, toxicological profile, refinery process and also an integrated step-by-step model for retrospective assessments. Chapter Three is written in the article format, in which the findings of the study are presented in readable and understandable format. Chapter Four is a final summary which addresses the hypothesis, results, and conclusion. Chapter Four also contains recommendations for future studies.

## Table 1: Contributions to the mini-dissertation and consent for use

| Researcher | Contribution | Consent |
|---|---|---|
| MM Young<br>(Student) | Designed and planned the study under supervision.<br>Captured and interpreted data and wrote the protocol and mini-dissertation. | |
| CJ van der Merwe<br>(Supervisor) | Assisted with the designing of the study, approval of the protocol and interpretation of the results.<br>Supervised the writing of the protocol and mini-dissertation. | |
| SJL Linde<br>(Co-Supervisor) | Assisted with the designing of the study, approval of the protocol and interpretation of the results.<br>Co-supervised the writing of the protocol and mini-dissertation. | |
| Prof JL du Plessis<br>(Assistant Supervisor) | Provided guidance with interpretation of the results.<br>Supervised the writing of the protocol and mini-dissertation in collaboration with the other supervisors. | |

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*"Ek self gee vir jou die opdrag. Wees sterk, wees vasberade. Moenie skrik nie moenie bang wees nie, want Ek, die Here jou God, is by jou oral waar jy gaan."*

*"Have I not commanded you? Be strong and courageous. Do not be afraid; do not be discouraged, for the Lord your God will be with you wherever you go."*

***Joshua 1:9***

# Summary

**Title:** A retrospective analysis of nickel exposure data at a South African base metal refinery.

**Background:** Nickel compounds are classified as a known human carcinogen causing lung and nasal cancer and nickel is a common cause of allergic contact dermatitis. Refinery workers in base metal refineries are occupationally exposed to soluble nickel and controlling nickel exposure is, therefore, essential. Control measures improved over time and consequently resulted in trends in soluble nickel exposure, which can be identified with a retrospective analysis of the exposure data.

**Aims and objectives:** This study aimed to analyse soluble nickel exposure data from a South African base metal refinery in order to identify trends in the exposure data during 1982 until 2014 in two tankhouses (i.e. Copper and Nickel Tankhouse). Furthermore, it aimed to identify specific trends in soluble nickel exposure within the sections inside the tankhouses and occupations, and to determine the number of excursions above the Time Weighted Average, Occupational Exposure Limit (TWA-OEL) for each of the different sections, as well as the different occupations. Finally, the effect of process changes on soluble nickel exposure was evaluated in both tankhouses.

**Methods:** Soluble nickel exposure data from two tankhouses (i.e. Copper and Nickel Tankhouse) of the base metal refinery were obtained and grouped into area and personal measurements. Exposure data were presented in an exposure matrix, which described exposure profiles for each of the pre-determined categories (sections inside tankhouses: Centre, East, West bays, North and South end, Contractor's tea room, Overhead crane and occupation categories: Cell worker, Crane driver, Supervisor, Miscellaneous activities) independently. One-way analyses of variances (ANOVA) were conducted to identify significant differences in exposures over time, and the trends were illustrated with linear regression graphs. Differences between sections inside the tankhouses as well as the different occupations were furthermore evaluated with Honest Significant Difference (HSD) Tukey tests, and the percentage of measurements above the TWA-OEL (0.1 mg/m$^3$) set by the Mine Health and Safety Act (MHSA) were calculated.

**Results:** Significant downward trends ($p \leq 0.0001$) were identified in area exposure data in the Copper Tankhouse between 1982 and 2011. Area exposure in the Copper Tankhouse decreased with a factor of 29 between 1982 and 1986.

However, after 1986 no significant downward trend was identified in area exposure. Furthermore, personal exposure decreased with a factor of three between 1991 and 2014 in the Copper Tankhouse, consequently, significant downward trends were identified in personal exposure ($p \leq 0.0001$). An eight-fold reduction in soluble nickel exposure of Cell workers and Crane drivers were identified, while a significant increase ($p \leq 0.05$) in exposure were identified for Supervisors when exposure increased with a factor of seven between 2001 and 2010. No significant trends were identified in area and personal exposure in the Nickel Tankhouse. Exposures measured for the Miscellaneous category and Supervisors were significantly different ($p \leq 0.05$) from Cell workers and Crane drivers. The highest percentage of OEL exceedances were determined for Cell workers (Copper Tankhouse, 64%; Nickel Tankhouse, 32%) and Crane drivers (Copper Tankhouse, 64%; Nickel Tankhouse, 19%), if Supervisors in the Nickel Tankhouse with limited measurements were not taken into account. The substantial decrease in area soluble nickel exposure (1982 – 1986) can be attributed to the polypropylene bead which were increased inside the electrowinning cells in 1986, and recent significant decreases in personal exposure in the Copper Tankhouse can be attributed to the movement of nickel production to the Nickel Tankhouse during 2009.

**Conclusion:** Significant downward trends in soluble nickel exposure inside the Copper Tankhouse were identified and may be ascribed to the implementation of various control measures and process changes. No exposure trend was established in the Nickel Tankhouse, as only four years of exposure data were available. A comprehensive exposure assessment is recommended to establish accurate exposure profiles for categories in which high soluble nickel exposure was identified (i.e. Supervisors and Contractor’s tea room). Furthermore, six measurements, quarterly, per occupation are recommended, due to the significant differences between the occupations. Finally, due to the carcinogenic effects of nickel compounds it is recommended to control exposure to the lowest possible level.

**Key words:** Historical exposure, soluble nickel, exposure matrix, nickel electrowinning, tankhouse.

# Opsomming

**Titel**: ŉ Retrospektiewe analise van nikkel blootstellingsdata by ŉ Suid-Afrikaanse basismetaal raffinadery.

**Agtergrond:** Nikkelverbindings word geklassifiseer as ŉ bekende menslike karsinogeen wat long en nasale kanker veroorsaak en nikkel is ŉ algemene oorsaak van allergiese kontak dermatitis. Raffinadery werkers van basismetaal raffinaderye word blootgestel aan oplosbare nikkel in hulle beroep, en daarom is dit belangrik om blootstelling aan nikkel te beheer. Beheermaatreëls verbeter met die verloop van tyd en mag ŉ tendens veroorsaak in nikkel blootstelling, wat geïdentifiseer kan word met ŉ retrospektiewe analise van die blootstellingsdata.

**Doelstelling en doelwitte:** Hierdie studie se doel was om oplosbare nikkel blootstellingsdata van ŉ Suid-Afrikaanse basismetaal raffinadery te analiseer, ten einde tendense in die blootstellingsdata tussen 1982 en 2014 te identifiseer in twee tenkhuise (nl. Koper en Nikkel Tenkhuis). Die doel was verder ook om spesifieke tendense in enige van die afdelings binne die tenkhuise of beroepe asook om die hoeveelheid oorskrydings van die Tyd-Beswaarde Gemiddelde, Beroepblootstellingsdrempel (TBG-BBD) vir elkeen van die verskillende afdelings, sowel as die verskillende beroepe te bepaal. Laastens, is die effek van proses veranderinge op blootstelling in beide tenkhuise geëvalueer.

**Metodes:** Oplosbare nikkel blootstellingsdata vanaf twee tenkhuise (nl. Koper en Nikkel Tenkhuis) in die basismetaal raffinadery is verkry en gegroepeer in area en persoonlike metings. Blootstellingsdata is voorgestel in ŉ blootstellingsmatriks, wat blootstellingsprofiele onafhanklik beskryf het vir elkeen van die vooraf bepaalde kategorieë (Afdelings binne die tenkhuise: Middel-, Oos- en Wes afdelings, Noordelike en Suidelike kante, Kontrakteur teekamer, Hyskraan asook die beroepskategorieë: Selwerker, Hyskraan-operateur, Toesighouer en Diverse aktiwiteite). Een-rigting analises van variansie (ANOVA) is gebruik om betekenisvolle verskille te identifiseer in blootstellings oor die jare, en die tendense is voorgestel in liniêre regressie grafieke. Vervolgens is die verskille tussen die afdelings in die tenkhuise asook die verskillende beroepe geëvalueer met HSD Tukey toetse, en die persentasie metings wat bo die TBG-BBD (0.1 mg/m$^3$) wat vasgestel is deur die Myn Gesondheid- en Veiligheidswet is bereken.

**Resultate:** Betekenisvolle afwaartse tendense ($p \leq 0.0001$) is geïdentifiseer in area blootstelling in die Koper Tenkhuis tussen 1982 en 2011. Area blootstelling in die Koper Tenkhuis het afgeneem met ŉ faktor van 29 tussen 1982 en 1986. Alhoewel, geen betekenisvolle tendens geïdentifiseer is na 1986 nie. Persoonlike blootstelling het afgeneem met ŉ faktor van drie tussen 1991 en 2014 in die Koper Tenkhuis, vervolgens is ŉ betekenisvolle tendens ($p \leq 0.0001$) geïdentifiseer in persoonlike blootstelling. ŉ Agtvoudige afname in oplosbare nikkel blootstelling van Selwerkers en Hyskraan-operateurs is geïdentifiseer, terwyl ŉ betekenisvolle verhoging in blootstelling vir Toesighouers geïdentifiseer is, toe blootstelling toegeneem het met ŉ faktor van sewe tussen 2001 en 2010. Daar is geen betekenisvolle tendense geïdentifiseer in area of persoonlike blootstellings in die Nikkel Tenkhuis nie. Blootstellings wat gemeet is vir die Diverse kategorie en Toesighouers is betekenisvol verskillend ($p \leq 0.05$) van Selwerkers en Hyskraan-operateurs. Die hoogste persentasie TBG-BBD oorskrydings is vir Sel werkers (Koper Tenkhuis: 64% en Nikkel Tenkhuis: 32%) en Hyskraan-operateurs (Koper Tenkhuis: 64%; Nikkel Tenkhuis: 19%) geïdentifiseer, as die Nikkel Tenkhuis se Toesighouers met beperkte metings nie in berekening gebring is nie. Die substansiële afname in area nikkel blootstelling (1982 – 1986) kan toegeskryf word aan meer polipropileen korrels binne die elektro-ontginning selle wat verhoog is in 1986, en die onlangse verlagings in persoonlike blootstelling in die Koper Tenkhuis kan toegeskryf word aan die verskuiwing van nikkel produksies na die Nikkel Tenkhuis in 2009.

**Gevolgtrekking:** Betekenisvolle afwaartse tendense in oplosbare nikkel blootstelling binne die Koper Tenkhuis is geïdentifiseer en mag toegereken word aan die implimentering van verskeie beheermaatreëls en proses veranderinge. Geen betekenisvolle tendense is vasgestel vir die Nikkel Tenkhuis nie, omdat net vier jaar se blootstellingsdata beskikbaar was. ŉ Volledige blootstellingsondersoek word aanbeveel om akkurate blootstellingsprofiele vas te stel vir die kategorieë waarvoor hoë oplosbare nikkel blootstelling geïdentifiseer is (nl. Toesighouers en Kontrakteur teekamer). Ses metings kwartaalliks word verder aanbeveel, a.g.v. die betekenisvolle verskille tussen die beroepe. Laastens, word daar aanbeveel om oplosbare nikkel blootstelling te beheer tot die laagste moontlike vlak a.g.v. die karsinogeniese effekte van nikkelverbindings.

**Sleutel terme:** Historiese blootstelling, oplosbare nikkel, blootstellingsmatriks, nikkel ontginning, tenkhuis.

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## List of abbreviations

| | |
|---|---|
| ACGIH | American Conference of Governmental Industrial Hygienists |
| AM | Arithmetic Mean |
| ANOVA | Analysis of Variance |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BMR | Base Metal Refinery |
| DEPA | Danish Environmental Protection Agency |
| EDM | Exposure Data Matrix |
| GM | Geometric Mean |
| HSE | Health and Safety Executive |
| IARC | International Agency for Research on Cancer |
| IOM | Institute of Occupational Medicine |
| LEV | Local Extraction Ventilation |
| LOD | Limit of Detection |
| MDHS | Methods for Determining Hazardous Substances |
| MHSA | Mine Health and Safety Act |
| MTD | Maximum Tolerated Dose |
| NIOSH | National Institute for Occupational Safety and Health |
| NMAM | NIOSH Manual of Analytical Methods |
| OEL | Occupational Exposure Limit |
| OESSM | Occupational Exposure Sampling Strategy Manual |
| OSHA | Occupational Safety and Health Administration |
| PGM | Platinum Group Metals |
| PPE | Personal Protection Equipment |
| SEG | Similar Exposure Group |
| SIR | Standard Incidence Ratios |
| TERA | Toxicology Excellence for Risk Assessment |
| TLV | Threshold Limit Value |
| TWA | Time Weighted Average |
| WHO | World Health Organisation |

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# CHAPTER 1: GENERAL INTRODUCTION

## 1.1 Introduction

Five percent of the worlds' nickel reserve is located in South Africa. Currently there is only one primary nickel mine in South Africa, the Nkomati nickel mine. The Nkomati mine only accounts for about 10% of South Africa's nickel production, while the majority of nickel production is mined as a co-product during platinum group metals (PGM) mining (Nickel Institute, 2009), as it is concentrated geologically with PGMs (Jones, 2005). Nickel has typical metallic properties as it is a good conductor of heat and electricity and also possesses ferromagnetic characteristics (ATSDR, 2005). Nickel is primarily used in alloys because of properties such as resistance to corrosion and heat, hardness and strength, while nickel salts have excellent adhesion properties and are, therefore, used in electroplating, ceramics, pigments and catalyst manufacturing. Nickel is also used in nickel-cadmium and nickel-metal hydride batteries (Nickel Institute, 2015). Nickel compounds are normally classified according to their solubility in water, hereafter referred to as soluble and insoluble nickel. Soluble nickel compounds include: nickel acetate, nickel chloride, nickel nitrate and nickel sulphate. Major insoluble nickel compounds include: nickel subsulphide, nickel sulphide, nickel carbonyl, nickel carbonate and nickel oxide (ATSDR, 2005).

Nickel compounds are classified as human carcinogens (Group 1), and metallic nickel and nickel alloys as possibly carcinogenic to humans (Group 2B), according to the International Agency for Research on Cancer (IARC). Nickel compounds are associated with lung cancer, more specifically insoluble nickel with lung cancer and nasal cancer and soluble nickel with lung cancer. Evidence of cancer elicited after exposure to metallic nickel alone is inconsistent (IARC, 2012). In addition to its carcinogenic properties, soluble nickel is also a respiratory and dermal sensitiser characterised with lung inflammation and atrophy of the nasal epithelium upon inhalation, and contact dermatitis after prolonged dermal exposure (ATSDR, 2005).

Refinery workers are exposed to various forms of nickel during the beneficiation of PGMs, depending on the stage of the refining and purification process at which they are employed. Exposure to sulphidic nickel tends to be higher during the milling and grinding of the ore, but after the concentrate is fed into the furnaces, exposure to sulphidic nickel decreases and exposure to oxidic nickel increases (Thomassen *et al.*, 1999; Werner *et al.*, 1999; Grimsrud *et al.*, 2002; Hughson *et al.*, 2009).

During metallurgical refining of nickel, exposure to soluble nickel compounds is higher (Thomassen *et al.*, 1999; Werner *et al.*, 1999; Grimsrud *et al.*, 2002; Hughson *et al.*, 2009). The last step of metallurgical refining takes place inside tankhouses where nickel and copper are electroplated into sheets during an electrowinning process (Lupi *et al.*, 2006). Soluble nickel exposure in the vicinity of copper and nickel electrowinning cells originates from a mist that is formed during the electrowinning process. During the anodic reaction hydronium and oxygen are produced and oxygen bubbles will rise through the electrolyte and burst at the surface of the liquid releasing a fine aerosol of electrolyte solution (Sigley *et al.*, 2003).

It is vital to control exposure to soluble nickel in the tankhouses, due to the health effects associated with nickel exposure. An occupational hygiene monitoring programme quantifies the exposure of workers to hazards, in order to monitor the effectiveness of the control measures in place to protect the health of workers. The monitoring programme not only indicates a failure in control measures but may also prevent occupational disease by identifying hazards early on and ensures that the base metal refinery (BMR) complies with health and safety regulations (MHSA, 1996). The occupational hygiene monitoring programme at the tankhouses of the BMR monitors, amongst others, the concentration of soluble nickel to which the workers are exposed to. The soluble nickel concentration, sampling method and conditions are then presented in an occupational hygiene report (Anon., 2002). Employers not only have the legal responsibility to protect the health and safety of their employees in general, but also to implement control measures with the aim of gradually reducing exposure to the lowest possible level (MHSA, 1996). A decrease in exposure is achieved by advancements of control measures that were developed to control exposure i.e. polypropylene beads, substitution, process enclosure and local extraction ventilation. Based upon the aforementioned, one would expect a decreasing trend in soluble nickel exposure should exposure data from available historical reports be collectively analysed. In order to identify a trend in nickel exposure at the BMR, a retrospective analysis of soluble nickel exposure data is required.

Two retrospective studies specifically linked nickel exposure trends to production changes in nickel refineries. Sivulka *et al.* (2014) reconstructed historical nickel exposures in a Welsh refinery. Three to 30-fold reductions in nickel exposure were not only attributed to changes in refinery processes but also to advancements in control measures. Grimsrud *et al.* (2000) assessed historical nickel exposure in a Norwegian refinery. Reductions in nickel exposure were reported in three departments after a major process change in 1978.

Nickel concentrations were reduced in roasting, electrolyte purification and copper leaching each by a factor of five, six and eight respectively (Grimsrud *et al.,* 2000). However, retrospective studies assessing nickel exposure have not been done in South Africa. Specifically, a retrospective study that will correlate historical soluble nickel exposure trends to refinery process changes and developing control measures are necessary in South Africa.

## 1.2 Research aim and objectives

### 1.2.1 Aim of the study

To assess historical soluble nickel exposure data from two tankhouses (i.e. Copper and Nickel Tankhouses) at a South African BMR, in order to identify if trends in exposure exist since the commissioning of the tankhouses until present.

### 1.2.2 Objectives

- To illustrate historical soluble nickel exposure data according to sections inside the tankhouses (area exposure) and occupations (personal exposure) over time.
- To identify if there is a trend in soluble nickel exposure for any of the sections or occupations.
- To establish the historical number of excursions above the time-weighted average occupational exposure limit (TWA-OEL) for soluble nickel in each section and occupation assessed.
- To establish the effect of process change(s) on soluble nickel exposure in both tankhouses.

## 1.3 Hypothesis

Previous retrospective studies conducted in Wales and Norway indicated a three to thirty-fold decrease in nickel exposure since the 1950's to 2014 (Grimsrud *et al.*, 2000; Sivulka *et al.*, 2014). It is, therefore, hypothesised that decreasing trends in soluble nickel exposure over time exist in the Copper and Nickel Tankhouses of a South African BMR.

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# CHAPTER 2: LITERATURE STUDY

This chapter provides a comprehensive literature overview of the properties and toxicological profile of nickel as well as a brief introduction to refinery processes where nickel exposure may occur. Finally, a step-by-step method for retrospective analyses which is integrated with six previous retrospective studies is discussed.

## 2.1 Physical and chemical properties of nickel

Nickel is a silver-white metal that belongs to the transition metal group (Group VIIIB) in the Periodic table, and can exist in various oxidation states, although Nickel(II) is more common under environmental conditions. Nickel is resistant to corrosion by air, water and alkalis, same as most of the transition metals. Nickel is, however, easily dissolved in dilute oxidising acids (Cempel and Nikel, 2006). Nickel is an ideal synergist in alloys, because of characteristics such as good conductance of heat and electricity, resistance to corrosion and heat, hardness and strength, as well as typical metallic properties such as ferromagnetic properties (ATSDR, 2005). Nickel salts are used in electroplating, ceramics, pigments and catalysts. Another use of nickel is in nickel-cadmium and nickel-metal hydride batteries. For a more extensive overview of nickel uses, the reader is referred to the Nickel Institute (Nickel Institute, 2015).

Nickel compounds are normally classified according to their solubility in water. The major nickel compounds soluble in water include: nickel acetate, nickel chloride, nickel nitrate and nickel sulphate. Major insoluble nickel compounds include: nickel subsulphide, nickel sulphide, nickel carbonyl, nickel carbonate and nickel oxide (ATSDR, 2005). Nickel sulphate is the primary source of nickel exposure in the electroplating of nickel and copper (discussed in Section 2.5), therefore, the physicochemical properties of nickel sulphate will be discussed in more detail. Nickel sulphate ($NiSO_4$) has a number of synonyms e.g. nickel monosulphate, nicklous sulphate, and nickel(II)sulphate. Nickel sulphate forms various hydrates depending on the temperature of the solution i.e. in a 30 °C solution, $NiSO_4 \cdot 7H_2O$ will be prevalent, and at temperatures from 35 °C up to 100 °C $NiSO_4 \cdot 6H_2O$ will prevail (DEPA, 2008). Temperatures in an electrowinning cell are normally between 60 °C and 65 °C, which means that nickel sulphate hexahydrate (NiSO4•6H2O) will be present in electrowinning cells (Anon., 2007).

## 2.2 Toxicological profile for Nickel

There are several physiological factors that may influence nickel absorption and the severity of the health effects associated with it. The toxicokinetic profile for nickel will be discussed according to the absorption, distribution, metabolism and excretion thereof in humans. There are two major routes of occupational exposure i.e. dermal and respiratory (ATSDR, 2005).

Deposition in the respiratory tract is determined by the size of nickel particles. Larger particles (5 – 30 μm) tend to deposit higher in the respiratory tract (nasopharyngeal region), smaller particles (1 – 5 μm) lower in the respiratory tract (trachea and bronchiolar region) and the smallest particles (<1 μm) in the alveolar region of the lungs, where diffusion and electrostatic precipitation are the main mechanisms of absorption. About 20% to 35% of the nickel that reaches the lungs will be absorbed into the bloodstream. The remainder of the inhaled nickel is either expectorated, swallowed or remains in the respiratory tract (ATSDR, 2005; Goodman *et al.*, 2011). Absorption rates of nickel in the respiratory tract are different for soluble and insoluble nickel. Soluble nickel is more easily absorbed from the respiratory tract than insoluble nickel, indicated by a higher nickel concentration in the urine of workers exposed to soluble nickel, than the workers exposed to insoluble nickel (Denkhaus and Salnikow, 2002; ATSDR, 2005; IARC, 2012).

Based on faecal excretion data, 18% to 49.6% of ingested nickel is absorbed from the gastrointestinal tract (Patriarca *et al.*, 1997). Nickel is absorbed from the intestinal tract via calcium or iron transporters or the divalent metal transport protein-1 (Liu *et al.*, 2008). Data from numerous studies (Sunderman *et al.,* 1989; Solomons *et al.,* 1982; Nielsen *et al.*, 1999 quoted from ATSDR, 2005), suggest that nickel absorption from the gastrointestinal tract decreases with food intake (ATSDR, 2005).

Dermal penetration varies with the different nickel compounds. Nickel(II)ions in a chloride solution permeated excised skin 50 times faster than nickel(II) ions in a sulphate solution. Dermal penetration is also affected by occlusion of the skin. If the skin is occluded, 3.5% of the nickel permeates the skin in contrast to only 0.23% when the skin it not occluded (ATSDR, 2005). Although there is evidence that nickel permeates the skin, it is, however, to a limited extent. An *in vitro* study by Larese Filon *et al.* (2009) compared absorption of metal powders between intact skin and damaged skin. This study determined that only 0.03% of the nickel dose penetrated through the skin, while 74.2% was retained in the skin.

Nickel distribution is dependent on the route of exposure and the solubility of the compound. Workers who are occupationally exposed by inhalation will typically have a higher concentration of nickel in the lungs. A higher concentration of nickel will be retained in the nasal mucosa of workers exposed to less-soluble nickel compounds, and workers exposed to soluble nickel will have a higher serum nickel concentration (ATSDR, 2005).

Goodman *et al.* (2011) supported the above mentioned solubility dependent distribution approach in the respiratory tract. This study reviewed nickel clearance in the lungs, and overall the lung clearance of soluble nickel salts were significantly faster than for insoluble nickel salts. Nickel oxide on its part had a dose-dependent retention time, whereas soluble nickel was unaffected by dose (Goodman *et al.*, 2011). The half-life for urinary elimination following nickel inhalation exposure ranged from 17 to 39 hours based on a study that monitored small groups of refinery workers exposed to nickel sulphate and nickel chloride (DEPA, 2008).

Nickel that was ingested will reach peak levels in the serum in one and a half to three hours after ingestion (ATSDR, 2005; DEPA, 2008). The half-life of nickel in the serum after ingestion of 5.6 mg nickel sulphate was 11 hours, and a strong positive correlation between nickel concentrations in the serum and urinary excretion was present in the same study (DEPA, 2008). Following absorption nickel is transported as a divalent ion ($Ni^{2+}$) in the serum that is either bound to albumin, histidine, or α2-microglobulin proteins (DEPA, 2008; Liu *et al.*, 2008).

There are two major mechanisms of cellular uptake of nickel i.e. endocytosis and ion-transport channels (Oller *et al.*, 1997; Goodman *et al.*, 2011). Solubility of nickel is an important factor that will determine cellular uptake of nickel. Dissolution of nickel compounds in extracellular fluids are easier if the compounds are water soluble, subsequently nickel ions tend to use ion-transport channels after dissolution (Oller *et al.*, 1997; Ke *et al.*, 2006; Goodman *et al.*, 2011). The calcium or magnesium ion-transport channels are the primary route of cellular uptake of nickel ions. Nickel's ionic radius (0.66 Å) is similar to calcium and magnesium and can, therefore, use the same ion-transport channel, but is limited by competition with calcium, magnesium and other metal ions. Calcium and magnesium concentrations in alveolar fluid limit nickel absorption because of the antagonistic behaviour between nickel and magnesium/calcium. *In vivo* the result is low intracellular uptake of nickel in the lungs (Ke *et al.*, 2006; Goodman *et al.*, 2011).

Nickel ions that do enter cells have the capacity to either bind to intracellular ligands or enter the nuclei. Nickel ions that do bind to intracellular ligands will increase cytotoxicity, but in turn will limit the amount of ions to enter the nuclei (Ke *et al.*, 2006; Goodman *et al.*, 2011). Insoluble nickel compounds rather enter the cells via endocytosis than the ion-transport channels, because of their impaired dissolution in extracellular fluids. Endocytosis is dependent on size and charge/structure of particulates, extracellular requirements, and influence of inhibitors (Oller *et al.*, 1997; Munoz and Costa, 2012). Nickel carbonyl is lipid soluble, and consequently large amounts will be absorbed after dermal or inhalation exposure (Munoz and Costa, 2012). Not only is the concentration of nickel inside the cells an important determinant of carcinogenicity but also the persistence of nickel inside the cells. Persistence of nickel ions inside cells is also dependant on nickel solubility. Insoluble nickel compounds ($Ni_3S_2$) persisted longer inside cells than soluble nickel ($NiCl_2$). Authors of this particular study suggested that retention of insoluble nickel inside cells may contribute to nickel bioavailability and consequently carcinogenicity (Ke *et al.*, 2006).

Excretion of soluble nickel is primarily through urine regardless of the route of exposure although trace amounts are also excreted through sweat, bile, hair and milk, while unabsorbed nickel is excreted through faeces (ATSDR, 2005; DEPA, 2008; Liu *et al.*, 2008). Urinary excretion of soluble nickel has 'n strong correlation with serum nickel levels, indicating effective excretion after absorption of soluble nickel (ATSDR, 2005; DEPA, 2008). Insoluble nickel compounds e.g. nickel oxide tend to be primarily excreted through the faeces and have a lower excretion rate than soluble nickel, because insoluble nickel compounds have a half-life of approximately 3.5 years in the nasal mucosa (ATSDR, 2005). Nickel retained in nasal mucosa may be expectorated and ingested which explains excretion through faeces of insoluble nickel (TERA, 1999; ATSDR, 2005; DEPA, 2008).

### 2.2.1 Health effects

The health effects of nickel on humans will be discussed according to acute and chronic toxicity and carcinogenicity. The solubility of nickel is an important consideration in determining the toxicity of nickel as soluble nickel is more toxic than less-soluble nickel, although the latter tends to be carcinogenic at the site of deposition (ATSDR, 2005; Goodman *et al.*, 2011). As exposure to nickel compounds usually involves a mixture of nickel compounds, a significant confounder in carcinogenicity, both will be discussed in Section 2.2.1.3.

#### 2.2.1.1 Acute toxicity

Data of acute toxicity in humans are limited to nickel carbonyl poisoning (Liu *et al.*, 2008). Lipid solubility is a major contributor to nickel carbonyl toxicity, as nickel carbonyl move effortlessly across cell membranes (Munoz and Costa, 2012). Nickel carbonyl is, therefore, highly toxic and acute exposure can lead to symptoms such as: headache, nausea, vomiting, and chest pains, followed by coughing, hyperpnoea, cyanosis, gastrointestinal symptoms and weakness. Symptoms may progress to pneumonia, respiratory failure and eventually cerebral oedema and death (Klein and Costa, 2007; Liu *et al.*, 2008).

#### 2.2.1.2 Chronic toxicity

Chronic toxicity will be discussed according to dermal and respiratory exposure to nickel. Dermal exposure to nickel that is airborne, in a solution or metal items containing nickel (piercings, prosthetics), cause skin irritation and after prolonged exposure allergic contact dermatitis. Allergic contact dermatitis is the result of nickel sensitisation, which is a type IV delayed hypersensitivity reaction. Skin irritation was elicited on intact skin after three days of exposure to a 20% nickel sulphate solution. On compromised skin, irritancy was caused with a 0.13% solution (DEPA, 2008).  Individuals that were previously sensitised to nickel will have a 100 to 1000 times' higher inflammatory reaction, than individuals who are exposed for the first time. Sensitisation symptoms will typically present at the site of exposure, but with prolonged exposure it can spread to other locations e.g. hands and forearms (ATSDR, 2005; DEPA, 2008).

Non-cancerous respiratory effects in animal studies after chronic exposure to nickel sulphate include inflammation, macrophage hyperplasia, alveolar epithelial hyperplasia, alveolar proteinosis, lung fibrosis and lymphoid hyperplasia (Oller *et al.*, 1997). Goodman *et al.* (2011) substantiated above mentioned chronic toxic effects in a study conducted on rats. Pulmonary inflammation, cytotoxicity and lung lesions contributed to respiratory toxicity after exposure to soluble nickel sulphate hexadrate ($NiSO_4{\bullet}6H_2O$) (Goodman *et al.*, 2011). Inflammatory effects of nickel sulphate may be due to increased secretion of inflammatory cytokines such as interleukin-1 and the activation of lipoxygenase pathway in leukocytes (produce leukotrienes which mediates allergic and inflammatory reactions). These effects are enhanced in a dose and time-dependant manner (Das and Büchner, 2007). Nickel sulphate has a steeper respiratory toxicity dose-response curve, resulting in the lowest maximum tolerated dose (MTD) among the nickel compounds (Goodman *et al.*, 2009).

Respiratory toxicity will ultimately influence carcinogenicity, as nickel compounds that are more toxic have a lower MTD and will, therefore, limit inhalation exposure and lung deposition. Nickel sulphate has a higher respiratory toxicity based on these animal studies, and nickel oxide has the lowest toxicity and the highest MTD, nickel oxide’s non-cancerous effects are, therefore, limited (Goodman *et al.*, 2009; Goodman *et al.*, 2011).

#### 2.2.1.3 Carcinogenicity

Limited epidemiological evidence for cancer at sites other than the respiratory tract has been found (IARC, 2012), there is, however, a study that reported elevated risks to develop stomach cancer among nickel refinery workers (Anttilla *et al.*, 1997). Site-specific cancer cases have been reported in IARC (2012), specifically, nickel industry workers had a higher risk for developing laryngeal and pharyngeal cancer. Studies that reported elevated risks for colon and kidney cancer did not relate risk with important confounders such as the duration of employment (IARC, 2012). Carcinogenicity will be discussed according to solubility, as solubility determines the toxicological profile for nickel.

Currently soluble and insoluble nickel are classified as human carcinogens (Group 1) by the IARC, with sufficient evidence of carcinogenicity in humans. Furthermore, the IARC classified metallic nickel and nickel alloys as possible human carcinogens (Group 2B), with limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals (IARC, 2006).

Inhalation of insoluble nickel compounds e.g. metallic nickel, nickel oxides and nickel subsulfide, is associated with lung and nasal cancers. Workers in calcination operations and plant cleaners, who were exposed to high levels of sulfidic and oxidic nickel had elevated risk to develop lung and nasal cancer (IARC, 2012). Smelter workers exposed to insoluble nickel had a significantly higher risk for developing cancer after a latent period of 20 years (Anttila *et al.*, 1997). Several studies reviewed the carcinogenicity of metallic nickel, but failed to show consistent evidence that could suggest that metallic nickel exposure alone causes lung cancer (IARC, 2012).

An elevated cancer risk was established in nickel refinery workers, who were exposed to soluble nickel and low concentrations of insoluble nickel. Workers in the refinery had an elevated risk for nasal cancer, which was positively correlated with latency and duration of employment (Anttila *et al.*, 1997).

Grimsrud *et al.* (2002) substantiated the dose-related association with the cancer risk of workers exposed to soluble nickel, but no dose relationship could be identified for insoluble nickel compounds. This relationship of lung cancer and cumulative exposure was deemed to be similar for nickel chloride and nickel sulphate, after similar standard incidence ratios (SIR) were calculated for both compounds (IARC, 2012).

The difference in carcinogenicity between soluble and insoluble nickel exposure under cumulative conditions can be explained by the different cellular uptake mechanisms. As discussed in Section 2.2, the low bioavailability of soluble nickel decreases the chance of nickel ions to induce mutagenesis directly (Oller *et al.*, 1997; Goodman *et al.*, 2009; Goodman *et al.*, 2011). However, after soluble nickel interacts with intracellular ligands, macrophages and polymorphonuclear leukocytes are recruited to the affected cells, and cytokines, proteases, growth factors and oxidants are secreted (inflammatory response). Cytotoxicity agents (cytokines and oxidants) will initially decrease the number of cells (apoptosis), but because of compensating proliferation (caused by growth factors), the tissue will be re-established. Proliferation is, however, limited in cells exposed solely to soluble nickel, because a number of background mutated cells are presumed to be low and would instead induce apoptosis (Oller *et al.*, 1997). A significant correlation between nickel-ion concentration and the degree of oxidative stress was illustrated by Wang *et al.* (2012), indicating that nickel-ion induced apoptosis is dose-dependent. Chronic inflammation caused by soluble nickel may enhance carcinogenicity of other substances, because of the growth factors that are secreted that may cause proliferation of insoluble nickel induced mutated cells (Oller *et al.*, 1997).

Insoluble nickel enters the cell via endocytosis and interaction with intracellular ligands is, therefore, limited, but the delivery to cell nucleus is higher than for soluble compounds (Goodman *et al.*, 2011). Nickel compounds in the endocytic vesicles dissolute into nickel ions after lysosomes fuses with the vesicles and nickel ions are released. Nickel ions enter the nucleus after the endocytic vesicles merge with the nuclear membrane. This mechanism ensures that a much higher concentration of nickel ions enters the nucleus and, therefore, the potential for mutagenicity is greater in cells exposed to insoluble nickel (Oller *et al.*, 1997).

In summary, evidence for carcinogenesis after exposure to a combination of soluble and insoluble nickel is overwhelming (IARC, 1990; Oller *et al.*, 1997; Goodman *et al.*, 2011; IARC, 2012), suggesting a synergistic relationship.

A synergistic effect was found for nickel compounds and other genotoxic or mutagenic agents (Oller *et al.*, 1997), substantiating the claim that the carcinogenesis of insoluble nickel may be enhanced by soluble nickel.

## 2.3 Nickel exposure

### 2.3.1 Environmental occurrence and consumer exposure

Nickel is the fifth most abundant element on Earth, even though it only ranks 24th in abundance in the Earth's crust. Nickel concentration increases towards the centre of the Earth ranging from between 0.22% in the Earth's mantle to 5.8% in the core. The nickel content in the atmosphere is not only attributed to the above mentioned natural sources, but also from combustion of fuel, municipal incineration, emissions from nickel refineries and steel production. The nickel concentration in the atmosphere varies between 5 ng/m$^3$ and 35 ng/m$^3$ depending on the natural sources of nickel and emissions from nickel industries can be as high as 150 ng/m$^3$ near sources (ATSDR, 2005; IARC, 2012).

Consumers may be exposed to nickel through food sources, drinking water, tobacco smoking and dermal contact with nickel-containing objects such as jewellery, coins and prosthetics, to name a few. Not only do various food sources naturally contain nickel, but nickel can also be released from stainless-steel cooking utensils, although some discrepancies about the amount of nickel being released exist (ATSDR, 2005; Klein and Costa, 2007; WHO, 2007). Nickel compounds in water is ascribed to natural sources such as the dissolution of pentlandite rocks and atmospheric deposition, or because of industrial effluent water, domestic waste water, landfill leachate or anthropogenic activities e.g. mining and smelting operations (WHO, 2007). Measurements done in the 1980's indicated average nickel concentrations in ground water of between 15 µg/l and 20 µg/l in surface water (ATSDR, 2005; IARC, 2012). In South Africa the nickel concentration were determined to be 6.49 µg/l in ground water near an old copper mine, which is below the World Health Organisation's permissible limit (Singo, 2013).

Another important source of nickel in drinking water is the nickel that is released from new stainless-steel pipes used to convey water for domestic use, although this phenomenon diminishes after a few weeks (WHO, 2007). Tobacco smoking was always considered to be a significant source of nickel exposure, according to a study from 1969 that estimated nickel concentration per cigarette to be between 2.2 µg and 2.3 µg per cigarette (Szadkowski *et al.*, 1969, quoted from IARC, 1990).

A study from 1986 estimated that 2 µg – 12 µg of nickel are inhaled per packet of cigarettes smoked (Sunderman, 1986, quoted from ATSDR, 2005). However, recently Torjussen *et al.* (2003) reported only 1.1% of the nickel content in cigarettes was recovered in the main stream smoke, and that most of the nickel was recovered in the ash. The study concluded that the nickel content of the refinery atmosphere were the main source of nickel exposure (Torjussen *et al.*, 2003).

### 2.3.2 Occupational exposure

Occupational nickel exposure may occur through dermal contact with solutions, aerosols or metals and alloys containing nickel, or by inhalation of such aerosols, dusts or fumes. The main industries where nickel exposure can occur include those of mining and refining operations, steel foundries, welding, thermal spraying of nickel and grinding and buffing of nickel containing metals (ATSDR, 2005).

The form of nickel that one will be exposed to depends on the source of nickel exposure. Exposure to nickel silicate, nickel subsulphide and nickel chloride are associated with more specialised industries, whereas nickel oxides, metallic nickel and nickel sulphate with combustion, incineration and refining operations (ATSDR, 2005; IARC, 2012). Specifically, occupational exposure to nickel sulphate is associated with the chemical industry, metal extraction industry, and electroplating operations (DEPA, 2008). Occupational exposure of refinery workers will be reviewed in more detail in Section 2.5, as it is relevant to this study.

## 2.4 Introduction to the refining of nickel

A brief introduction to nickel refinery processes is required to understand where nickel exposure may occur during the refinery process. Nickel exposure occurs in refinery processes where nickel-copper matte is beneficiated, either during nickel and copper mining or as a by-product during platinum group metals (PGM) mining. During PGM mining, base metals such as nickel and copper (often associated with sulphides) must first be separated from the precious metals through a number of beneficiation steps. The main beneficiation processes are comminution, flotation, smelting, converting and hydrometallurgical treatment (Jones, 2005).

During comminution, mined ore is degraded into smaller particles by milling the ore, and a gravity concentrate is extracted (Jones, 1999). The gravity concentrate containing approximately 30 percent precious minerals is subjected to flotation (Vermaak, 1995).

Flotation is a process during which sulphides (associated with ore minerals) are concentrated. Chemicals are added to the concentrate, which makes the minerals in the ore hydrophobic, while gangue particles (unusable material) remain hydrophilic. A froth is created by forcing air through the slurry, or by adding additional chemicals, that also supresses unwanted minerals (such as talc). The surface froth, containing nickel and copper, which is still associated with precious metals, is skimmed off and allowed to thicken (Vermaak, 1995). The froth is concentrated further in a spray or flash drier that will reduce water content of the concentrate and, therefore, also energy required for smelting (Jones, 1999). The sulphide concentrate is dried and pelletized, after which the concentrate is fed into furnaces to be smelted (Vermaak, 1995).

Smelting is a process that melts the concentrate that will separate into two liquid phases: a lighter silicate and iron-rich slag, and a denser molten matte that settles out from under the slag. The matte is tapped into ladles at the opposite end of the furnace from which the slag is tapped. This furnace matte is transported by crane to a converter vessel for further processing (Jones, 2005).

During converting, iron and sulphur are removed from the matte by blowing air into the molten matte, to oxidise as much of the iron and sulphur as possible (Vermaak, 1995). Silica sand is added to the converter to remove the iron oxide by forming an iron silicate slag ($2FeO \bullet SiO_2$), which is periodically tapped from the converter vessel. Sulphur leaves the system as sulphur dioxide ($SO_2$). The converter matte can be cast into cast-iron moulds, or refractory-lined pits and crushed, or it can be granulated by a fast-flowing water stream, after the iron content is satisfactory. Some of the base metals may dissolve in the converter slag, as these base metals oxidise in the slag. Therefore, converter slag is commonly either looped back to the primary smelting furnace or granulated and subjected to milling and flotation once more, to remove the remnant of base metals. Alternatively, the converter slag can be introduced to a slag-cleaning furnace. The converter matte now contains nickel, copper and iron sulfides ($Ni_3S_2$, $Cu_2S$, FeS), small amounts of cobalt, and precious metals (Jones, 2005).

Converter matte is chill-casted into refractory-lined moulds and covered with a lid for a day and left to slow cool for approximately five days. This slow-cooling process allows for the iron-nickel phase and the copper-nickel alloy phase to separate. PGM's concentrate in a small amount of magnetic nickel-copper-iron alloy (Vermaak, 1995). After crushing and milling, the alloy can be magnetically separated, and directly processed in a precious metals refinery. The non-magnetic phase containing the nickel-copper phase is transported to a BMR for further processing (Archery, 2005).

At a BMR the nickel-copper matte is subjected to two stages of leaching: In the first stage of leaching copper is removed through a precipitation process that will convert soluble copper to insoluble copper sulphide or antlerite (Archery, 2005). This first stage of leaching takes place inside five tanks arranged in a cascade. Oxygen and sulphuric acid are added to the converter matte and nickel and copper separate into a liquid/solid phase inside the thickener (Vermaak, 1995). Nickel is removed from the overflow and fed into the nickel purification circuit. Copper sulphide or antlerite is removed from the underflow and subjected to a second stage of leaching. In the second stage leaching the copper removal residue is pumped into a lead and brick-lined autoclave. The primary objective of the second stage is to complete removal of nickel and iron (Archery, 2005). Nickel, copper and cobalt sulphides are converted to sulphates at temperatures between 150 °C and 165 °C and at a pressure of $9.8 \times 10^6$ kPa. The discharge from the autoclave is depressurised and pumped through two pressure filters in series. Precious metals collect on the filters and the copper rich filtrate is transferred to a copper electrowinning circuit, after selenium is filtered and leached with sodium hydroxide (Vermaak, 1995).

In the nickel purification circuit, lead is precipitated from the solution by injecting barium hydroxide. Secondly, cobalt is filtered out from the nickel rich solution that can now be transported to the nickel electrowinning circuit (Archery, 2005). The final step in hydrometallurgical treatment is electrolysis of the base metal solutions received from leaching and purification. Electrolysis takes place inside tankhouses consisting of electrowinning cells (Anon., 2007). In an electrowinning cell an electrical current is applied to the solution received from the leaching and purification department to yield copper and nickel plates. In a nickel electrowinning circuit the electrical current is applied to the electrolyte consisting of the nickel-rich solution and sulphuric acid (Lupi *et al.*, 2006).

Nickel deposits on the cathode according to the following reactions (Lupi *et al.*, 2006):

**Cathode reactions:**

$Ni^{2+} + 2e^{-} \rightarrow Ni$

$2H_3O^{+} + 2e^{-} \rightarrow H_2 + 2H_2O$

**Anode reaction:**

$6H_2O \rightarrow 4H_3O^{+} + O_2 + 4e^{-}$

Electroplated cathodes are hoisted from the electrowinning cells with an overhead crane. During production-pulling of the cathodes, cell workers assist with connecting the bailer to cathode hanger bars. Cathodes are hoisted from the cells and kept in this position to allow excess solution to drip back into the cell. The cathodes are transported to wash tanks, with the cell workers assisting and guiding the cathodes if necessary. After the cathodes are placed into the wash tank (completely submerged), the crane moves to a boric acid holding cell to collect starter sheets to be placed back into the electrowinning cell. This process is repeated until all of the electroplated cathodes are submerged in the wash tank and new starter sheets are in the electrowinning cell. Cell workers assist during this entire process of hooking and unhooking the cathodes. Cathodes are then extracted from the wash tank and transported to a drop-out well, where the cathodes are unloaded in the basement. Cathodes in the basement are sorted into rough and smooth cathodes and stored in a temporary storage where they are prepared for marketing and trading. Production-pulling of electroplated cathodes are normally done in a six-day cycle and during each cycle there is a crane operator, cell workers and a supervisor present (Anon., 2007).

## 2.5 Nickel exposure in tankhouses

According to the anodic reaction in Section 2.4, oxygen bubbles are formed and will migrate through the electrolyte bursting at the electrolyte/air interface, which will liberate some of the electrolyte solution into the ambient atmosphere (Sigley *et al.*, 2003). Two types of droplets are formed from the oxygen bubble migration process viz. film (Figure 1) and jet (Figure 2) droplets. Film droplets are generated when the film layer of the bubble collapses (Al Shakarji, 2012).

After the bubble has collapsed, liquid rushes to the centre and a droplet rises from the solution as a liquid jet (Al Shakarji, 2012). The result is the presence of an aerosol in the tankhouse atmosphere that consists of the acidic electrolyte (Sigley *et al.*, 2003).

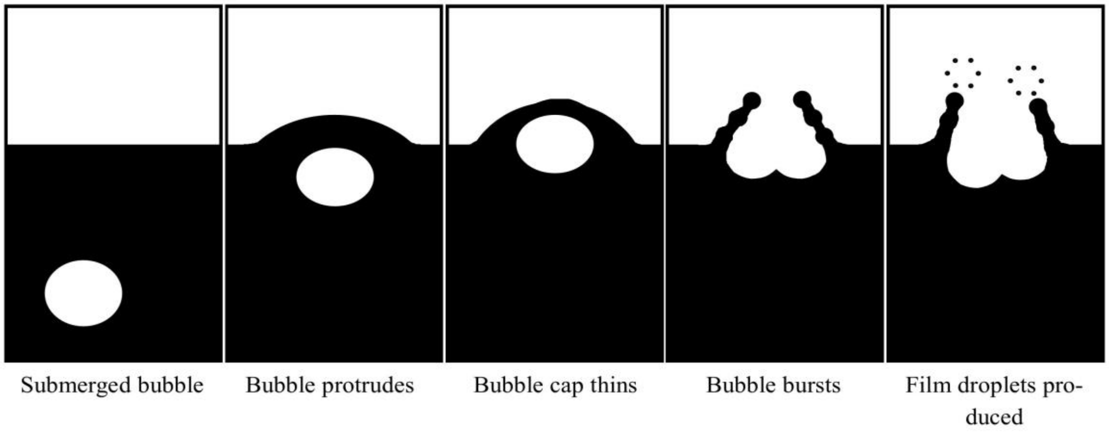


**Figure 1: Formation of film droplet in electrolyte (Bhattacharyya *et al.*, 2010).**

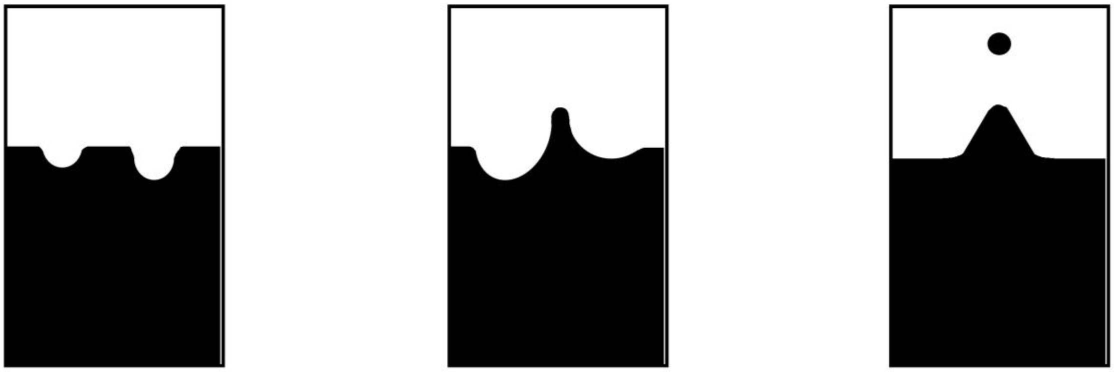


**Figure 2: Formation of jet droplet in electrolyte (Barlowe & Patton, 2011).**

There are several factors that may influence aerosol formation based on the above mentioned mechanisms e.g. current density, temperature, age of anode, presence of mist suppressants and solution acidity (Al Shakarji, 2012). According to Al Shakarji (2012), temperature had the largest effect on aerosol generation, followed by the presence of mist suppressants and current density. At higher temperatures, 40.6 mg/m$^3$ more aerosol was present in the atmosphere than at lower temperatures. Under high current density conditions, 8 mg/m$^3$ more aerosol was generated and in the absence of mist suppressants an additional 39.9 mg/m$^3$ aerosol was present.

Effectiveness of floating mist suppressants were influenced by their coverage of free surface area of the electrolyte and the height above the electrolyte. Floating barriers with lower densities proved to be more effective, because they were more buoyant in the solution and, therefore, covered the solution more effectively and also successfully intercepted acid drops (Al Shakrji, 2012). Cell workers, crane drivers and supervisors working in the tankhouse will be exposed to this nickel acid aerosol, and consequently be susceptible to the health effects associated with exposure to the aerosol discussed in Section 2.2.1.

### 2.5.1 Occupational hygiene monitoring conducted in tankhouses

In light of the previous section and the health effects associated with exposure, it is apparent why occupational hygiene monitoring is conducted at a BMR in the tankhouses. A brief overview of the sampling method for aerosols, conducted during an occupational hygiene monitoring programme, is necessary to understand the type of data that are used in a retrospective analysis. In the interest of staying inside the scope of this study only aerosol sampling, specifically that for nickel sulphate will be discussed.

According to the Health and Safety Executive (HSE) report on methods for determining hazardous substances (MDHS 14/4), aerosol sampling should be conducted in such a way that the sample is representative of the exposure a worker will experience in a full working shift. A minimum of 25% of the shift should be sampled, however, it is not recommended to sample less than 4 hours to determine a worker's time-weighted average (TWA) exposure (HSE, 2014). Occupational Safety and Health Administration (OSHA) recommends a minimum sampling period of 7 hours, for the sample to be representative of the worker's true exposure (OSHA, 1994), but according to the Occupational Exposure Sampling Strategy Manual (OESSM), a sampling period of 70% to 80% of the shift is recommended (Leidel *et al.*, 1977).

Despite these contradictions, all the above associations agree that the sample time should be representative of the worker's exposure, as far as is reasonably practicable (Leidel *et al.*, 1977; OSHA, 1994; HSE, 2014). Equipment needed to conduct aerosol sampling includes: A sampler, collection media, personal sampling pump, flexible tubing, a mass balance and a portable flow meter. A sampler that is designed to collect the size-fraction of interest (e.g. inhalable, thoracic or respirable) should be used. In the case of the aerosol present in the tankhouses (inhalable fraction), an Institute of Occupational Medicine (IOM) sampler is recommended (HSE, 2014).

Furthermore, a cellulose ester membrane with a 0.8 µm pore size as prescribed by the NIOSH 7300 analytical method to determine nickel content (NMAM, 2003) is used. For a full description of the preparation and assembly of the sampling media, the reader is referred to HSE (2014). In summary, the sampling media is assembled and the sampler is placed within the breathing zone of the worker (30 cm from the nose-mouth region) and the sampling pump attached to the workers belt. For general area samples, the sampling media is placed on a fixed position with the sampler approximately head height, away from obstructions and strong winds. The sampler is allowed to run for a period of at least 70% to 80% of the shift, and removed at the end of the shift (HSE, 2014). The collection media is transported to an analytical laboratory to determine the nickel concentration on the collection media, and also to do a speciation analysis (determines nickel species). The analytical method used to determine nickel concentration is the NIOSH 7300 analytical method (NMAM, 2003). Each worker's 8-hour TWA is calculated from the nickel concentration received from the laboratory, and these data are captured in an occupational hygiene report, as required by the Mine Health and Safety Act (MHSA) (MHSA, 1996). According to the MHSA, a person who is qualified in occupational hygiene must be employed to measure levels of exposure to hazards. Furthermore, employees are required to comply with the requirements of the MHSA and to co-operate with any person appointed to implement the MHSA requirements (MHSA, 1996).

Exposure data from occupational hygiene reports are used in a retrospective study, to evaluate exposure levels over a period of time. The time period over which a retrospective study stretch is, more often than not, decades, and with that a few challenges come to light (Smith *et al.,* 2005). One of these challenges is that the sampling method for collecting aerosols, changes over the years as newer technology becomes available. Consequently, an occupational hygiene database will have measurements that were taken with different samplers that have different collection efficiencies (Kenny *et al.*, 1997). Kenny *et al.* (1997) investigated eight different inhalable samplers viz. IOM, seven-hole, GSP, PAS-6, PERSPEC, CIP 10-I, 37-mm cassette open face and 37-mm cassette closed face. The IOM sampler is accepted as the personal sampler of choice to sample the inhalable fraction of aerosols (DEPA, 2008). According to Kenny *et al.* (1997), the sampling ratio between the IOM and seven-hole sampler was 1.17, in other words to convert the 'total' aerosol measurement from the seven-hole sampler to the inhalable fraction, the measurements need to be multiplied by a factor of 1.17.

The 37-mm cassette tended to under-sample with a factor of 2 – 3 times lower than the IOM during field tests but under laboratory conditions the ratio was 1.2 at an air velocity of 1 m/s (Kenny *et al.*, 1997).

The Danish Environmental Protection Agency (DEPA) reviewed regression results and sampling efficiencies of multiple studies comparing the IOM and 37-mm closed face samplers. Regression coefficients for the IOM and 37-mm sampler in the electroplating industry ranged from 0.7 to 0.87. To convert total aerosol concentrations measured with the 37-mm cassette (open or closed configuration and flow rate = 2 l/min) to the inhalable fraction, a correction factor of 3.0, is proposed by DEPA for scenarios where aerosol droplets are predominant (DEPA, 2008).

## 2.6 Characterisation of nickel exposure in refinery processes

Workers in a refinery are exposed to different nickel compounds, depending on the refining stage and purification step they are working on. Exposure to sulphidic nickel tends to be higher during the milling and grinding of the ore. After the ore is fed into furnaces, exposure to sulphidic nickel decreases with a concurrent rise in oxidic nickel exposure. During metallurgical refining of nickel, exposure to soluble nickel compounds will be higher. (Thomassen *et al.*, 1999; Werner *et al.*, 1999; Grimsrud *et al.*, 2000; Hughson *et al.*, 2009). A study conducted in a Russian nickel refinery characterised nickel exposure to different departments in the refinery. In the electrorefining department soluble nickel represented 55% – 99% of the total nickel exposure. Oxidic nickel represented 13% – 34% of the total nickel in half of the samples taken at the electrorefining department (Thomassen *et al.*, 1999).

Ratios of different nickel compounds are an important factor that needs to be taken into account when evaluating nickel exposure. Multiple studies suggest that it is not soluble nickel alone that is responsible for cancer incidents in the electrorefining industry, but rather exposure to a combination of different nickel compounds (Oller *et al.*, 1997; Thomassen *et al.*, 1999; Das and Buchner, 2007; Goodmann *et al.*, 2011).

## 2.7 Previous historical data assessments

In light of the previous sections, which explains the chronic health effects and exposure of nickel, the importance of historical reconstruction of nickel exposure data becomes clear.

Historical data are analysed and evaluated not only to investigate chronic health effects of substances in the work place, but also for epidemiological studies and to use in toxic tort cases (Stewart, 1999). The purpose of the retrospective study will ultimately determine the method that will be used to assess the historical data. Methodologies between retrospective studies will, therefore, differ to some extent, but will follow the same recipe of five basic steps i.e. collection of descriptive data, identifying the type of hazard, selecting an exposure metric, formation of exposure groups and estimating exposure (Seixas and Checkoway, 1995; Stewart and Stenzel, 2000). A comprehensive review of six retrospective studies' methodologies (Van Tongeren *et al.*, 1998; Glass *et al.*, 2000; Grimsrud *et al.*, 2000; Virji *et al.*, 2012; Friesen *et al.*, 2014; Sivulka *et al.*, 2014), will be discussed according to the five steps of historical reconstruction proposed by Stewart and Stenzel (2000). The six retrospective studies were selected based on their similarity to the present study.

### 2.7.1 Collection of descriptive data

Descriptive data include toxicological data and health effects of any substance in the workplace and a description of the site e.g. occupations, process information, engineering and administrative control measures (Stewart and Stenzel, 2000). All six retrospective studies reported chronic diseases after exposure to the investigated substance, and thus the purpose of the retrospective assessment – to construct an exposure matrix and evaluate exposure trends (Van Tongeren *et al.*, 1998; Glass *et al.*, 2000; Grimsrud *et al.*, 2000; Virji *et al.*, 2012; Friesen *et al.*, 2014; Sivulka *et al.*, 2014). Job titles are often used to differentiate between different groups of exposure. Care should, however, be taken as the exposure of the same job title may differ significantly across different industries. A detailed description of the site is necessary to assess exposure adequately (Smith *et al.*, 2005). Typically the site from which data were collected will be described, specifically departments and occupations but also process changes that would have significantly affected exposures (Van Tongeren *et al.*, 1998; Glass *et al.*, 2000; Grimsrud *et al.*, 2000; Virji *et al.*, 2012; Friesen *et al.*, 2014; Sivulka *et al.*, 2014). For instance Grimrud *et al.* (2000) documented a process change in 1978, when a nickel refinery switched from the Hybinette method to a chlorine leaching process. This change dramatically affected the exposure in the roasting, electrolyte purification, and copper leaching departments, with a factor of five, six and eight respectively. Glass *et al.* (2000) collected extensive descriptive data on job histories of employees in the Australian petroleum industry. The job histories included employment site, job title, duration of employment and hours worked per week.

Furthermore, data were collected on benzene content of materials handled, task frequencies and technologies used. These data were later identified as exposure modifying factors and used in a formula to calculate exposure estimates (Glass *et al.,* 2000). In some retrospective studies exposure is related to medical surveillance data, to determine an exposure-response relationship. Heederik *et al.* (2014) collected medical surveillance data on respiratory sensitisation after exposure to platinum salts.

### 2.7.2 Hazard identification

Information to identify and characterise hazards in a retrospective study should accompany the descriptive data. Such information should classify the type of hazard, identify the route of exposure, and contain details on whether more than one hazard is present and the physical and toxicological characteristics thereof (Stewart and Stenzel, 2000). The characteristics of the hazard will firstly determine the health effects experienced by the workers, and secondly, determine the sampling method in an occupational hygiene programme and consequently the exposure data in a retrospective study. Health effects were discussed in Section 2.2.1, but recall the deposition of nickel particles in the respiratory tract based on particle sizes and also the difference in carcinogenicity based on the solubility of nickel (ATSDR, 2005; IARC, 2012). With this premise in mind the researchers of the retrospective studies, aimed to characterise the type of hazard according to the descriptive data of the site. For example, Grimsrud *et al.* (2000) characterised different nickel species to the different departments in the nickel refinery. Exposure to insoluble nickel compounds will be higher during comminution of the ore and during metallurgical refining exposure to soluble nickel compounds will be higher. Virji *et al.* (2012) characterised exposure to beryllium compounds according to particle sizes i.e. respirable and submicron particles collected with a personal cascade impactor sampler. The size-dependant measurements were, furthermore, compared to measurements taken with a 37-mm cassette sampler that represented the ‘total’ beryllium exposure (Virji *et al.*, 2012). Characteristics of the hazard assessed provide a preliminary category in which data are grouped into and applied to the descriptive data. Categorising of the data facilitates the construction of an exposure matrix in which exposure metrics can be applied (Seixas and Checkoway, 1995).

### 2.7.3 Selection of an exposure metric

In most cases arithmetic (AM) and geometric means (GM) and time-weighted averages (TWA) are used as exposure metrics. Means and TWA adequately describe exposure, but they are not the ideal method to predict occupational disease (Stewart and Stenzel, 2000).

The type of exposure metric used in a study is dependant, as mentioned, on the aim of the study (e.g. characterising exposure or predicting disease) and the toxicological mechanism of the hazard. It is, however, recommended to use more than one metric to evaluate exposure, to make sure that all the variables are accounted for and that the aim of the study is achieved (Stewart and Stenzel, 2000). In historical analyses, sampling strategies in an occupational hygiene programme change over time, consequently the exposure metric will differ between the different samplers used in the occupational hygiene programme. As described in Section 2.5.1, the collection efficiency between the samplers are different and can, therefore, not be categorised together in an exposure matrix without the use of conversion factors (Kenny *et al.*, 1997). Sivulka *et al.* (2014) conducted a site-specific inter-sampler comparison programme to generate conversion factors to convert measurements of the 37-mm cassette sampler to the IOM. As a result inhalable particulate measurements could be combined regardless of the sampler and categorised in different departments and in personal or area samples (Sivulka *et al.*, 2014). After the exposure metric is standardised across the study, preliminary retrospective assessment begins with descriptive statistics. All six retrospective studies began statistical analyses with AM's and GM's to describe exposure in each worksite (Van Tongeren *et al.*, 1998; Glass *et al.*, 2000; Grimsrud *et al.*, 2000; Virji *et al.*, 2012; Friesen *et al.*, 2014; Sivulka *et al.*, 2014).

### 2.7.4 Formation of exposure groups

In an occupational hygiene monitoring programme, workers are grouped into similar exposure groups (SEGs), to monitor exposures based on similar departments, job titles and tasks. The OESSM recommendation is used to group workers correctly into SEGs and makes it substantially easier to estimate exposures, because workers in a SEG should have similar, average exposures, percentiles, 8-hour TWAs and any other exposure metrics (Leidel *et al.*, 1977; Stewart and Stenzel, 2000).

This method is used with the assumption that no day–to–day variation exists between workers in the same SEG. In reality, inter–worker variation may significantly influence homogeneity of the SEG. Factors that may contribute to inter–worker variation include work experience, technical skill, work habits, posture and body shape. Although eliminating inter–worker variation may be a substantial and impractical task, it remains critical as inter–worker variation may lead to misclassification and the lack of a dose-response relationship for the whole group (Smith *et al.*, 2005).

The SEGs that are formed during an occupational hygiene survey are used to construct an exposure matrix (Table 1). SEGs will be part of the dimensions in an exposure matrix (Seixas and Checkoway, 1995). For example, exposure data from a tankhouse in a nickel refinery are normally grouped into different sections of the tankhouse as illustrated in Table 1, thus section will be one dimension in the exposure matrix, and for retrospective studies, time (years of exposure) will be the second dimension. The size of dimensions can, furthermore, be determined by another exposure determinant, e.g. the time dimension can be divided into significant intervals (determined by sampling methods or process changes etc.) (Seixas and Checkoway, 1995).

**Table 1: Example of exposure matrix for nickel exposure data from a nickel refinery (Seixas and Checkoway, 1995).**

| **Dimension 1: Time** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Dimension 2: Area** | East bay | 1980 – 1984 | 1985 – 1989 | 1990 – 1994 | 1995 – 1999 | 2000 – 2004 | 2005 – 2009 | 2010 – 2014 |
| | | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ |
| | Centre bay | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ |
| | West bay | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ | $[Ni]_{(mg/m^3)}$ |

Exposure matrices will differ between retrospective studies, as the data available and the aim of each study will be different. Retrospective studies with the aim to construct an exposure matrix for epidemiological studies, tend to group data according to departments and chemical forms of the hazard (Van Tongeren *et al.*, 1998; Grimrud *et al.*, 2000; Virji *et al.*, 2012; Sivulka *et al.*, 2014).

Other studies that evaluate exposure of one chemical across industries and the different occupations within the industries, tend to group the data according to industries and occupations within the industries (Glass *et al.*, 2000; Friesen *et al.*, 2014).

Furthermore, studies may have a similar aim, but data available can be different between them. Grimsrud *et al.* (2000) had more than 500 area samples and 5900 personal samples and could, therefore, group the data into stationary and personal samples while Sivulka *et al.* (2014) only used personal samples in the analysis. Both studies did, however, build an exposure matrix for epidemiological studies (Grimsrud *et al.*, 2000; Sivulka *et al.*, 2014). Glass *et al.* (2000) conducted an extensive job history investigation and, therefore, had comprehensive descriptive data that could be categorised specifically according to industry, job title, tasks and frequency of a task.

An additional determinant of the dimensions in an exposure matrix is exclusion criteria, which two of the retrospective studies reported explicitly (Glass *et al.*, 2000; Grimrud *et al.*, 2000). Grimsrud *et al.* (2000) excluded departments with 10 or less measurements, measurements that had a running time of 5 hours or less, and exposure concentrations that were higher than 50 mg/m$^3$. Glass *et al.* (2000) exclusively used personal monitoring data and excluded any data which were incomplete e.g. not reporting year of measurement, or details on tasks that were performed. Samples that had a running time of less than 180 minutes were also excluded. Finally, before exposure can be estimated, the limit of detection (LOD) of the analytical method used to determine concentrations on the sample media should be considered in order to determine a value with which to substitute LOD values. Two of the retrospective studies substituted the value of the LOD as half of the LOD (Glass *et al.*, 2000; Grimsrud *et al.*, 2000). The $\beta$–substitution method is however, considered to be superior to the substitution of half of the LOD or LOD divided by the square root of two, as it produces unbiased results. This method uses the observed data to calculate a $\beta$ factor, which is multiplied by the LOD to estimate the unknown below the detection limit (BDL) values (Ganser and Hewett, 2010). Once exposure groups are formed, it is possible to estimate exposure in a retrospective analysis correctly (Stewart and Stenzel, 2000).

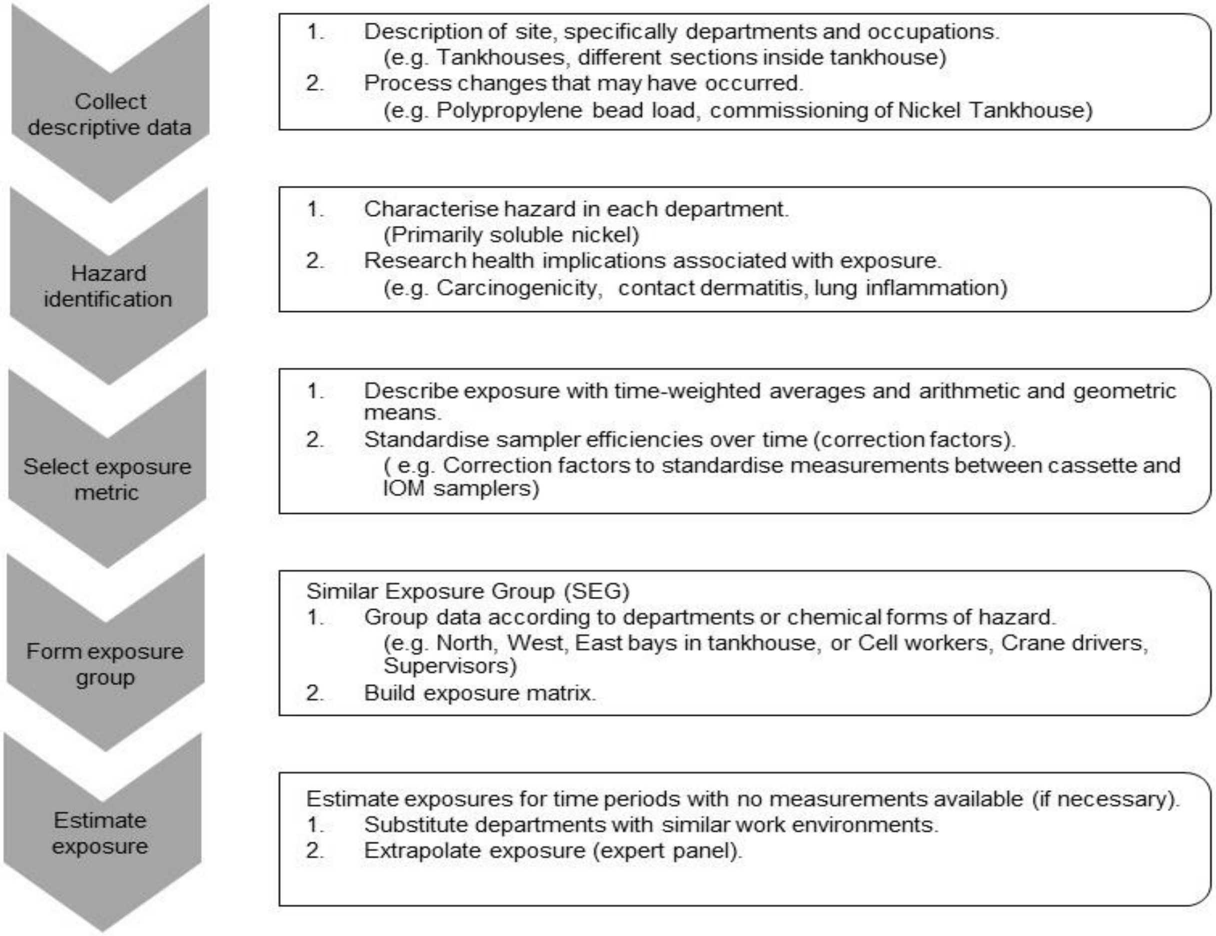
### 2.7.5 Estimation of exposures

The last step of a retrospective analysis, is the estimation of exposures. The previous four steps are vital to build an appropriate exposure matrix, from which exposures can be estimated (Stewart and Stenzel, 2000).

Based on the exposure metric used, exposures can be estimated on a semi-quantitative scale (e.g. a numeric value of 1 – 10, or low, medium or high), a defined range of measurements (e.g. 0.01 – 0.09 mg/m$^3$) or point estimates (e.g. 0.09 mg/m$^3$). Exposure estimates are ultimately used to evaluate the health effects related to exposure to the hazard (Stewart and Stenzel, 2000). Descriptive statistics were the first step in estimating exposures in all six retrospective studies (Van Tongeren *et al.*, 1998; Glass *et al.*, 2000; Grimsrud *et al.*, 2000; Virji *et al.*, 2012; Friesen *et al.*, 2014; Sivulka *et al.*, 2014).

One of the challenges in retrospective studies is the estimation of exposures for time periods and departments, with no measurement data. This challenge can be approached in two ways; firstly measurements from departments with similar work environments that will yield similar exposure to the hazard can be assigned to the departments with no measurements. Secondly, exposures can be estimated by extrapolating exposures. In the latter case an expert panel is usually used to take into account any processes, technologies, shut-downs, etc. that may have influenced exposures at that time (Van Tongeren *et al.*, 1998; Grimrud *et al.*, 2000; Sivulka *et al.*, 2014). Both Glass *et al.* (2000) and Friesen *et al.* (2014) aimed to estimate exposures of a hazard across the entire industry. These studies, therefore, had to account for multiple variances within the data, and used multivariable models to estimate the exposures. This is not the case with the present study, as the data will not be used to estimate exposures and it is, therefore, unnecessary to describe the statistical models used in the last mentioned studies. When variation between process operations and/or different occupations was investigated, Sivulka *et al.* (2014) used an ANOVA analysis. Variation over a time period was assessed by three of the six studies by using trend coefficients and linked to the descriptive data (e.g. process changes) (Van Tongeren *et al.*, 1998; Grimrud *et al.*, 2000; Sivulka *et al.*, 2014). Virji *et al.* (2012) used stationary area samples to evaluate time trends with regression models. Historical exposure estimates were calculated by applying temporal factors to the baseline exposure estimates of workers. Temporal factors were calculated with stationary area samples (that estimated changes in exposures from 1994 to 1999) and work histories and profiles of workers. Furthermore, exposures were summarised in average, cumulative and highest-ever job exposure (Virji *et al.*, 2012).

Based upon the aforementioned, the proposed model by Stewart and Stenzel (2000), can be applied to the present study. However, as mentioned previously, retrospective assessments may differ from each another to some extent and, therefore, the proposed model was adjusted to this study (Figure 3, next page).



1. Description of site, specifically departments and occupations.
   (e.g. Tankhouses, different sections inside tankhouse)
2. Process changes that may have occurred.
   (e.g. Polypropylene bead load, commissioning of Nickel Tankhouse)

1. Characterise hazard in each department.
   (Primarily soluble nickel)
2. Research health implications associated with exposure.
   (e.g. Carcinogenicity, contact dermatitis, lung inflammation)

1. Describe exposure with time-weighted averages and arithmetic and geometric means.
2. Standardise sampler efficiencies over time (correction factors).
   ( e.g. Correction factors to standardise measurements between cassette and IOM samplers)

Similar Exposure Group (SEG)
1. Group data according to departments or chemical forms of hazard.
   (e.g. North, West, East bays in tankhouse, or Cell workers, Crane drivers, Supervisors)
2. Build exposure matrix.

Estimate exposures for time periods with no measurements available (if necessary).
1. Substitute departments with similar work environments.
2. Extrapolate exposure (expert panel).

**Figure 3: Adjusted model for present retrospective assessment, (model first proposed by Stewart and Stenzel, 2000)**

In conclusion, nickel compounds have various chronic health effects including allergic contact dermatitis, lung inflammation and also causes nasal and lung cancer (ATSDR, 2005). Refinery workers in a base metal refinery, specifically in the electrowinning department are exposed to soluble nickel (DEPA, 2008). Control measures implemented over time, to minimise exposure to soluble nickel, result in a trend in soluble nickel exposure. Retrospective assessments collectively analyse all of the exposure data from occupational hygiene monitoring reports by building an exposure matrix to identify the trend in exposure (Seixas and Checkoway, 1995). The exposure matrix can ultimately be used to link exposure to response, and illustrate the entire exposure-response relationship in an epidemiological study (Smith *et al.,* 2005).

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# CHAPTER 3: ARTICLE

This article will be submitted to the journal: *The Annals of Occupational Hygiene* to be considered for publication. *The Annals of Occupational Hygiene* publishes original research and development material that helps reduce risk of ill-health resulting from work.

## 3.1 Instructions to authors (excerpt)

*Structure of paper.* Papers should generally conform to the pattern: Introduction, Methods, Results, Discussion and Conclusions – consult a recent issue for style of headings. A paper must be prefaced by an abstract of the argument and findings, which may be arranged under the headings: Objectives, Methods, Results and Conclusions. Keywords should be given after the list of authors.

*Brevity:* The necessary length of a paper depends on the subject, but any submission must be as brief as possible consistent with clarity. The number of words, excluding the abstract, references, tables and figures, must be stated as a message to the editor at the time of submission. If this length is more than 5000 words, a statement must be included justifying the extra length. Papers without this information may be returned unread.

*Units and symbols:* SI units must be used, though their equivalent in other systems may be given as well.

*Figures:* Good quality low resolution electronic copies of figures, which include photographs, diagrams and charts, should be sent with the first submission. It is helpful to reviewers to incorporate them in the word-processor text or at the end. The revised version, after review, should be accompanied by high resolution electronic copies in a form and of a quality suitable for reproduction. They should be about the size they are to be reproduced in, with font size at least 6 point, using the standard Adobe set of fonts.

*Tables:* Tables should be numbered consecutively and given a suitable caption, and each table typed on a separate page. Footnotes to tables should be typed below the table and should be referred to by superscript lowercase letters.

*References:* References should only be included if essential to the development of an argument or hypothesis, or which describe methods for which the original account is too long to be reproduced, only publications which can be obtained by the reader should be referenced. References in the text should be in the form Jones (1995), or Jones and Brown (1995), or Jones *et al.* (1995) if there are more than two authors. For example: Jones and Brown (1995) observed total breakdown control… or Total breakdown of control has sometimes been observed (Jones and Brown, 1995).

At the end of the paper, references should be listed in alphabetical order by name of first author, using the Vancouver Style of abbreviation and punctuation. Examples are given below. ISBNs should be given for books and other publications where appropriate. Material unobtainable by readers should not be cited. Personal Communications, if essential, should be cited in the text in the form (Professor S.M. Rappaport, University of California). References will not be checked editorially, and their accuracy is the responsibility of authors.

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# A retrospective analysis of nickel exposure data at a South African base metal refinery

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## 3.2 Abstract

Refinery workers in base metal refineries are occupationally exposed to soluble nickel and, controlling soluble nickel exposure is, therefore, essential. Control measures improved over time and consequently resulted in trends in soluble nickel exposure, which can be identified with a retrospective analysis of the exposure data. This study aimed to analyse soluble nickel exposure data from a South African base metal refinery (BMR), to identify trends in the exposure data from 1982 until 2014 in two tankhouses (i.e. Copper and Nickel Tankhouse). Exposure data were presented in an exposure matrix, which described exposure profiles for the sections inside tankhouses and the different occupations independently. One-way analyses of variances (ANOVA) were conducted to identify significant differences in exposures from 1982 until 2014, and the trends illustrated with linear regression graphs. Differences between sections inside the tankhouses as well as the different occupations were evaluated, and the percentage of measurements above the time-weighted average, occupational exposure limit (TWA-OEL) were calculated. Significant downward ($p \leq 0.0001$) trends were identified in area exposure in the Copper Tankhouse between 1982 and 2011. Area exposure in the Copper Tankhouse decreased with a factor of 29 between 1982 and 1986. However, after 1986 no significant downward trend was identified in area exposure. Furthermore, personal exposure significantly ($p \leq 0.0001$) decreased with a factor of three between 1991 and 2014 in the Copper Tankhouse. No significant trends were identified in area and personal exposure in the Nickel Tankhouse. The highest percentage of OEL exceedances were determined for Cell workers (Copper Tankhouse, 64%; Nickel Tankhouse, 32%) and Crane drivers (Copper Tankhouse, 64%; Nickel Tankhouse, 19%), if Supervisors in the Nickel Tankhouse with limited measurements were not taken into account. In conclusion, downward trends in the Copper Tankhouse were identified and may be ascribed to the implementation of various control measures and process changes. No exposure trend was established in the Nickel Tankhouse, as only four years of exposure data were available.

## 3.3 Introduction

Nickel is essential for the manufacturing of numerous products including alloys, ceramics, pigments, catalysts and is also used in various electroplating processes (Nickel Institute, 2015). Approximately 25 000 tons of nickel are produced by South Africa annually, of which 90% is produced as a co-product from platinum group metals (PGM) mining (Nickel Institute, 2009).

Each stage during the purification and refining of nickel is characterised by exposure to different nickel compounds. Exposure to sulphidic nickel tends to be higher during the milling and grinding of the ore, but after the nickel ore is fed into the furnaces, exposure to oxidic nickel is higher (Thomassen *et al.,* 1999). Refinery workers are primarily exposed to nickel sulphate (referred to as soluble nickel), during the electrolysis of nickel (Grimsrud *et al.*, 2000). Electrolysis of nickel takes place inside tankhouses, where an electrical current is applied to a nickel sulphate solution and consequently, nickel deposits on the cathode of the electrowinning cell (Lupi *et al.*, 2006). During nickel electrolysis, oxygen bubbles are formed at the anode and will rise through the electrolyte solution, bursting at the liquid-air interface, producing an aerosol of the electrolyte solution (Sigley *et al.*, 2003). Therefore, an aerosol containing soluble nickel is present in the tankhouse atmosphere, and increased exposure to this aerosol is imminent for workers aiding in the removal process of electroplated cathodes. Specifically, cell workers and crane drivers are considered to be at maximum risk employees, due to their proximity to the electrowinning cell during the removal of the electroplated cathodes (Anon., 2007).

Exposure to nickel compounds may lead to dermal and respiratory health effects. Chronic dermal exposure to nickel compounds which is either airborne or in a solution may elicit allergic contact dermatitis (DEPA, 2008). Furthermore, chronic respiratory exposure to nickel compounds causes lung inflammation and atrophy of the nasal epithelium (Goodman *et al.,* 2011). Nickel compounds are currently classified as human carcinogens (Group 1) by the International Agency for Research on Cancer (IARC), (IARC, 2012). Several studies indicated a significant increase in lung and nasal cancer risk, following cumulative exposure to soluble nickel (Anttila *et al.,* 1998; Grimsrud *et al.,* 2002; Beveridge *et al.,* 2010; Binazzi *et al.,* 2015). Specifically, Anttila *et al.* (1998) determined a positive association between increased lung cancer risk and duration of employment. Chronic diseases, in occupational settings, may develop after prolonged exposure to toxic substances such as asbestos, nickel and lead. A retrospective assessment of the exposure to these substances is often used to illustrate the complete exposure-response relationship (Smith *et al.,* 2005). For soluble nickel such an exposure-response relationship is considered to span over at least 20 years (Anttila *et al.,* 1998).

Two retrospective studies, one conducted at a Welsh nickel refinery and the other at a Norwegian nickel refinery, evaluated historical nickel exposure data, from 1953 to 2000 (Welsh refinery), and 1973 to 1994 (Norwegian refinery) (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014).

On average, two-fold reductions were associated with process changes in both of the refineries, and overall nickel exposure decreased 30-fold in the Welsh refinery and six-fold in the Norwegian refinery. Results for both of these retrospective studies were used in combination with epidemiological studies to evaluate cancer risks for the refinery workers (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014). For the Welsh refinery an increased lung cancer risk existed for workers hired before 1929, but decreased dramatically thereafter (Doll *et al.*, 1990). An increased lung cancer risk, associated with exposure to soluble nickel in the electrolysis department, was established by Andersen *et al.* (1996) in the Norwegian refinery. Evidently, the absence of reliable nickel exposure estimates dating back to the commissioning of the refineries made it difficult to determine whether the cancer risks were solely related to nickel exposure. Therefore, earlier exposures were estimated at both refineries, by extrapolating exposures from similar departments, taking into account knowledge of the processes in operation and working conditions during that time, to build an exposure matrix (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014).

As with most retrospective studies, estimation of exposures for which no data are available and to process variations in exposure over time adequately, are some of the challenges that need to be taken into account. Variations in the exposure measurements may lead to misclassification within the matrix and significantly influence the final exposure matrix (Smith *et al.,* 2005). For example, Glass *et al.* (2000) exclusively used personal monitoring data and excluded any data which were incomplete e.g. not reporting year of measurement, or details on tasks that were performed. Samples that had a running time of less than 180 minutes were also excluded. A correctly applied exclusion criteria is, therefore, essential for an accurate exposure matrix which can provide a description of past exposures to link to epidemiological studies (Smith *et al.,* 2005).

An exposure matrix is not only useful in epidemiological studies, but also in providing a comprehensive description of past exposures, and the effect of process changes and control measures on exposure. A description of historical soluble nickel exposure has not been done at South African base metal refineries. The aim of this study is to assess historical soluble nickel exposure inside two tankhouses (i.e. Copper and Nickel Tankhouse) at a South African base metal refinery. An exposure matrix will also be constructed to simplify trend analysis for each section inside the tankhouses and occupations. The exposure matrix is subsequently used to evaluate the effect of process changes on soluble nickel exposure inside the Copper and Nickel Tankhouse.

## 3.4 Methods

This study has been approved by the Human Research Ethics Committee of the North-West University (Ethics clearance number: NWU-00195-15-S1).

### 3.4.1 The base metal refinery

Electrolysis of nickel at the base metal refinery (BMR) takes place inside the two tankhouses. The leach and purification department separates the base metal phase (non-magnetic) into a copper-rich solution and a nickel-rich solution. After leaching, both solutions are transported to the tankhouses to commence their respective electrowinning circuits. Nickel is electroplated from a nickel sulphate solution, and during this reaction nickel is reduced at the cathode and water oxidises at the anode in sulphate media. The BMR commissioned the first tankhouse in 1981 (hereafter referred to as the Copper Tankhouse), which was until 2009, responsible for copper and nickel production. In 2009 a second tankhouse was commissioned (hereafter referred to as the Nickel Tankhouse), which was responsible for nickel production thereafter. Before 2009, the Copper Tankhouse was divided into three production bays: West bay, responsible for copper production and Centre and East bay, responsible for nickel production (Anon., 2012).

### 3.4.2 Historical data

Anonymised nickel exposure data from both tankhouses were obtained from the BMR. Exposure data were processed as a random sample from all of the nickel exposures measured over 32 years at the BMR. Exposure data for the Copper Tankhouse were available from 1982 to 2014, and for the Nickel Tankhouse from 2011 to 2014. The data consisted of area and personal measurements for both tankhouses, and were either taken with a 37-mm cassette or an Institute of Occupational Medicine (IOM) sampler. The methods to assess soluble nickel exposures varied over the years, but followed in principle the Methods for Determining Hazardous Substances (MDHS 14/3; 14/4), published by the Health and Safety Executive (HSE, 1983; HSE, 2014). The different samplers used over the years were, however, taken into account in order to standardise exposures as an inhalable fraction. As soluble nickel is classified as inhalable particulate (DME, 2002), the Danish Environmental Protection Agency (DEPA) recommends an IOM sampler to measure airborne soluble nickel concentrations.

To convert total aerosol concentrations measured with the 37-mm cassette (open or closed configuration and flow rate = 2 l/min) to the inhalable fraction, a correction factor (3.0), as proposed by DEPA for scenarios where aerosol droplets are predominant (DEPA, 2008), was applied. A total of 1038 measurements (i.e. 487 area and 551 personal measurements), from the total measurements (N = 1426) were converted to the inhalable fraction.

#### 3.4.2.1 Exclusion criteria

Measurements conducted with a duration of less than 70% of an eight hour working shift (i.e. 336 minutes / five hours 36 minutes) were excluded from the database. This was based on the recommendation in the Occupational Exposure Sampling Strategy Manual (OESSM), which recommends a sampling period of at least 70% to 80% of the shift for the measurement to be representative of true exposure (Leidel *et al.*, 1977). Ten personal measurements from the Copper Tankhouse and 36 measurements (29 area and 7 personal) for the Nickel Tankhouse were excluded based on this criterion. Furthermore, measurements taken with samplers other than 37-mm cassette or IOM samplers, for which no correction factors are available were excluded from the study (n = 160).

After the exclusion criteria was applied, a total of 554 area measurements of the Copper Tankhouse from 1982 to 2011 remained. These measurements were taken at fixed locations at the three bays of the tankhouse (West, Centre, East bays) and additionally North and South ends of the tankhouse, inside the Contractor’s tea room and Overhead crane. A total of 695 personal measurements taken at the Copper Tankhouse from 1991 to 2014 were eligible for use in this study. The majority of the data for the Nickel Tankhouse consisted of personal measurements (n = 173) measured during 2011 to 2014, and only four area measurements for the East and Centre bay, measured during 2013, were available. Some of the measurements were only reported as general area or personal measurements, without explicitly reporting the respective bay or occupation that was measured. Consequently, these measurements were processed as unspecified measurements in an additional category.

Personal measurements for both tankhouses were grouped into four occupation categories namely: Cell workers, Crane drivers, Supervisors and Miscellaneous activities. Cell workers are responsible for removal of electroplated cathodes, stripping starter sheets and fault finding of the electrowinning cells. Crane drivers are responsible for operating overhead cranes, used to remove and replace cathodes of electrowinning cells. Supervisors are in charge of overseeing all of the daily activities within the tankhouse.

The Miscellaneous activities category contains exposure data for housekeeping workers and contractors grouped together as they were all intermittently exposed and exposure data available were limited.

### 3.4.4 Statistical Analysis

An exposure matrix was constructed by initial grouping of data from both tankhouses according to the sample type i.e. area and personal measurements. Area measurements were again grouped into the different sections inside both tankhouses and personal measurements according to the four occupational categories. The Copper Tankhouse exposure data were grouped into five year intervals in order to build a compact exposure matrix for which descriptive statistics on similar exposure circumstances could be applied. Exposure data for the Nickel Tankhouse, however, only consisted of data for four years, and were therefore summarised per year.

Measurement values that were below the limit of detection (LOD = 0.8 µg/m$^3$), were substituted with a value calculated by the β–substitution method. This method uses the observed data to calculate a β-factor, which is multiplied by the LOD to estimate the unknown below the detection limit (BDL) values. The β–substitution method produces unbiased results and is considered superior to the substitution of half of the LOD or LOD divided by square root of two (Ganser and Hewett, 2010). Seven percent of all of the exposure data were below the LOD and substituted with the respective β–estimated values.

As the data were approximately log-normal distributed, it was deemed appropriate to log transform the data and calculate geometric means (GM) and confidence intervals (CI: 5% – 95%) for each category to provide a preliminary description of the data. GMs and CI (95%) were calculated from the antilog (to the base 10) of the log-transformed data. A one-way analysis of variance (ANOVA) followed by post-hoc Tukey HSD (Honest Significant Difference) test, were conducted on the log transformed data to identify any differences in mean nickel exposure influenced firstly, by the year intervals, and secondly by the different categories (i.e. respective sections or occupations) for both area and personal exposure data ($p \leq 0.05$, as statistically significant).

Effect sizes are often used in empirical research to determine the importance of the statistical significant ($p \leq 0.05$) differences between groups being evaluated (Steyn, 2009).

Effect sizes are determined from partial eta squared values (i.e. small effect ≤ 0.01; medium effect ≈ 0.06; and large effect ≥ 0.13), which represents the proportion of the variance that is accounted for by the independent variable. This proportion can, therefore, also be reported as a percentage e.g. 1%, small effect (Steyn, 2009). Effect sizes were calculated in conjunction with ANOVA's and, therefore, determined the importance of statistical differences between the respective year intervals and also between the different categories (i.e. respective bays or occupations).

All figures were generated using GraphPad Prism® version 5.03 (GraphPad Software) and all statistical analyses were conducted in Statistica, version 12 (Stat Soft, Inc. 2015).

## 3.5 Results

The majority of soluble nickel exposure data were obtained from the Copper Tankhouse, as it was longer in operation and the primary producer of nickel and copper electroplated sheets prior to 2009.

### 3.5.1 Area exposures in the Copper Tankhouse

A summary of the area inhalable nickel exposure data is presented in an exposure matrix (Table 1) for the Copper Tankhouse. Area exposures in the Copper Tankhouse ranged between the BDL and 14.400 mg/m$^3$ with a geometric mean soluble nickel exposure of 0.105 mg/m$^3$. The Centre and East bays that were responsible for nickel production before 2009, had geometric mean area exposures of 0.157 mg/m$^3$ and 0.145 mg/m$^3$ respectively (both above the TWA-OEL = 0.1 mg/m$^3$). Soluble nickel exposure in the West bay which was responsible for copper production before 2009, had a geometric mean exposure of 0.136 mg/m$^3$ and the exposure ranged between the BDL and 11.400 mg/m$^3$.

In addition to exposure monitoring in the three bays, a series of measurements were conducted inside the overhead crane and inside the Contractor's tea room, and geometric mean exposures of 0.086 mg/m$^3$ and 0.053 mg/m$^3$ were calculated respectively. Area exposures for the Unspecified tankhouse areas had a geometric mean exposure of 0.089 mg/m$^3$.

**Table 1: Summary of inhalable soluble nickel area exposure ($mg/m^3$) for the Copper Tankhouse (1982 – 2011).**

| | Time period | n | GM ($mg/m^3$) | Median ($mg/m^3$) | CI (95%) ($mg/m^3$) | Above OEL (%) |
|---|---|---|---|---|---|---|
| Centre bay | 1982 – 1985[a – c] | 11 | 2.285 | 3.810 | 0.755, 6.914 | 91 |
| | 1986 – 1990[a] | 20 | 0.046 | 0.073 | 0.015, 0.136 | 40 |
| | 1991 – 1995[b] | 6 | 0.094 | 0.205 | 0.002, 3.752 | 83 |
| | 1996 – 2000[c] | 16 | 0.132 | 0.375 | 0.028, 0.621 | 75 |
| | 2001 – 2005 | 1 | 0.360 | – | – – | 100 |
| | **1982 – 2005** | **54** | **0.157** | **0.224** | **0.073, 0.342** | **67** |
| East bay | 1982 – 1985[d – f] | 8 | 1.035 | 0.943 | 0.291, 3.671 | 100 |
| | 1986 – 1990[d] | 19 | 0.042 | 0.120 | 0.010, 0.169 | 53 |
| | 1991 – 1995[e] | 6 | 0.098 | 0.186 | 0.002, 4.059 | 83 |
| | 1996 – 2000[f] | 12 | 0.332 | 0.780 | 0.058, 1.889 | 83 |
| | **1982 – 2000** | **45** | **0.145** | **0.240** | **0.060, 0.350** | **73** |
| West bay | 1982 – 1985[g – i] | 10 | 2.004 | 2.488 | 0.650, 6.174 | 100 |
| | 1986 – 1990[g] | 74 | 0.098 | 0.150 | 0.055, 0.174 | 65 |
| | 1991 – 1995[h] | 4 | 0.026 | 0.088 | BDL, 11.734 | 50 |
| | 1996 – 2000[i] | 9 | 0.213 | 0.180 | 0.126, 0.360 | 78 |
| | **1982 – 2000** | **97** | **0.136** | **0.180** | **0.082, 0.227** | **69** |
| North end | **1991 – 1995** | **6** | **0.133** | **0.311** | **0.011, 1.588** | **83** |
| South end | **1991 – 1995** | **6** | **0.037** | **0.076** | **0.001, 0.960** | **50** |
| Overhead crane | 1991 – 1995 | 1 | BDL | BDL | – – | 0 |
| | 2006 – 2010 | 12 | 0.151 | 0.230 | 0.065, 0.352 | 83 |
| | **1991 – 2010** | **13** | **0.086** | **0.198** | **0.020, 0.367** | **77** |
| Contractors' tea room | **2006 – 2010** | **4** | **0.053** | **0.047** | **0.028, 0.098** | **0** |
| Unspecified areas | 1991 – 1995 | 31 | 0.102 | 0.210 | 0.046, 0.227 | 61 |
| | 1996 – 2000 | 163 | 0.077 | 0.180 | 0.048, 0.122 | 56 |
| | 2001 – 2005 | 52 | 0.120 | 0.306 | 0.052, 0.278 | 75 |
| | 2006 – 2010 | 28 | 0.123 | 0.119 | 0.063, 0.240 | 54 |
| | 2011 | 55 | 0.083 | 0.130 | 0.054, 0.128 | 58 |
| | **1991 – 2011** | **329** | **0.089** | **0.173** | **0.067, 0.119** | **60** |
| **Area measurements** | **1982 – 2011** | **N = 554** | **0.105** | **0.181** | **0.084, 0.131** | **63** |

[a – i] Significant differences ($p \leq 0.0001$) in soluble nickel exposures between the year groups.

The lowest mean exposure was measured at the South end (0.037 $mg/m^3$) of the Copper Tankhouse. No significant difference was determined in mean soluble nickel exposures between the bays of the Copper Tankhouse ($p = 0.874$), substantiated with the partial eta squared value of 0.011 (small effect), for the effect size between the bays and soluble nickel concentration. Geometric mean area exposure for 1982 – 1985 were overall statistically significantly higher than in the subsequent years in the Centre, East and West bays.

After 1982 – 1985 there was a sharp decline in soluble nickel exposure, evidently the lowest exposures for the Centre (0.046; CI: 0.015 – 0.136) and East bay (0.042; CI: 0.010 – 0.169) were measured between 1986 and 1990. Trends in area exposures for the Copper Tankhouse are illustrated in Figure 1.

An ANOVA indicated a significant difference ($p \leq 0.0001$) in all of the area soluble nickel exposure between 1982 and 2011, with a partial eta squared value (0.066) of medium effect size (6%), and the significant downward trend is illustrated in Figure 1A. No significant trend was, however, determined after 1986 (Figure 1C), and the significant downward trend was attributed to the substantial decrease in exposures between 1982 and 1986, with a factor of 29 (Figure 1B).

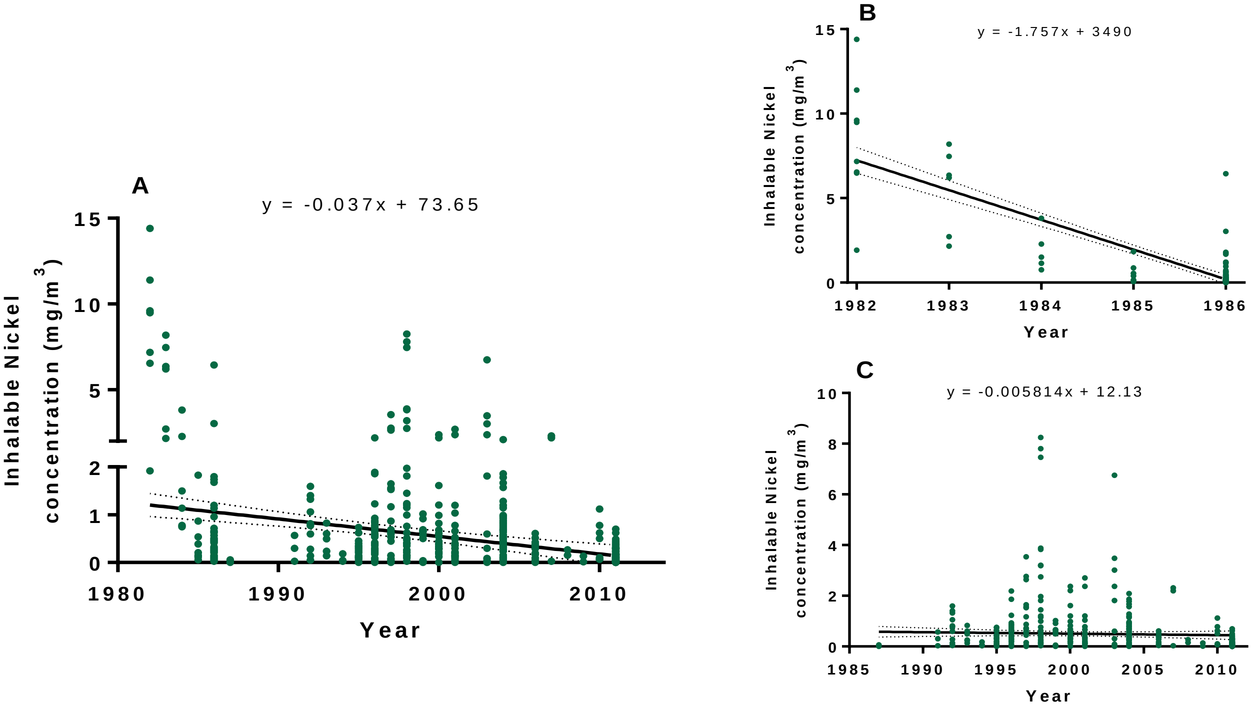

**Figure 1: Linear regression of area inhalable soluble nickel exposures for the Copper Tankhouse, A (1982 – 2011); B (1982 – 1986); C (1987 – 2011).**

### 3.5.2 Personal exposures in the Copper Tankhouse

The exposure matrix (Table 2) for personal exposures in the Copper Tankhouse, illustrates personal exposures which ranged between the BDL and 4.453 mg/m$^3$. Specifically, Cell workers and Crane drivers who are considered maximum at risk employees, had geometric mean exposures of 0.113 mg/m$^3$ and 0.106 mg/m$^3$ respectively (both above the TWA-OEL = 0.1 mg/m$^3$). Supervisors' exposure in the Copper Tankhouse ranged between the BDL and 1.617 mg/m$^3$ and workers grouped into the Miscellaneous category had a geometric mean exposure of 0.014 mg/m$^3$.

An ANOVA indicated similar exposure for Cell workers and Crane drivers in the Copper Tankhouse, although when both of these occupations were compared to the Miscellaneous category, statistically significant different exposures were established ($p \le 0.05$). However, a small effect size (partial eta value = 0.03) was determined for the influence of occupation category on soluble nickel exposure.

**Table 2: Summary of inhalable soluble nickel personal exposure (mg/m$^3$) for the Copper Tankhouse (1991 – 2010).**

|  | Time period | n | GM (mg/m$^3$) | Median (mg/m$^3$) | CI (95%) (mg/m$^3$) | Above OEL (%) |
|---|---|---|---|---|---|---|
| Cell worker [i] | 1991 – 1995[a] | 1 | 0.295 | 0.295 |  | 100 |
|  | 1996 – 2000[b] | 97 | 0.347 | 0.366 | 0.270, 0.445 | 90 |
|  | 2001 – 2005[a-c] | 126 | 0.052 | 0.161 | 0.033, 0.084 | 56 |
|  | 2006 – 2010[c] | 79 | 0.265 | 0.339 | 0.189, 0.371 | 77 |
|  | 2011 – 2014[a-c] | 57 | 0.028 | 0.036 | 0.017, 0.044 | 23 |
|  | **1991 – 2014** | **360** | **0.113** | **0.234** | **0.090, 0.143** | **64** |
| Crane driver [j] | 1996 – 2000[d] | 52 | 0.272 | 0.329 | 0.181, 0.409 | 87 |
|  | 2001 – 2005[d,e] | 13 | 0.027 | 0.211 | 0.003, 0.222 | 54 |
|  | 2006 – 2010[e] | 3 | 0.852 | 1.076 | 0.211, 3.432 | 100 |
|  | 2011 – 2014[d,e] | 18 | 0.013 | 0.020 | 0.006, 0.026 | 0 |
|  | **1996 – 2014** | **86** | **0.106** | **0.210** | **0.065, 0.174** | **64** |
| Miscellaneous activities [i, j] | **2001 – 2005** | **14** | **0.014** | **0.039** | **0.002, 0.102** | **43** |
| Supervisor | 2001 – 2005[f] | 17 | 0.024 | 0.034 | 0.007, 0.080 | 29 |
|  | 2006 – 2010[f] | 14 | 0.161 | 0.257 | 0.064, 0.404 | 57 |
|  | **2001 – 2010** | **31** | **0.057** | **0.051** | **0.025, 0.129** | **42** |
| Unspecified occupations | 2001 – 2005[g] | 68 | 0.079 | 0.389 | 0.034, 0.181 | 62 |
|  | 2006 – 2010[g, h] | 69 | 0.267 | 0.339 | 0.200, 0.356 | 83 |
|  | 2011 – 2014[h] | 67 | 0.059 | 0.092 | 0.041, 0.085 | 45 |
|  | **2001 – 2014** | **204** | **0.108** | **0.179** | **0.078, 0.150** | **63** |
| **Personal measurements** [i – j] | **1991 – 2014** [a-h] | **N = 695** | **0.103** | **0.208** | **0.087, 0.123** | **63** |

[a-e] Significant differences ($p \le 0.0001$) in soluble nickel exposures between the year groups.

[f-h] Significant differences ($p \le 0.05$) in soluble nickel exposures between the year groups.

[i, j] Significant differences ($p \le 0.05$) between indicated occupation categories.

Geometric mean personal soluble nickel exposures declined (three-fold) over the years (1991 – 2014), with the lowest exposures measured during 2011 – 2014 (0.013; CI: 0.006 – 0.026). The overall decrease in personal soluble nickel exposures from 1991 to 2014 (Figure 2), were substantiated by an ANOVA ($p \le 0.0001$) with an effect size of 17% (partial eta squared = 0.166, large effect). Significant decreases ($p \le 0.0001$) in exposures were specifically determined for Cell workers and Crane drivers during 2001 – 2005 and 2011 – 2014 with effect sizes of 21% and 36% (large effects) respectively. Between 2006 and 2010 mean soluble nickel exposures peaked for Crane drivers, although only three measurements were available for Crane drivers during this period. Furthermore, Supervisors' soluble nickel exposures increased significantly ($p \le 0.05$) from 2001 to 2006 (seven-fold), with an effect size of 19% (large effect).

Furthermore, a significant increase ($p \leq 0.05$) in exposure was identified for the unspecified proportion of personal exposures during 2006 – 2010.

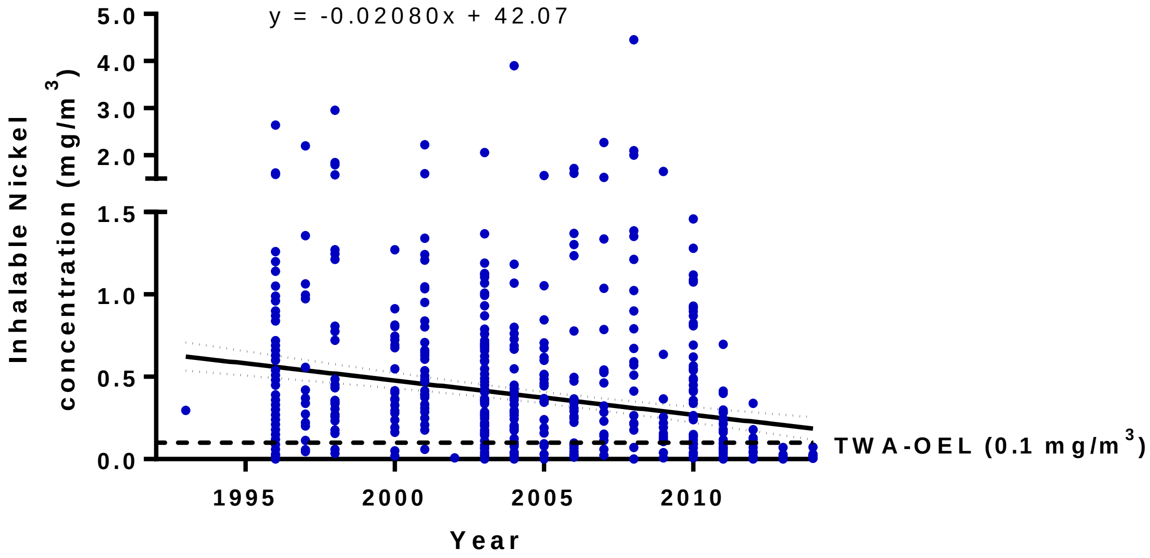

**Figure 2: Linear regression of personal inhalable soluble nickel exposure in the Copper Tankhouse (1991 – 2014).**

### 3.5.3 Area and Personal exposures in the Nickel Tankhouse

An exposure matrix for soluble nickel exposure in the Nickel Tankhouse is presented in Table 3. Only four area measurements were obtained for the Nickel Tankhouse, of which three of the measurements were measured in the East bay (0.009; CI: 0.002 – 0.030).

Personal exposure in the Nickel Tankhouse ranged between the BDL and 0.672 mg/m$^3$. Cell workers had a geometric mean exposure of 0.043 mg/m$^3$ and Crane drivers 0.021 mg/m$^3$, which were both below the TWA-OEL (0.1 mg/m$^3$). Cell workers and Crane drivers had similar exposure to soluble nickel in the Nickel Tankhouse as determined by a Tukey HSD test ($p = 0.116$). The highest personal exposure was identified for Supervisors with a geometric mean exposure of 0.320 mg/m$^3$, however, only two measurements were available and may not be representative of their true exposure. The Miscellaneous category of the Nickel Tankhouse had a geometric mean exposure of 0.008 mg/m$^3$, although only exposures for 2014 were obtained. Occupation categories had a significant influence on soluble nickel exposure ($p \leq 0.05$) in the Nickel Tankhouse, with a 10% effect size (moderate to large effect).

The variance was attributed to the Miscellaneous category in comparison with Supervisors ($p = 0.020$) and Cell workers ($p = 0.009$). Significant differences ($p \leq 0.05$) for all personal exposures in the Nickel Tankhouse (2011 – 2014) were determined by an ANOVA, although no specific influence of a particular year could be identified, as illustrated in Figure 3.

**Table 3: Summary of area and personal inhalable soluble nickel exposure (mg/m$^3$) for the Nickel Tankhouse (2011-2014).**

| | Time period | n | GM (mg/m$^3$) | Median (mg/m$^3$) | CI (95%) (mg/m$^3$) | Above OEL (%) |
|---|---|---|---|---|---|---|
| Centre bay | **2013** | **1** | **0.064** | **0.064** | **– –** | **0** |
| East bay | **2013** | **3** | **0.009** | **0.007** | **0.002, 0.030** | **0** |
| **Area measurements** | **2013** | **4** | **0.014** | **0.010** | **0.003, 0.080** | **0** |
| Cell worker [b] | 2011 | 7 | 0.020 | 0.016 | 0.011, 0.038 | 0 |
| | 2012 | 9 | 0.065 | 0.097 | 0.024, 0.180 | 44 |
| | 2013 | 11 | 0.089 | 0.155 | 0.025, 0.316 | 55 |
| | 2014 | 17 | 0.029 | 0.036 | 0.013, 0.065 | 24 |
| | **2011 – 2014** | **44** | **0.043** | **0.040** | **0.027, 0.069** | **32** |
| Crane driver | 2011 | 39 | 0.019 | 0.020 | 0.010, 0.035 | 26 |
| | 2013 | 40 | 0.023 | 0.022 | 0.014, 0.038 | 13 |
| | **2011, 2013** | **79** | **0.021** | **0.021** | **0.014, 0.031** | **19** |
| Miscellaneous activities [b, c] | **2014** | **12** | **0.008** | **0.017** | **0.002, 0.026** | **0** |
| Supervisor [c] | **2013** | **2** | **0.320** | **0.320** | **– –** | **100** |
| Unspecified | 2011 | 10 | 0.013 | 0.016 | 0.006, 0.030 | 0 |
| | 2012 | 25 | 0.034 | 0.052 | 0.018, 0.064 | 28 |
| | 2013 | 1 | 0.160 | – | – – | 100 |
| | **2011 – 2013** | **36** | **0.027** | **0.030** | **0.017, 0.045** | **22** |
| **Personal measurements** | **2011 – 2014[a]** | **N = 173** | **0.026** | **0.027** | **0.020, 0.033** | **4** |

[a] Significant decreases ($p \leq 0.05$) in soluble nickel exposures for all personal measurements.

[b, c] Significant differences ($p \leq 0.05$) between indicated occupation categories.

The effect size of time period on overall personal exposure was calculated to be a 5% influence on the total variance (a moderate effect), and with an intercept partial eta value of 0.817, indicated that 80% of the variance is accounted for by variance between the measurements. Furthermore, no specific decreases in exposures in any particular year could be identified for Cell workers or Crane drivers after conducting Tukey HSD tests.

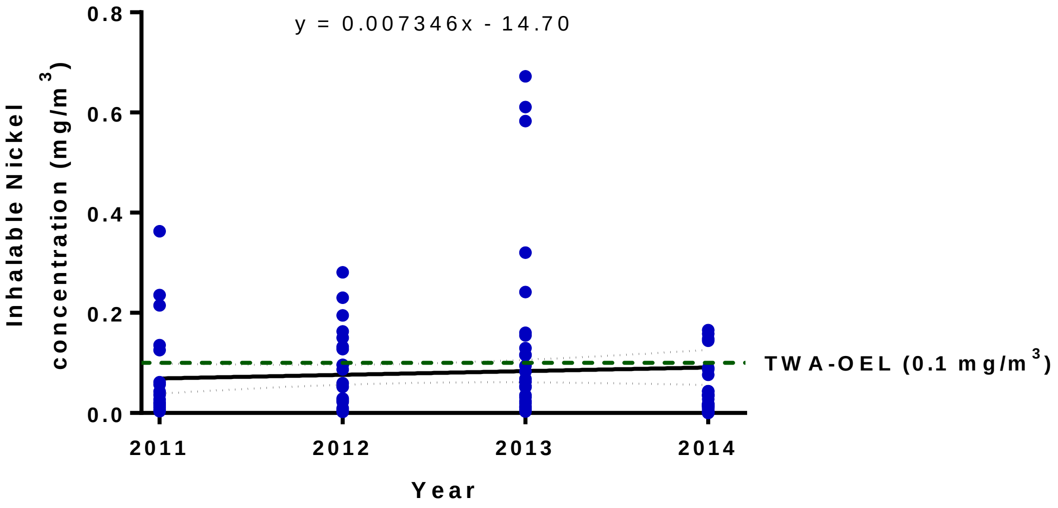

**Figure 3: Linear regression of personal inhalable soluble nickel exposures for the Nickel Tankhouse (2011 – 2014).**

### 3.5.4 Occupational exposure limit (TWA-OEL) exceedances

The fraction of measurements of area and personal exposures in Table 1 and 2, that exceeded the time weighted average (TWA)-OEL (0.1 mg/m$^3$) in the Copper Tankhouse, exceeded 50%. During 1982 – 1985, more than 90% of the area measurements exceeded the TWA-OEL in the Copper Tankhouse. None of the area measurements in Table 3 for the Nickel Tankhouse exceeded the TWA-OEL, and only 4% of all the personal measurements did exceed the TWA-OEL. Cell workers (64%) and Crane drivers (64%) had the highest percentage of TWA-OEL exceedances in the Copper Tankhouse and Supervisors (100%) in the Nickel Tankhouse. In 2011 – 2014 a lower percentage of measurements exceeded the TWA-OEL for Cell workers in the Copper Tankhouse (23%) than in the Nickel Tankhouse (32%). Similar results were determined for Crane drivers, in 2011 – 2014 none of the measurements for Crane drivers in the Copper Tankhouse were above the TWA-OEL, compared to 19% of the Crane drivers in the Nickel Tankhouse.

Although, during 2006 – 2010 all of the measurements for Crane drivers in the Copper Tankhouse exceeded the TWA-OEL. The number of measurements for Supervisors that exceeded the TWA-OEL in the Copper Tankhouse increased from 29% (2001 – 2005) to 57% (2006 – 2010), and all of the Supervisors' measurements in the Nickel Tankhouse exceeded the TWA-OEL.

The number of measurements above the TWA-OEL for Cell workers in the Copper Tankhouse decreased over the years with the lowest percentage during the 2011 – 2014 interval, although Cell workers' exposures marginally increased between 2013 (0.002 mg/m$^3$) and 2014 (0.016 mg/m$^3$), none of the exposures were above the TWA-OEL.

## 3.6 Discussion

Soluble nickel exposure data which were used for this retrospective assessment consisted of a large number of area measurements from 1982 to 2011, after which personal measurements were more often used to evaluate nickel exposure of the workers in the tankhouses. General area soluble nickel exposure in the Copper Tankhouse decreased significantly with a factor of 29, between 1982 and 1986, which may have been caused by more polypropylene beads that were added to the electrowinning cells in 1986 (Anon. 2012). No further significant trends in general area exposure could be identified in the Copper Tankhouse (Table 1), as progressively more personal measurements were used to assess exposures in the tankhouses. The effect sizes indicated that different sections in the Copper Tankhouse had a small to medium influence on exposure.

Personal exposure in the Copper Tankhouse decreased three-fold between 1991 and 2014, and subsequently had a significant downward trend, with the exception of Supervisors which had a significant increasing trend (seven-fold increase) from 2001 to 2010. Exposure data from the Nickel Tankhouse were only available from 2011, even though the Nickel Tankhouse was commissioned in 2009. Therefore, only four years exposure data were available for the Nickel Tankhouse and consequently, no significant downward trend was identified for personal exposures in the Nickel Tankhouse.

Previous historical studies at nickel refineries in Wales and Norway also used personal measurements predominantly in their analyses, but did not report specific occupations. Nevertheless, downward trends in the electrolysis departments were identified at both refineries. Soluble nickel exposures decreased with a factor of four in the electrolysis departments at both refineries in approximately 20 years (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014), whereas personal exposures in this study decreased with a factor of three in the Copper Tankhouse in approximately 20 years.

Cell workers in the Copper Tankhouse had a significant downward trend in exposures during 2011 – 2014, specifically during 2013 when exposures were reduced with a factor of 27 from 2011 (Table 2).

This substantial reduction in exposures for Cell workers may be ascribed to less nickel electrowinning cells in the Copper Tankhouse, as nickel production were progressively moved to the Nickel Tankhouse with the commissioning of the Nickel Tankhouse in 2009. There was still soluble nickel exposure in the Copper Tankhouse in the immediate past (2001 – 2014), when personal exposure had a geometric mean of 0.03 $mg/m^3$, even though nickel productions were moved to the Nickel Tankhouse.

Soluble nickel exposure of Cell workers in the Nickel Tankhouse (Table 3) were at a maximum during 2013, and may be ascribed to more nickel solution that was introduced to the electrowinning cells. Furthermore, Supervisors in the Nickel Tankhouse also had high exposures during 2013, although only two measurements were available, but still corresponded with the high exposures for Cell workers. High exposures for Cell workers and Supervisors in the Nickel Tankhouse may have been caused by technical issues that were experienced with the commissioning of the new tankhouse. Technical difficulties were specifically caused by a shorting problem and with the introduction of more nickel solution in the Nickel Tankhouse (Anon, 2013). After the technical challenges were addressed, exposures decreased three-fold in 2014. Elevated exposures were not only identified for Supervisors in the Nickel Tankhouse, but Supervisors in the Copper Tankhouse also revealed an increasing exposure trend. The number of measurements conducted for Supervisors in both tankhouses were, however, limited and, therefore, not necessarily representative of the true exposure. The influence of occupation category on exposure in the Nickel Tankhouse had a large effect, consequently an employee’s occupation and tasks associated with the occupation, will have a large effect on soluble nickel exposure.

Exposures measured for the Miscellaneous category were approximately 79% lower than in the other three occupation categories at both tankhouses. Low exposures for the Miscellaneous category were, however, expected as these workers were only intermittently exposed, and may not have been in close proximity to the electrowinning cells. Sivulka *et al.* (2014) evaluated workers grouped in a category named ESWA (Engineering and Site-Wide Activities) or non-process workers, for which exposure was only 13% lower when compared to process workers. When the ESWA workers were compared to the Miscellaneous category of this study in both tankhouses, the exposures were 11% higher than the Miscellaneous category, although no recent exposure data were available for the ESWA category (1990 – 1994).

Soluble nickel exposure in the Contractors' tea room were at the action level of soluble nickel (0.05 mg/m$^3$), and workers may be significantly exposed in this area, considered that this is demarcated as a common room in which no personal protective equipment (PPE) is worn.

Exposure matrices from the Welsh and Norwegian studies were compared with the exposure matrix of the Copper Tankhouse (Table 1) for exposures measured between 1986 and 1990, and did correlate to some extent. Even though the measurements from the Welsh and Norwegian studies were personal exposures and only corresponding area exposures from the Copper Tankhouse were available, on average the exposures of this study were 19% higher than the Welsh refinery and 68% higher than in the Norwegian refinery (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014). Soluble nickel exposures were additionally compared to exposures measured in the electrorefining departments in Russian and Scandinavian nickel refineries. Exposure in the Copper Tankhouse was approximately 32% lower than in the Russian refinery (Thomassen *et al.,* 1999), however, approximately 74% higher than the Scandinavian refinery (Werner *et al.* 1999), in corresponding years.

The majority of the earlier exposures in the Copper Tankhouse exceeded the current TWA-OEL for soluble nickel (0.1 mg/m$^3$). However, during 1982-1985 exposures were regulated according to a Threshold Limit Value (TLV) determined by the American Conference of Governmental Industrial Hygienists (ACGIH). Furthermore, the TLV to which nickel exposures in the Copper Tankhouse were regulated against (1982 – 1985), was for total nickel (TLV = 1.0 mg/m$^3$) and not soluble nickel (Anon., 1987). However, even if the TLV that was used during this time is taken into consideration, mean measurements in the Copper Tankhouse were still almost double the TLV. TWA-OEL exceedances did decrease over the years in the Copper Tankhouse, with the lowest fraction of exceedances during 2011 – 2014. TWA-OEL exceedances in the Nickel Tankhouse did increase during 2013, when more than 50% of the exposures measured for Cell workers were above the TWA-OEL. This increase TWA-OEL exceedances corresponds with the high exposures associated with the technical challenges experienced during 2013.

The high percentage of TWA-OEL exceedances in the tankhouses is a cause for concern for refinery workers who are occupationally exposed to soluble nickel, especially if the elimination half life time after inhalation exposure is taken into account. Urinary elimination half life time for soluble nickel after inhalation exposure was determined to be between 17 to 39 hours (DEPA, 2008). Therefore, cumulative exposure to soluble nickel may be present in refinery workers who are exposed on a daily basis.

Cumulative exposure to soluble nickel is associated with lung inflammation, atrophy of nasal epithelium (Goodman *et al.,* 2011) and an increased lung cancer risk (Anttila *et al.,* 1998; Grimsrud *et al.,* 2002; Beveridge *et al.,* 2010; Binazzi *et al.,* 2015).

Monitoring and controlling soluble nickel exposures is, therefore, essential, specifically in the occupation categories for which limited measurements were obtained (i.e. Supervisors and Miscellaneous activities).

## 3.7 Conclusion

Supervisors in the Nickel Tankhouse had the highest exposure to soluble nickel, and an increasing trend in exposure for Supervisors in the Copper Tankhouse was identified. The Miscellaneous category had significantly lower exposures compared to the other occupation categories in both tankhouses. Soluble nickel exposures measured at the South African BMR were in general higher, than in the Welsh, Norwegian and Scandinavian refineries for corresponding years. Advances in controlling soluble nickel exposure in the tankhouses have been made since 1981, and process changes had a significant influence on exposure. A statistically significant downward trend in area exposures was identified in the Copper Tankhouse and may be due to the polypropylene bead load that was increased in 1986, as a mist suppressant. Personal exposures had significant downward trends in the Copper Tankhouse, which can be ascribed to the movement of nickel productions to the Nickel Tankhouse in 2009. The introduction of more nickel solution to the electrowinning cells in the Nickel Tankhouse led to an increase in exposure and consequently that more than 50% of Cell workers’ exposure exceeded the TWA-OEL.

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# CHAPTER 4: CONCLUDING CHAPTER

In this concluding chapter, the aims, objectives and hypothesis are discussed according to the conclusions of the study. Recommendations are made to ensure future adequate monitoring of all tankhouse employees, who are occupationally exposed to soluble nickel. The limitations of this retrospective assessment study are discussed and finally, suggestions for future studies will be made.

## 4.1 Conclusions

This study aimed to assess historical nickel exposure data from two tankhouses at a South African base metal refinery (BMR). Historical nickel exposure data obtained from two tankhouses (i.e. Copper and Nickel Tankhouse) at the BMR, were presented in exposure matrices (Chapter 3, Tables 1 – 3). These tables characterised area exposure according to the different sections in the tankhouses, and personal exposures according to the different occupations, thus achieving the first objective. The second objective was to identify trends in any of the sections or occupations. The exposure matrix not only made the trend analyses easier, it also integrated the trend analyses into the predetermined categories (sections inside the tankhouses and occupations). Specifically, soluble nickel exposure data were assessed to identify any trends in exposure for any of the sections inside the tankhouses and occupations. This objective was achieved when a significant downward trend ($p \leq 0.0001$) was identified in area soluble nickel exposure data from 1982 to 2011 in the Copper Tankhouse. Area exposure in the Copper Tankhouse decreased with a factor of 29 between 1982 and 1986, however, no trend was established should exposures from 1986 to 2011 be analysed independently. A three-fold reduction in personal exposure was identified in the Copper Tankhouse, consequently a significant downward trend ($p \leq 0.0001$) was established for personal exposure data. Significant downward trends ($p \leq 0.05$) were established specifically for Cell workers and Crane drivers. Cell workers and Crane drivers had on average an eight-fold reduction in soluble nickel exposure during 2001 – 2005 and 2011 – 2014. The downward trend in personal exposure (1991 – 2014) in the Copper Tankhouse could be ascribed to the movement of nickel productions to the Nickel Tankhouse in 2009. Personal exposures for Supervisors had a significant increasing trend ($p \leq 0.05$), as exposure from 2010 were approximately seven times higher than in 2001.

No personal exposure data of Supervisors were available to establish whether this trend discontinued during 2011 – 2014. Since limited data from only 2001 – 2005 were available, no trend could be identified for the Miscellaneous category.

No significant downward trends in area or personal exposures in the Nickel Tankhouse were identified, as only four area measurements could be used after the exclusion criteria were applied, and only four years of exposure data were obtained since the commissioning of the Nickel Tankhouse in 2009.

The number of time-weighted average, occupational exposure limit (TWA-OEL) exceedances were determined for each of the occupations and sections inside both tankhouses. A large proportion (63%) of area exposures in the Copper Tankhouse exceeded the current TWA-OEL for soluble nickel (0.1 mg/m$^3$), and no significant decreases ($p = 0.994$) in exceedances were determined for area exposures (1986 – 2011). Personal TWA-OEL exceedances in the Copper Tankhouse did, however, significantly decrease with 34% between 1991 and 2014, as nickel productions were progressively moved to the Nickel Tankhouse, which corresponds with the decreasing trend in personal exposure for Cell workers and Crane drivers.

The third objective was to establish the historical number of excursion above the TWA-OEL for each section and occupation assessed. The number of TWA-OEL exceedances for Supervisors in the Copper Tankhouse, increased with 28% during 2001 to 2006, while the Miscellaneous category had the lowest number of TWA-OEL exceedances. None of the area exposures in the Nickel Tankhouse exceeded the TWA-OEL, although the four area measurements cannot be considered as representative of exposure over time. A small percentage (4%) of personal exposures in the Nickel Tankhouse did exceed the TWA-OEL, and no significant trend was identified. The percentage of TWA-OEL exceedances for Cell workers and Crane drivers were higher in the Copper Tankhouse than in the Nickel Tankhouse, with the exception of recent exposure (2011 – 2014). Technical difficulties experienced after the commissioning of the Nickel Tankhouse may have been responsible for higher personal exposures in the Nickel Tankhouse during 2013 (Anon, 2013), and the movement of nickel productions to the Nickel Tankhouse for the low percentage (23%) of TWA-OEL exceedances in the Copper Tankhouse.

Finally, the effect of process changes on soluble nickel exposure in the tankhouses was evaluated, as demonstrated by the differences in nickel exposure measured in the immediate past (2011 – 2014), thus achieving the final objective. Technical difficulties with the introduction of a higher volume nickel solution to the electrowinning cells, led to an increase in exposure for Cell workers during 2013 in the Nickel Tankhouse (Table 3).

Cell workers' exposure in the Copper Tankhouse decreased significantly ($p \leq 0.0001$) between 2011 and 2013 when nickel production was progressively moved to the Nickel Tankhouse. In addition to the recent advancements in control measures, exposures in the Copper Tankhouse decreased significantly between 1985 and 1986, when the polypropylene bead load was increased in the electrowinning cells, as a mist suppressant.

Previous retrospective studies conducted in Wales and Norway indicated a three to thirty-fold decrease in nickel exposure since the 1950's to 2014 (Grimsrud *et al.*, 2000; Sivulka *et al.*, 2014). It was, therefore, hypothesised that decreasing trends in nickel exposure over time exist in the Copper and Nickel Tankhouses of a South African BMR. The hypothesis is, therefore, partially accepted as a significant decreasing trend in area and personal exposure was only identified for the Copper Tankhouse, which can be attributed to the increase polypropylene bead load and the movement of nickel productions to the Nickel Tankhouse in 2009. Only four years of exposure data were available for the Nickel Tankhouse, while previous retrospective assessments were conducted on at least 20 years of data (Grimrud *et al.,* 2000; Sivulka *et al.,* 2014), in which trends in exposure could be identified.

## 4.2 Recommendations

Recommendations will be made in the following section to ensure future adequate monitoring of all tankhouse employees, who are occupationally exposed to soluble nickel.

### 4.2.1 Number of samples

Currently, the occupational hygiene monitoring programme at the BMR is based on the Department of Mineral Resources (DMR) guidelines, which classifies employees in the tankhouses into a similar exposure group (SEG), Category A. The DMR requires a minimum of 5% of the employees, or at least five employees to be sampled quarterly, whichever is greater (DME, 2002a). Consequently, only 20 employees are sampled annually (Total employees exposed = 47).

**Recommendation 1:** Due to the significant differences identified between the occupation categories, the American Industrial Hygienist Association (AIHA) recommends six measurements for each category to establish accurate exposure profiles for all of the occupation categories. Six measurements are recommended based on practicability and to estimate the population mean accurately, with minimum variance (Mulhausen *et al.,* 2006a).

For example, if the four proposed occupation categories from this study are used in an exposure assessment, at least 24 measurements are recommended quarterly and, therefore, 96 measurements annually.

**Recommendation 2**: Numerous area measurements (n = 27) from the Nickel Tankhouse were excluded from this study due to non-representative short sampling periods.

Cathodes are extracted from the electrowinning cells in a six day cycle during the morning shift and, therefore, will result in a cyclic variation in soluble nickel exposure inside the tankhouses (Anon, 2007). Area measurements are, therefore, necessary to evaluate the exposure trend in the tankhouses during the day. Furthermore, area exposures should be measured in longer representative sampling periods (e.g. min of 70% of an 8-hour working shift), to ensure that the cyclic variation in exposure is accounted for (Sadhra, 2005).

### 4.2.2 High exposure in under-sampled categories

High exposures were measured for Nickel Tankhouse Supervisors, and in the Contractor's tea room where the geometric mean was at the action level (50% of the TWA-OEL) for soluble nickel. Despite this, very few measurements were obtained for both of these categories and may, therefore, not necessarily represent true exposure conditions. Soluble nickel exposure which is at the action level in the Contractor's tea room, are alarming as this is demarcated as a common room in which no exposure is supposed to be present and personal protective equipment (PPE) is not worn.

**Recommendation 3:** Guidelines under the Mine Health and Safety Act (Act 29 of 1996), requires a system of occupational hygiene measurements to be implemented if the concentration of an aerosol is half of the TWA-OEL (DME, 2002b). A comprehensive exposure assessment (area and personal measurements) is, therefore, recommended in the Contractor's tea room and more personal measurements for Supervisors, to establish an accurate exposure profile as described in Section 4.2.1. Should exposure in the Contractor's tea room be established to be at the action level after the comprehensive exposure assessment and the reason for contamination identified, is it recommended to eliminate the source of contamination or to implement adequate control measures when elimination is not practicable. However, if the exposure is determined to be lower than the action level after the exposure assessment, the quality of monitoring demarcated sections should be revised.

### 4.2.3 Supplementary data

Collecting supplementary data or descriptive data as proposed by Stewart and Stenzel (2000), is the first step in constructing an exposure matrix described in Section 2.7.1. Incomplete supplementary data made it difficult to explain the high soluble nickel exposure for Nickel Tankhouse Supervisors, the increasing trend in exposure for Copper Tankhouse Supervisors, and the high exposure in the Contractor's tea room.

Supplementary data describing sampling conditions, for example, may have explained why Supervisors who are expected to be only intermittently exposed had high exposures in 2013 in the Nickel Tankhouse and an increasing trend in exposure in the Copper Tankhouse. Although the high exposure in 2013 correlates with the high exposure for Cell workers during that time associated with the shorting problem, supplementary data on the Supervisors may have described the Supervisors aiding the Cell workers with identifying the fault in the electrowinning cells. Furthermore, a potential unaccounted contamination source may be present in the Contractor's tea room, although the cause for the high exposure in a demarcated common room is difficult to identify without descriptive supplementary data.

**Recommendation 4**: In the exposure matrices of this study an additional category was created to include measurements for which sections or occupations as supplementary data indicating the specific section of occupation sampled were not available. Detailed supplementary data are, therefore, recommended to accompany exposure data, to identify potential unaccounted for hazards.

### 4.2.4 TWA-OEL exceedances

The number of TWA-OEL exceedances in the tankhouses and the exposure in the Contractor's tea room which is at the action level for soluble nickel, is alarming when the health effects associated with exposure are considered.

Soluble nickel not only causes contact dermatitis and chronic lung inflammation but is also classified as a known human carcinogen (IARC, 2012), specifically a higher lung cancer risk is associated with cumulative exposure (Anttila *et al.,* 1998). International legislations revised their TWA-OEL for soluble nickel to take the health effects associated with soluble nickel exposure into account. The Occupational Safety and Health Administration (OSHA) and the European Chemicals Agency (ECHA) recommend a permissible exposure limit (PEL) for soluble nickel of 0.05 mg/m$^3$ (ECHA, 2006; OSHA, 2013).

**Recommendation 4:** It is, therefore, recommended to lower soluble nickel exposure to the lowest possible level, considering that international PELs are 50% lower than in South Africa, and that nickel compounds are classified as a human carcinogen. The success of the local extraction ventilation (LEV) systems is evident from the low percentage of personal OEL exceedances in the Nickel Tankhouse, however, high exposure can be prevented by implementing additional administrative controls (e.g. rotating shifts) to minimise cumulative exposure of the employees.

One of the developing control measures to prevent employees' high exposure, is to predict hypothetical exposure by using Bayesian methods associated with a process change, as described in the following section (Mulhasusen *et al.,* 2006).

### 4.2.5 Predictive modelling

**Recommendation 6:** The exposure matrix from this study can be used to predict future exposure in the tankhouses. Predictive modelling uses knowledge of the source of contaminant, control measures in place, exogenous factors (e.g. temperature, pressure, and humidity), activities performed and worker interactions (Mulhausen *et al.,* 2006b). Predictive modelling is based on the same principle of estimating past exposure for which no exposure data are available. For example, Bayesian methods to estimate past exposures were applied to estimate past exposures for employees in a nickel smelter (Ramachandran, 2001). Bayesian methods can, therefore, be used to extrapolate known exposure to predict future exposures when certain conditions (e.g. in the tankhouses) prevail (Mulhausen *et al.,* 2006b). When the exposure matrix is linked to process changes and control measures, it provides a framework of exposures during certain circumstances. This can be used to predict hypothetical exposure during process changes. For instance, a multiplication factor (e.g. four-fold increase in exposure) can be calculated for the effect of the introduction of more nickel solution on exposure in the Nickel Tankhouse, and be used to predict exposures in a similar circumstance. The necessary control measures can then be prearranged and be in place before the process change takes place.

## 4.3 Limitations of the study

### 4.3.1 Incomplete supplementary data

Retrospective studies often use exposure data which span over 20 years or more (Grimsrud *et al.,* 2000; Sivulka *et al.,* 2014). Unfortunately, apart from varying sampling methods which need to be taken into account in the retrospective analysis, supplementary data accompanying exposure data will also vary over time. Different sampling methods have a direct influence on the exposures measured and can be compensated for in some instances with correction factors. The amount and detail of supplementary data (e.g. sampling time, area sampled, work shift sampled etc.) will differ depending on the occupational hygienist responsible for the monitoring programme, legislative requirements and the monitoring programme implemented at the time (Smith *et al.,* 2005).

A retrospective study can only be conducted on supplementary data available and the supplementary data influences the categorisation of the historical exposure data. Incomplete supplementary data can be processed in two ways, firstly exposure without adequate supplementary data can be excluded from the analysis entirely (Glass *et al.,* 2000), or these exposures can be grouped as a separate category. In this study sections or occupations which were not explicitly reported were grouped into an unspecified category and processed as an independent category in the exposure matrix. As discussed in Section 4.2.3, incomplete supplementary data made it difficult to identify the cause of high exposure measured in the Contractor's tea room and for Supervisors in the Nickel Tankhouse. Supplementary data accompanying the exposure data may have explained the high exposure and identify the cause or source of contamination, which need to be eliminated or adequately controlled to an acceptable level.

### 4.3.2 Estimation of missing exposures

As with incomplete supplementary data, exposure data are not always available for all of the departments, occupations and time periods. Exposure data can be missing entirely for a category or only a few measurements may be available. Exposure is usually estimated when no data are available for a certain category and are either extrapolated or substituted with exposures from a similar category taking into account knowledge of previous processes and exposure circumstances (Van Tongeren *et al.*, 1998; Grimrud *et al.*, 2000; Sivulka *et al.*, 2014). Substituting missing exposures with exposures from similar categories is, however, a subjective task and an expert panel (e.g. Occupational Hygienist, Engineer, and Statistician) is needed to ensure that this is done correctly (Smith *et al.,* 2005).

In the present study neither of these methods were practicable and the limitations in exposures (e.g. sparse measurements for Supervisors) were reported as such.

### 4.3.3 Bias during the measurement of exposures

The monitoring programme implemented and legislative guidelines often determine that exposure be measured in worst-case scenarios, and consequently lead to biased mean exposure (Smith *et al.,* 2005). Supplementary data (if available) such as information on the prevailing conditions, tasks being performed and process information can be used to categorise and analyse these measurements accurately. The only worst case scenario identified in this retrospective analysis was when a higher volume nickel solution was introduced in the Nickel Tankhouse, and the accompanying high exposure was reported.

## 4.4 Future studies

This study constructed an exposure matrix based on soluble nickel exposure levels as measured inside the tankhouses of the BMR. This exposure matrix can in future be linked to medical records and job histories to conduct an epidemiological study. Specifically, cancer incidence ratios can be calculated for the employees in the tankhouses by linking the cumulative soluble nickel exposure data to the medical records of the employees. Medical records should, however, be available and detailed to be used in an epidemiological study.

If employees' job histories are considered, it is unlikely that one employee worked in one department only for his entire career. The expansion of the current retrospective analysis is necessary to include other departments from the base metal refinery where the employees may have worked. Job histories from the epidemiological study can be used as a guideline to determine which departments need to be included in the analysis, to give a complete exposure matrix of the employees.

Previous retrospective studies (Grimsrud *et al.,* 2000; Virji *et al.,* 2012) were conducted across different departments and exposure could be characterised to each department. As the carcinogenic effect of nickel is influenced by solubility (Oller *et al.,* 1997), a study characterising nickel compounds across the refinery is necessary. Exposure to a mixture of soluble and insoluble nickel has a significant influence on lung cancer risk and, therefore, complementary to the epidemiological study, characterising nickel exposure will complete a comprehensive dose-response relationship for the refinery employees.

A study testing the accuracy of the predictive modelling suggested in Section 4.2.5, is recommended by using the exposure matrix. Predictive modelling can be used to prearrange control measures to compensate for certain high exposure scenarios.

In this study a predictive model can be constructed to predict a hypothetical situation and assessed according to actual measurements taken in such a situation.

The retrospective assessment can be expanded to include data from more refineries. At least three refineries’ historical data can be presented in an exposure matrix and compared to each other. Similar process changes at the refineries can be used to calculate temporal factors on the exposure and, furthermore, calculate one uniform multiplication factor for a process change which can be applied to other refineries. Multiplication factors can be used in a predictive exposure model, as mentioned earlier.

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