



Association between respiratory exposure and urinary excretion of both soluble platinum and rhodium at a precious metals refinery

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DECLARATION

Contributions of the research team:

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Prof SJL Linde	Supervisor • Assisted with the planning and designing of the study. • Assisted with the ethics application. • Approving protocol and assisted with the interpretation of the results. • Extended support with the statistical analysis of the data and interpretation of the results. • Provided guidance and gave recommendations. • Provided supervision with the writing of the dissertation.
Prof A Franken	Co-supervisor • Assisted with the planning and designing of the study. • Approving protocol. • Assisted with the interpretation of the results. • Provided guidance and gave recommendations. • Provided co-supervision with the writing of the dissertation.

The following is a statement from the supervisors that confirms each individual's role in the study:

I declare that I have approved the article and that my role in the study as indicated above is representative of my actual contribution and that I hereby give my consent that it may be published as part of Stephanie Smit's dissertation



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Prof A Franken: Co-supervisor

PREFACE

The dissertation was written according to the specifications of the Manual for Higher Degrees Studies (2020) of the North-West University (NWU). The article in Chapter 3 was written using British spelling for publishing in the *International Journal of Hygiene and Environmental Health* and, for uniformity, the International Journal of Hygiene and Environmental Health reference style was applied throughout this dissertation for referencing the sources used in the study. The International Journal of Hygiene and Environmental Health suggest using the “List of Title Word Abbreviations” (<https://www.issn.org/services/online-services/access-to-the-ltwa/>) for journal abbreviations in the reference list .

The outline of the dissertation is as follows:

- Chapter 1: For the introductory purposes, this chapter contains background information, occupational exposure, legislation, problem statement, aims and objectives, and lastly the hypotheses.
- Chapter 2: Literature study on information relevant to this dissertation.
- Chapter 3: Contains a research article where the method and results are discussed.
- Chapter 4: The final chapter concludes on the key findings of this study, discusses the recommendations, limitations and future studies.
- Appendix A: Ethics approval letter.
- Appendix B: Proof of language editing.
- Appendix C: Turn-it-in report.

DISCLAIMER

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1 Tessalonisense 5:16-18

¹⁶Wees altyd vol blydskap. ¹⁷ Moenie ophou bid nie. ¹⁸Wees in alle omstandighede dankbaar, want dit is wat God van julle vewag omdat julle met Christus Jesus verenig is.

EXECUTIVE SUMMARY

Title: Association between respiratory exposure and urinary excretion of both soluble platinum and rhodium at a precious metals refinery

Background: In 2025, South Africa supplied more than 56% of the total worldwide platinum (Pt) and rhodium (Rh). During the refining of Pt and Rh, soluble Pt and Rh salts are formed as by-products of the extraction process. Metallic Pt and Rh have low toxicity; however, soluble Pt and Rh salts are especially sensitising. Soluble Rh is only a dermal sensitiser, whereas soluble Pt is both a dermal and a respiratory sensitiser. The primary route of exposure to soluble Pt and Rh is inhalation, with less exposure through the dermal and ingestion routes. The excretion of Pt and Rh via the urine has been reported to occur in refinery workers following exposure via various routes.

Aims and objectives:

This retrospective study aimed to evaluate the association between respiratory exposure and urinary excretion of workers exposed to soluble Pt and Rh at a precious metals refinery (PMR) in South Africa and to determine the optimal time for performing urinary biological monitoring. This was done by using retrospective data received from a PMR. The objectives of the study were to correlate workers' respiratory exposure to soluble Pt/Rh in the PMR to the concentration of urinary Pt/Rh measured in urine collected before and after their shifts. Additionally, to describe how workers' urinary Pt and Rh excretion fluctuated over the sampling period and to determine when the optimal time would be to collect urine samples for Pt or Rh exposure monitoring.

Method:

The retrospective data received from the PMR was collected in 2024 and included data for respiratory exposure to soluble Pt and Rh, urinary Pt and Rh concentrations, as well as creatinine concentrations for six refinery workers. Respiratory exposure was monitored during five consecutive shifts (Monday to Friday) and urine samples were collected pre- and post-shift during five consecutive shifts (Monday to Friday) with an additional pre-shift sample collected on Saturday morning. Three workers were anticipated to be primarily exposed to soluble Pt, and the other three were anticipated to be primarily exposed to soluble Rh. The respiratory exposure was monitored for both soluble Pt and Rh, and the urine samples were analysed for Pt, Rh, and creatinine for all six participants. All the data for the project were analysed and graphically represented using GraphPad Prism 10 (GraphPad® software). β -substitution was used to

substitute urine samples and respiratory results with results below the detection limit. The D'Agostino & Pearson test was used to test the distribution of the data. Pearson correlations were used to investigate the relationship between respiratory exposure and urinary Pt and Rh excretion, as well as the relationship between creatinine concentration in urine and urinary Pt and Rh concentrations. Paired t-tests were performed on the data to compare pre- and post-shift urinary Pt and Rh excretion results.

Results:

The exposure to soluble Pt ranged between 0.015 and 99.224 $\mu\text{g}/\text{m}^3$, and Rh exposure ranged between below detection limit (BDL) and 6.782 $\mu\text{g}/\text{m}^3$ via inhalation. However, only the participants who had relatively high respiratory exposure when compared to other participants who had lower respiratory Pt or Rh exposure, or performed high-exposure activities, had detectable levels of urinary Pt (range: BDL to 7.116 $\mu\text{g}/\text{g}$ creatinine) or Rh (range: BDL to 4.995 $\mu\text{g}/\text{g}$ creatinine). Three participants had detectable levels of urinary Pt, and two participants had detectable levels of urinary Rh. There was no significant correlation between respiratory exposure and excretion of the metal on an individual level; however, there was a significant relationship for the results on a group level, including all six participants, for Pt ($r = 0.487$; $p = 0.006$) and for Rh ($r = 0.691$; $p < 0.0001$). Additionally, there was no significant difference between pre- and post-shift urinary metal excretion and no clear indication if pre- or post-shift samples best represented exposure via inhalation.

Discussion and conclusions:

Even though the method used to analyse urinary Pt and Rh had a high limit of detection (LOD) compared to other studies in literature, participants with higher Pt or Rh body burden could be identified. Three participants had detectable levels of urinary Pt, and two participants had detectable levels of urinary Rh. The urinary Pt and Rh excretion of workers could be linked to their respiratory exposure, work activities and years of employment in the specific area (accumulation in body burden of Pt and Rh). One participant anticipated to be mainly exposed to soluble Rh, was one of the three participants with detectable levels of urinary Pt excretion; however, none of the participants mainly exposed to Pt had detectable levels of urinary Rh excretion. Although there was a significant positive correlation for all six participants between both soluble Pt and Rh exposure and both pre- and post-shift Pt and Rh concentrations for the group-level analysis, the individual-level comparisons did not show a significant correlation on the day-to-day results. Therefore, individually, there was no significant relationship between respiratory exposure and urinary excretion of Pt and Rh. Furthermore, there was no consistent pattern of

excretion for Pt or Rh and therefore, the specific days of peak exposure or the optimal time of sampling could not be determined using the results for urinary Pt or Rh.

Recommendations:

This analytical method used to analyse urinary Pt and Rh excretion is not a commercial method used by a pathology laboratory, but a method reported in literature by Crespo-Alonso *et al.* (2015) (“A simple, sensitive analytical method for platinum trace determination in human urine”) using ICP-MS. This method required dilution of urine samples which resulted in the high LOD for Pt and Rh. Therefore, the method for analysing urinary Pt and Rh needs to be improved for possible future use by the refinery, or another laboratory reporting lower LOD should be used. The use of a personal direct reading optical particle counter could assist future studies in the identification of the exact time of peak respiratory exposure, which could be used to explain the variation in pre- and post-shift urinary excretion concentrations. The optimal time to conduct biological monitoring of refinery workers for Pt and Rh could be more accurately identified if the exact time of peak exposure can be identified.

Word count: 1021 words

Keywords: Soluble platinum, soluble rhodium, platinum group metals, urinary platinum, urinary rhodium, biological monitoring, MDHS 46/2.

LIST OF UNITS

$\mu\text{g}/\text{m}^3$	microgram per cubic metre
ng/L	nanogram per litre
$\mu\text{g}/\text{g}$ creatinine	microgram per gram of creatinine
$\mu\text{g Pt}/\text{g}$ creatinine	microgram of platinum per gram of creatinine
$\mu\text{g Rh}/\text{g}$ creatinine	microgram of rhodium per gram of creatinine
$\mu\text{g Pt}/\text{cm}^2$	microgram of platinum per centimetre squared
μm	micrometre
g/L	grams per litre
L/min	litre per minute
m^2	square metre
mg/m^3	milligram per cubic metre
mL	millilitre
mmol/L	millimoles per litre
ng/g	nanogram per gram
nm	nanometre

LIST OF ABBREVIATIONS

$\leq$	less than or equal to
$<$	less than
BDL	below detection limit
CI	confidence interval
Co	cobalt
CV	coefficient of variation
DNA	deoxyribonucleic acid
DSEN	dermal sensitisation
Eds.	editors
<i>et al.</i>	<i>et alii</i> (and others)
GM	geometric mean
HCA	hazardous chemical agent
HCl	hydrochloric acid
HESCom	Health and Environmental Science Committee
HNO ₃	nitric acid
HR-ICP-MS	high resolution inductively coupled plasma-mass spectrometry
ICP-MS	inductively coupled plasma-mass spectrometry
IDMS	isotope dilution mass spectrometry
IFCC	International Federation of Clinical Chemistry and laboratory medicine
Ig	immunoglobulin
IOM	Institute of Occupational Medicine

LIST OF ABBREVIATIONS (CONTINUED)

IPA	International Platinum Group Metals Association
Ir	iridium
K ₂ PtCl ₄	potassium tetrachloroplatinate
K ₂ PtCl ₆	potassium hexachloroplatinate
Kg	kilogram
LOD	limit of detection
MCE	mixed cellulose ester
MDHS	Methods for the Determination of Hazardous Substances
Na ₂ PtCl ₄ ·6H ₂ O	sodium tetrachloroplatinate
Na ₂ PtCl ₆ ·6H ₂ O	sodium hexachloroplatinate
Na ₃ RhCl ₆ ·12H ₂ O	sodium Rh chloride
NaHSO ₄	sodium bisulphate
(NH ₄) ₂ PtCl ₆	ammonium hexachloroplatinate
(NH ₄) ₂ PtCl ₄	ammonium tetrachloroplatinate
NH ₄	ammonium
Ni	nickel
OEL	occupational exposure limit
OEL-RL	occupational exposure limit-restricted limit
OHS Act	Occupational Health and Safety Act 85 of 1993
Os	osmium
Pb	lead

LIST OF ABBREVIATIONS (CONTINUED)

Pd	palladium
PGM	platinum group metal
PMR	precious metals refinery
PPE	personal protective equipment
Pt	platinum
Rh	rhodium
RHCA	Regulations for Hazardous Chemical Agents
RhCl ₃	Rhodium(III) Chloride
RNA	ribonucleic acid
RSEN	respiratory sensitisation
Ru	ruthenium
SANAS	South African National Accreditation System
STEL	short-term exposure limit
TWA	time-weighted average
US CDC	United States Centers for Disease Control

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CHAPTER 1: INTRODUCTION

1.1 Introduction

The six metals that form part of the platinum group metals (PGMs) are platinum (Pt), rhodium (Rh), palladium (Pd), iridium (Ir), ruthenium (Ru) and osmium (Os). Along with the other four PGMs, Pt and Rh form part of the ever-evolving world of technology, with catalytic converters being one of their main uses (Iavicoli and Leso, 2022; Rao and Reddi, 2000; Santonen *et al.*, 2022). South Africa is one of the world's major suppliers of PGMs. In 2025, South Africa supplied more than 56% of the total worldwide Pt contribution, with an estimated Pt supply of 121.3 tonnes compared to the total global supply of 215.4 tonnes. Most of the Pt demand stems from automotive, jewellery and chemical industries (Johnson Matthey, 2025). In 2025, South Africa supplied more than 56% of the total worldwide Rh contribution, consisting of an estimated Rh supply of 17.4 tonnes compared to the total global supply of 30.9 tonnes. The Rh demands are mainly from the automotive industry, and smaller demands from other industries such as the chemical industry (Johnson Matthey, 2025).

Platinum and Rh are found in mined ore together with base metals such as cobalt, copper, iron and nickel, other precious metals such as gold and silver, and the remaining PGMs, Pd, Ir, Ru and Os. After the ore has been mined, smelted, and concentrated, the PGM-containing material firstly undergoes a separation process where the base metals are extracted and separated from the precious metals (Crundwell, 2011; Seymour and O'Farrelly, 2012). Thereafter, the precious metals are removed by either conventional precipitation or solvent extraction processes for refining (Seymour and O'Farrelly, 2012). The refinery involved in this retrospective study relies primarily on the conventional precipitation process to refine the PGMs.

Conventional precipitation is a process involving precipitation techniques and several dissolution stages. Firstly, aqua regia, which is a combination of concentrated hydrochloric and nitric acid, is added to the PGM-containing concentrate to dissolve Pt and Pd from the mixture, separating the rest of the PGMs as a residue. Secondly, ammonium chloride is added to the Pt and Pd mixture to extract the Pt in the form of ammonium hexachloroplatinate $[(\text{NH}_4)_2\text{PtCl}_6]$ precipitate. Glove boxes and filter presses are used to recover the $(\text{NH}_4)_2\text{PtCl}_6$ precipitate, which is then transported to the furnaces where calcination of the precipitate occurs. It is during these processes where employees are at an increased risk of soluble Pt exposure, as they are required to handle the salt form of the $(\text{NH}_4)_2\text{PtCl}_6$ precipitate by removing it from the glove boxes and filter presses. The

solvent extraction process has a higher separation efficiency than the conventional precipitation process. Therefore, the conventional precipitation process requires repetition of filtration and washing processes (Seymour and O'Farrelly, 2012).

The diagram provided by Seymour and O'Farrelly (2012) (Figure 1-1) summarises the refining process for base metals as well as precious metals using conventional precipitation. Marked with red crosses on Figure 1-1 is where exposure to soluble Pt and Rh is expected (Seymour and O'Farrelly, 2012). Exposure to soluble Pt or Rh may induce a sensitising reaction, leading to symptoms such as coughing, wheezing, shortness of breath (Santonen *et al.*, 2022), urticaria and less commonly contact dermatitis (Santucci *et al.*, 2000; Cristaudo *et al.*, 2007). Metallic Pt and Rh are considered to be a lower risk to employees' health, as they are inert and unlikely to cause a sensitising reaction after respiratory or dermal exposure (Iavicoli *et al.*, 2007).

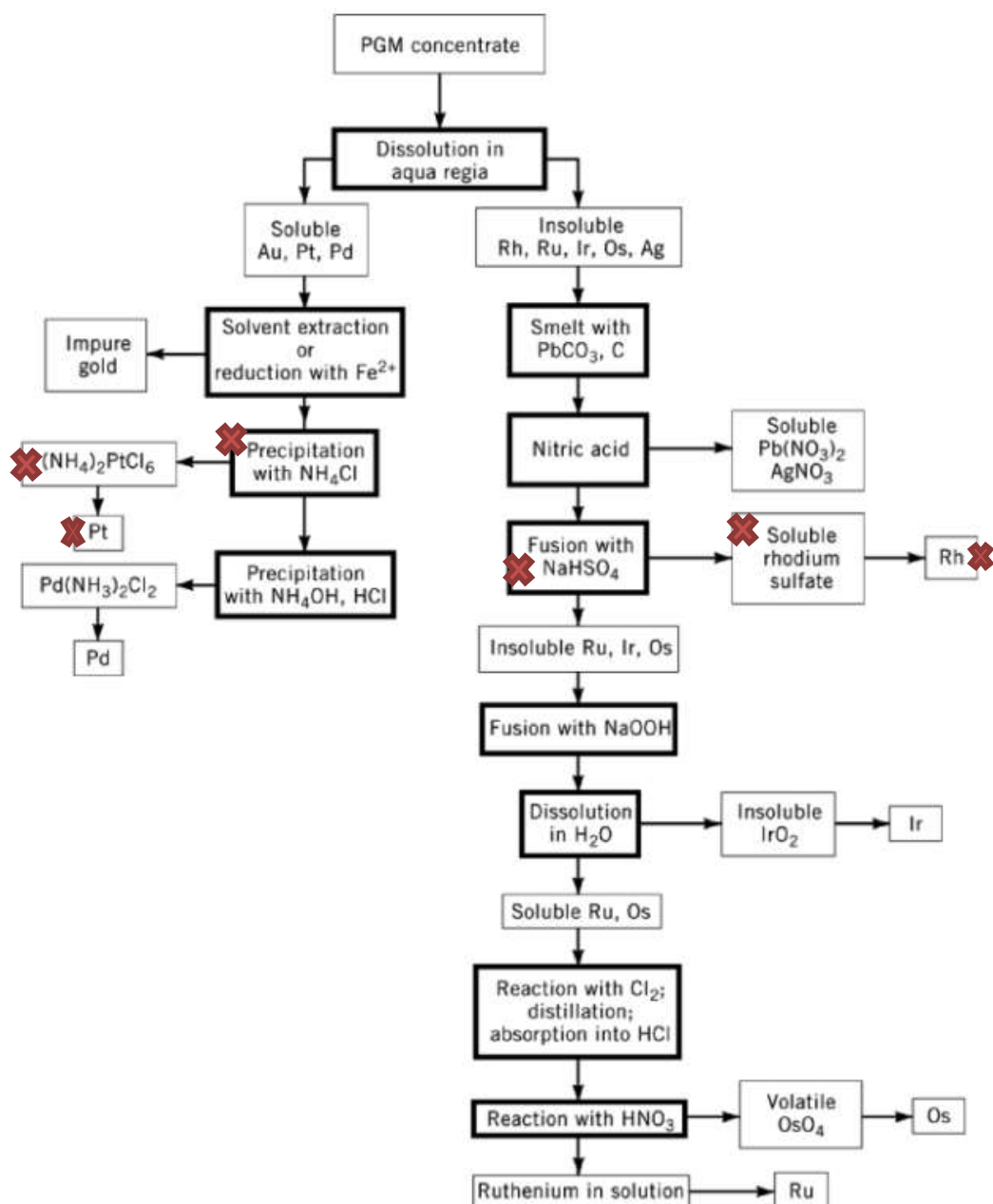


Figure 1-1: Process of refining Pt and Rh (Seymour and O'Farrelly, 2012). Red crosses represent areas in the process where exposure to soluble Pt and Rh is expected.

1.2 Human health effects

Respiratory exposure to soluble Pt leads to symptoms such as dyspnoea (shortness of breath), wheezing (tightening of the bronchial tubes), coughing, and allergic asthma (narrowing of the airway) (Santonen *et al.*, 2022). Furthermore, exposure to soluble Pt has been shown to cause irritation of the nasal cavity, sensitisation or irritation of the skin, including urticaria, cyanosis, lymphocytosis, rhinitis and, less frequently, type 4 delayed sensitisation response leading to contact dermatitis (Santucci *et al.*, 2000; Santonen *et al.*, 2022).

Metallic Pt is not considered a respiratory sensitiser (Maynard *et al.*, 1997) as it is regarded as biologically inert and hypoallergenic (Iavicoli *et al.*, 2007). Conversely, soluble Pt is a well-known type 1 respiratory sensitiser that triggers the production of specific Immunoglobulin (Ig) E antibodies. Employees who are atopic (sensitive to allergens) or who are smokers are far more likely to develop a hypersensitivity to Pt. The sensitisation is primarily linked to respiratory exposure, with respiratory symptoms improving or subsiding approximately an hour after the worker has been removed from the area of exposure (Santonen *et al.*, 2022). Nevertheless, soluble Pt sensitisation has major implications for employees. After an employee has been sensitised to soluble Pt, they could still experience symptoms like asthma years after they have been moved to a job with little to no exposure to soluble Pt (Merget *et al.*, 2017).

Limited information is available regarding human health effects when exposed to soluble Rh. Soluble Rh is a dermal sensitiser and therefore could cause allergic contact dermatitis when dermal exposure takes place (Goossens *et al.*, 2011; Department of Employment and Labour, 2021). In addition, studies have shown that soluble Rh has the potential to be a respiratory sensitiser in occupational settings such as a refinery and a goldsmith. Studies also reported allergic reactions such as respiratory symptoms, or dermal symptoms such as urticaria, and contact dermatitis in workers exposed to soluble Rh (Bedello *et al.*, 1987; De La Cuadra and Grau–Massanéés, 1991; Santucci *et al.*, 2000; Goossens *et al.*, 2011). Rhodium metal or Rh-plated metal is allergenically safe, as the metallic form is considered to be inert and unable to elicit any physiological reaction in the body (Iavicoli *et al.*, 2007).

1.3 Occupational exposure

1.3.1 Inhalation

Respiratory exposure to soluble Pt and Rh could potentially occur in several areas in the refinery. The highest exposure will possibly occur in areas where workers are directly exposed to soluble Pt and Rh during the handling of the concentrate or PGM salts. These areas include actions such as material handling, PGM separation, crushing and ignition, and handling of precious metals. Other areas in the refinery also hold a possibility for soluble Pt and Rh exposure; however, exposure will likely be significantly lower. These areas include other production and non-production activities, security and the health clinic area (Linde *et al.*, 2018).

1.3.2 Skin permeability

The skin is the largest organ in the human body, and, for the most part, the skin acts as a barrier to foreign organisms it encounters. The skin consists of two layers, namely: the epidermis (outer

layer) and the dermis (layer beneath the epidermis). The stratum corneum is the top layer of the epidermis and consists of four to five layers, depending on the area of the body. The stratum corneum is responsible for the prevention of fluid loss and acts as a barrier preventing absorption of foreign organisms and contaminants into the body. The dermis has a network of blood vessels supplying both the epidermis and dermis with blood flow. Foreign contaminants can penetrate the body not only through the epidermis but also penetrate the skin through hair follicles, sweat glands and sebaceous glands (Lehman–McKeeman, 2015).

Franken *et al.* (2014) and Jansen Van Rensburg *et al.* (2017) conducted studies that found that soluble Pt and Rh can permeate through intact human skin. Their research showed that soluble Pt and Rh not only permeate through the intact skin but are also retained inside the layers of the skin, causing the formation of a reservoir (Franken *et al.*, 2015a). Franken *et al.* (2015b) showed the permeation of soluble Pt through African and Caucasian skin. Jansen Van Rensburg *et al.* (2017) investigated the permeation of soluble Rh and how different pH levels affect the ability of soluble Rh to permeate the skin. Soluble Rh was able to permeate the skin at both pH 4.5 and pH 6.5. It is expected that the skin surface pH of refinery workers is lower than pH 6.5 (Jansen Van Rensburg *et al.*, 2017).

1.3.3 Excretion of Pt or Rh after occupational exposure

According to Schierl *et al.* (1998), maximum urinary Pt excretion happens 10 hours after soluble Pt inhalation exposure. Excretion of Pt in the urine occurs over two phases, the first half-life at 50 hours with a 95% confidence interval (CI) of 36 to 66 hours, and the second half-life was 24 days with a 95% CI of 18 to 33 days. Urine samples taken after employees were away on holiday for two weeks reported no decrease in urinary Pt excretion. Additionally, employees who had not been occupationally exposed to soluble Pt for two to six years still had 25-fold higher urinary Pt excretion compared to the control group. This could be an indication that Pt has slow excretion kinetics (Schierl *et al.*, 1998). There are currently no studies reporting on the half-life of soluble Rh after exposure has occurred in humans. Czerczak *et al.* (2012) conducted a study on rats, administering Rh chloride (RhCl_3) in the rats' drinking water, where urinary Rh excretion happened over two phases. During the first phase of urinary Rh excretion, 45% of the absorbed RhCl_3 dose was excreted via the urine in the first 24 hours following exposure, and during the second phase, a decrease in urinary Rh excretion was observed. Rhodium chloride has been found to be absorbed in the gastrointestinal tract and excreted via the faeces.

1.4 Legislation

The health and safety procedures at the refinery to be investigated are regulated by the Occupational Health and Safety Act 85 of 1993 (OHS Act) and its Regulations. Hazardous chemical agents (HCA) with an occupational exposure limit-restricted limit (OEL-RL) can be found in Annexure 2, Table 3 of the Regulations for Hazardous Chemical Agents (RHCA) of 2021 (Department of Employment and Labour, 2021). Hazardous chemical agents listed as OEL-RL are possibly non-carcinogenic according to current knowledge and would possibly not cause harm if exposure to the substances is kept below the OEL-RL. Therefore, respiratory exposure below the OEL-RL will deem control measures to be adequate. Soluble Pt has a respiratory OEL-RL of 0.002 mg/m^3 ($2 \text{ }\mu\text{g/m}^3$) and has the potential to cause dermal sensitisation (DSEN) and respiratory sensitisation (RSEN), as indicated by the notations. Soluble Rh has an OEL-RL of 0.02 mg/m^3 ($20 \text{ }\mu\text{g/m}^3$) and has the potential to cause dermal sensitisation as indicated by the notation (Department of Employment and Labour, 2021). Sensitisation could occur when exposed to low levels of soluble Pt and Rh, even at exposure levels below their respective OEL-RL limits and can potentially cause adverse health effects (Merget *et al.*, 2017). Therefore, exposure to soluble Pt and Rh should be kept as low as reasonably practicable.

1.5 Retrospective exposure data analysis

Often, workplaces such as a refinery do not have the capacity, time or resources to do comprehensive data analyses and these studies are often performed by researchers not employed by the company. Retrospective studies may offer valuable information following the analysis of complex exposure results. Extensive analysis of data can be done by using pre-existing information supplied by the workplace, which needs to include, at the very least, monitoring data, personal information of each participant and monitoring results. A retrospective study is non-interventional, as it collects information from past studies, including information regarding previous patients or employees (Powell and Sweeting, 2015; de Sanctis *et al.*, 2022). There are four important purposes of a retrospective study; namely, (1) to compare present or future practice with historical data, (2) to investigate a proposed hypothesis about possible risk factors in connection with a particular outcome, (3) to establish the sample population size and information needed for a proposed study, and (4) to explore uncommon events (Powell and Sweeting, 2015). A retrospective study could assist future researchers in finding the best methodology and prevent mistakes made by previous studies (Riley, 2014).

1.6 Problem statement

Precious metals refinery workers are exposed daily to soluble Pt and Rh. After sensitisation has occurred and workers are removed from the refinery, the risk of developing adverse health effects such as chronic asthma later in life, are not eliminated (Merget *et al.*, 2017). The Department of Employment and Labour (2021) requires that, where employees are exposed to HCAs such as soluble Pt and Rh, personal air monitoring should be conducted at least every 24 months. In addition to this requirement, the refinery under study collects urine samples as per its medical surveillance programme. According to the International Platinum Group Metals Association's (IPA) Health and Environmental Science Committee (HESCom), there is still uncertainty regarding the monitoring of urinary excretion levels of PGMs and the interpretation of those results. For example, when should urine samples be collected and how should the results be interpreted? (IPA, 2022). To help answer this question, the refinery involved in this study organised and performed the air monitoring and biomonitoring of the six refinery workers. However, the refinery lacked the capacity to carry out comprehensive data analyses, which resulted in this study performing a thorough analysis of the retrospective data to determine how the urinary excretion results can be used to evaluate exposure to Pt and Rh exposure in the workplace.

1.7 Aim and objectives

1.7.1 Aim

The retrospective study aimed to evaluate the association between respiratory exposure and urinary excretion of workers exposed to soluble Pt and Rh at a PMR in South Africa and to determine the optimal time for performing urinary biological monitoring. This was done using retrospective data received from a PMR, where respiratory exposure and urine samples were collected during five consecutive shifts for six workers. Three workers were anticipated to be primarily exposed to soluble Pt, and the other three were anticipated to be primarily exposed to soluble Rh. The urine of all six workers was analysed for both Pt and Rh, as well as creatinine.

1.7.2 Objectives

The objectives of the study were to:

1. Correlate PMR workers' respiratory exposure to soluble Pt to the concentration of urinary Pt obtained from urine collected before and after their shift.
2. Correlate PMR workers' respiratory exposure to soluble Rh to the concentration of urinary Rh

obtained from urine collected before and after their shift.

3. Describe how workers' urinary Pt and Rh excretion fluctuated over the sampling period.
4. Determine the optimal time to collect urine samples for Pt or Rh exposure monitoring.

1.8 Hypotheses

1. Based on the research of Linde *et al.* (2018), employees at a PMR, who were directly exposed to soluble Pt, had higher urinary Pt excretion compared to employees who were indirectly exposed. A positive correlation was found between the workers' urinary Pt excretion and their respiratory exposure.
 - a. It is therefore hypothesised that the retrospective data from the PMR will show a statistically significant positive correlation between respiratory exposure and urinary excretion for Pt.
 - b. It is therefore hypothesised that the retrospective data from the PMR will show a statistically significant positive correlation between respiratory exposure and urinary excretion for Rh.
2. According to Schierl *et al.* (1998), the maximum urinary Pt excretion occurs 10 hours after exposure, with the first half-life being 50 hours and the second half-life 24 days. Based on the data from Schierl *et al.* (1998), Linde *et al.* (2018) collected urine samples in the morning after exposure occurred and reported a low degree of variability of Pt in urine samples collected over three consecutive mornings. This was concluded to be likely due to the frequent exposure experienced by workers and the long half-life of the metal.
 - a. It is therefore hypothesised that the optimal time to take urine samples will be in the morning before their shift, following exposure to soluble Pt the previous day. Morning urine samples are expected to be the most concentrated and therefore provide the most accurate measure of Pt exposure.
 - b. No information is available reporting on the urinary Rh excretion of PMR workers. However, PGMs are similar in physical properties. Therefore, it is hypothesised that the optimal time to take urine samples will be in the morning before their shift, following exposure to soluble Rh the previous day. Morning urine samples are expected to be the most concentrated and therefore provide the most accurate measure of Rh exposure.

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CHAPTER 2: LITERATURE REVIEW

This literature study will focus on available scientific literature that reports exposure of refinery workers to platinum (Pt) and rhodium (Rh) through inhalation, and how the Pt and Rh are excreted through urine. Information about Pt and Rh will be discussed, such as: physical and chemical characteristics, how the metals are mined and refined, exposure routes, adverse health effects when exposed to soluble Pt and Rh, and the biomonitoring of Pt and Rh. Limited information is available on respiratory and dermal exposure to Rh in an occupational setting, such as refineries and the excretion thereof.

2.1 Physical and chemical characteristics

Palladium (Pd), ruthenium (Ru), osmium (Os), iridium (Ir), Pt and Rh are the six recyclable silvery white metals in the platinum group metals (PGMs) (IPA, 2022a). In the 15th century, the Spanish Conquistadors were panning for gold and found plenty of a metal which they called “platina”. Later in the 1800s, metallic Pt was successfully melted when a Swedish researcher made a breakthrough by adding oxygen to the melting process (Minerals Council South Africa, 2023). Rhodium was discovered by William Hyde Wollaston between 1803 and 1804 after he extracted Pt and Pd from a Pt ore acquired from South America. After extracting the Pt and Pd from the Pt ore, there was a dark red powder residue. The dark red powder was sodium Rh chloride ($\text{Na}_3\text{RhCl}_6 \cdot 12\text{H}_2\text{O}$) (Iavicoli and Leso, 2022; National Center for Biotechnology Information, 2025). The discovery of PGMs in South Africa’s Bushveld took place in 1924 when Mr Andries Lombaard was panning in a dry riverbed on the farm Maandagshoek and found grey-white metallic granules which Hans Merensky (geologist) confirmed to be Pt (Sibanye Stilwater, 2025).

Platinum group metals are highly durable and have great catalytic qualities; they are resistant to tarnish and chemical exposure (IPA, 2022a). Rhodium and Ir are less likely to corrode due to chemical exposure, in contrast to Pt, Pd, Ru and Os. The primary use for Pt and Rh is in catalytic converters (autocatalysts). Platinum and Rh have a unique key application in the electrical, jewellery, chemical and other industries (Iavicoli and Leso, 2022; Santonen *et al.*, 2022). Rhodium is primarily used as an alloying element to Pt and Pd to enhance their hardness. The newly formed alloys have high resistance to corrosion and display good conductivity at the point of contact. Therefore, the alloys are used in electric laboratory furnaces, a container for high temperature gas, and for welding space technology electrodes (Rinkovec, 2019). Oxidative forms of Pt are +1, +5, and +6, but the main oxidative states are +2 and +4 (Santonen *et al.*, 2022). Chloroplatinates are Pt salts that contain halogens, and examples include ammonium tetrachloroplatinate

$[(\text{NH}_4)_2\text{PtCl}_4]$, ammonium hexachloroplatinate $[(\text{NH}_4)_2\text{PtCl}_6]$, potassium tetrachloroplatinate $(\text{K}_2\text{PtCl}_4)$, potassium hexachloroplatinate $(\text{K}_2\text{PtCl}_6)$, sodium tetrachloroplatinate $(\text{Na}_2\text{PtCl}_4 \cdot 6\text{H}_2\text{O})$ and sodium hexachloroplatinate $(\text{Na}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O})$. Oxidative forms of Rh are +0 to +6, but the main oxidative state is +3 (Iavicoli and Leso, 2022). Rhodium chloride (RhCl_3) and chlorotris(triphenylphosphine)Rh(I) ($\text{RhCl}[\text{P}(\text{C}_6\text{H}_5)_3]_3$) are outstanding catalysts (Michalke *et al.*, 2024).

2.2 Mining and refining of PGMs

Rhodium and Pt are mined in the following locations, in descending order of quantity: South Africa, Russia, Zimbabwe, North America and others. South Africa is currently abundant in reserves for PGMs, while in Russia and Canada, Pt is a by-product of their nickel and copper mining processes, and in North America, Pt is a by-product of their Pd mining process (Johnson Matthey, 2023).

There are two processes which could be followed for refining PGMs. These two processes are conventional refining and solvent extraction. The flaw of conventional refining is that there is not a 100% separation of metals during the dissolution and reprecipitation processes, and conventional refining can be a long and labour-intensive process. The metal being filtered can become trapped when coprecipitation occurs. Solvent extraction refining could be quite expensive; however, this process is quicker and more efficient in extracting metals (Seymour and O'Farrelly, 2012). The refinery involved in this study uses a precipitation process to refine PGMs from the concentrated material.

Conventional refining of PGMs involves acid treatment, precipitation, and dissolution in inorganic (acids and oxidants) and organic additives (Petrucci *et al.*, 2005). The concentrate received from the base metal's refinery is combined with aqua regia (Seymour and O'Farrelly, 2012). Aqua regia is a solution containing concentrated hydrochloric acid (HCl) and nitric acid (HNO_3) with a volume ratio of 3:1 (Ding *et al.*, 2022). The aqua regia dissolves Pt, Pd and gold from the concentrate. Gold is extracted by using the method of solvent extraction or by using ferrous salts to reduce it to metallic gold. The rest of the solution is treated with an ammonium (NH_4) salt of HCl (ammonium chloride) to precipitate ammonium hexachloroplatinate (IV) $[(\text{NH}_4)_2\text{PtCl}_6]$ (Seymour and O'Farrelly, 2012). The precipitate $(\text{NH}_4)_2\text{PtCl}_6$ powder is calcinated into Pt sponge (99.99% pure Pt) (Petrucci *et al.*, 2005; Seymour and O'Farrelly, 2012). The Pt sponge then undergoes extended purification. The remainder of the insoluble metals from the aqua regia process is left as a residue. The residue is merged with sodium bisulphate (NaHSO_4), to form

soluble Rh sulphate. Rhodium sulphate undergoes several stages of dissolution and recrystallisation to form pure Rh (Semour and O'Farrelly, 2012).

The solvent extraction process involves the PGM concentration going through dissolution, solvent extraction, neutralisation, distillation and reduction processes. Tri-*n*-octylamine is used as a solvent extractant, and HCl and ammonium chloride (NH₄Cl) are used to strip Pt from the PGM concentrate. Furthermore, oxidation and solvent extraction are done before ion exchange can happen to produce Rh (Semour and O'Farrelly, 2012).

2.3 Occupational exposure

In the mining industry, workers are exposed to metallic PGMs, and refinery workers are additionally exposed to soluble PGMs during the process of refining (Maynard *et al.*, 1997; Goossens *et al.*, 2011). In the refinery, exposure to soluble Pt and Rh can occur by inhalation (Heederik *et al.*, 2016) or dermal exposure (Linde *et al.*, 2018). Respiratory Pt exposure has been monitored in several studies (Fothergill *et al.*, 1945; Hunter *et al.*, 1945; Johnson *et al.*, 1976; Baker *et al.*, 1990; Calverley *et al.*, 1995; Maynard *et al.*, 1997; Merget *et al.*, 2000; Petrucci *et al.*, 2005; Cristaudo *et al.*, 2007; Heederik *et al.*, 2016; Linde *et al.*, 2017; Linde *et al.*, 2018; Linde *et al.*, 2021; Smit *et al.*, 2023; Smit *et al.*, 2025). Compared to soluble Pt, respiratory exposure to soluble Rh has been the topic of fewer studies (Petrucci *et al.*, 2004; Cristaudo *et al.*, 2007; Linde *et al.*, 2021). The consequence of dermal exposure for workers exposed to PGMs will likely result in the permeation of Pt and Rh through the skin (Franken *et al.*, 2014).

The legislation does not list skin notations [stating that hazardous chemical agents (HCA) can penetrate through intact skin and thus become absorbed into the body (Department of Employment and Labour, 2021)] for either soluble Pt or Rh. Additionally, these HCAs are not included in Annexure 2, Table 4 of the Regulations for Hazardous Chemical Agents (RHCA) of 2021, which contains the information for biological exposure indices for HCAs. However, the study conducted by Linde *et al.* (2018) found that exposure to soluble Pt takes place via both the respiratory and skin exposure routes and that urinary excretion of Pt can be used as a tool to assess total Pt body burden. Furthermore, according to the results from Franken *et al.* (2014, 2015) and Jansen Van Rensburg *et al.* (2017), both soluble Pt and Rh can permeate healthy intact skin. The permeation of soluble Pt and Rh through the skin can, therefore, increase the total body burden of these HCAs and could increase the risk of sensitising reactions for employees who are sensitive toward PGM salts.

2.4 Adverse health effects of Pt and Rh salts

Platinum toxicity and health effects depend on the solubility of the Pt compound (Kiilunen *et al.*, 2015). There is a definitive exposure-response to Pt salt and related sensitisation for workers at Pt recycling and refining industries (Heederik *et al.*, 2016). Platinum salts such as chloroplatinates can cause irritation to the skin and eyes, and are more toxic than Pt oxides (Kiilunen *et al.*, 2015). Pt is a respiratory sensitiser and exposure to Pt could lead to irritation and inflammation of the respiratory tract, resulting in symptoms that include dyspnoea, wheezing, coughing and allergic asthma (Santonen *et al.*, 2022). Limited information is available on adverse human health effects following exposure to Rh. However, Merget *et al.* (2010) found the operator at an electroplating plant to have a higher sensitivity (respiratory and dermal) to Rh exposure in comparison to Pt exposure. The operator experienced symptoms such as rhinitis and asthma following Rh chloride exposure. Maynard *et al.* (1997) reported that workers had sensitisation reaction even with respiratory exposure below the occupational exposure limit (OEL); therefore, the sensitisation could have been due to low soluble Pt respiratory exposure, otherwise it could have been an alternative route of exposure such as dermal exposure, which was a possibility at each site leading to sensitisation reactions (Maynard *et al.*, 1997). Studies have concluded that the severity of sensitising reaction is directly associated with the frequency and duration of exposure. After removing workers from the source of soluble Pt and Rh exposure, sensitising symptoms should decrease (Heederik *et al.*, 2016; Merget *et al.*, 2017).

2.5 Exposure routes

2.5.1 Respiratory exposure

The respiratory system consists of the nasopharynx, pharynx, trachea, bronchus, bronchi, alveolar duct and alveoli. The alveoli are where gas exchange takes place with an effective surface of $\pm 70 \text{ m}^2$ (Schröder, 2014). Particles $\leq 10 \text{ }\mu\text{m}$ have a 50% possibility of depositing in the bronchioles after entering the respiratory system (Department of Employment and Labour, 2021). Particles larger than $6 \text{ }\mu\text{m}$ inhaled through the nasal passage will most likely not reach the lungs, due to the effective turbulence mechanisms of air being obstructed by the conchae, the septum and pharyngeal wall. Particulates between $1\text{--}5 \text{ }\mu\text{m}$ will most likely reach and deposit in the small bronchioles (thoracic fraction) due to gravitational precipitation. Particles $\leq 1 \text{ }\mu\text{m}$ will likely diffuse against the alveoli walls and stick to the alveolar fluid. Lastly, particles smaller than $0.5 \text{ }\mu\text{m}$ have a $\pm 33\%$ probability of precipitation against any of the sections in the respiratory system, therefore $\pm 67\%$ of the particles smaller than $0.5 \text{ }\mu\text{m}$ are removed via exhalation (Hall, 2016). Significant health risks are associated with the inhalation exposure of soluble Pt and Rh, commonly in the

respiratory tract (Heederik *et al.*, 2016). Inhalation is one of the main exposure routes of concern in comparison to exposure by ingestion when it comes to health risks associated with exposure to soluble Pt and Rh (Linde *et al.*, 2017). Respiratory exposure to soluble Pt in precious metals refineries (PMR) has been investigated since 1945 (Hunter *et al.*, 1945; Fothergill *et al.*, 1945). Linde *et al.* (2017) reviewed numerous studies reporting on respiratory soluble Pt exposure since 1945, which included information, amongst many, from Hunter *et al.* (1945) and Fothergill *et al.* (1945). The reported information used different techniques and is situated in different countries. From their investigation, the reported range of respiratory soluble Pt exposure was between 0.159 and 1700 $\mu\text{g}/\text{m}^3$.

In a study performed in two South African refineries, employees directly exposed to soluble Pt and Rh in South African refineries had job descriptions such as handling PGM concentrate, separating PGMs, handling PGM salts and maintenance, and experienced respiratory exposure to soluble Pt between 0.006 $\mu\text{g}/\text{m}^3$ and 73.270 $\mu\text{g}/\text{m}^3$, and respiratory exposure to soluble Rh of between 0.002 $\mu\text{g}/\text{m}^3$ and 24.060 $\mu\text{g}/\text{m}^3$. Other occupations at risk of indirect respiratory soluble Pt and Rh exposure were security, laundry and laboratory workers and were reported to experience respiratory exposure to soluble Pt between 0.002 $\mu\text{g}/\text{m}^3$ and 11.600 $\mu\text{g}/\text{m}^3$, and respiratory exposure to soluble Rh of between 0.002 $\mu\text{g}/\text{m}^3$ and 2.400 $\mu\text{g}/\text{m}^3$. Although the employees indirectly exposed to soluble Pt and Rh are significantly less at risk of respiratory and dermal sensitisation, the risk remains (Linde *et al.*, 2021).

2.5.1.1 Respiratory exposure sampling method

The sampling train attached to the employee consists of a filter cassette attached to a pump with tubing. The pump is pre- and post-calibrated to 2 L/min, not exceeding a difference of more than 5% between the pre- and post-calibration averages. The filter is marked with a unique identification number and is weighed before use, and after being used. The filter size and cassette depend on the method used for sampling. For this study, MDHS 46/2 was used. MDHS 46/2 recommends the use of an Institute of Occupational Medicine (IOM) sampler in an inhalable sampling head. The IOM contains a 25 mm mixed cellulose ester (MCE) filter. The pump is placed around the employee's waist by clipping it to the belt of the employee or using a harness to hold the pump, and the IOM is placed within the breathing zone of the employee (as close as possible to the nose and mouth). The sampling time will depend on the maximum volume prescribed by the method (IPA, 2016).

2.5.2 Dermal exposure

Dermal exposure was measured by using pre-moistened wipes to wipe anatomical areas which could be occupationally exposed to soluble Pt and Rh, such as the neck, palm, wrist and forehead (Linde *et al.*, 2021). Dermal exposure to Pt is possible for workers at a refinery (Maynard *et al.*, 1997). Linde *et al.* (2021) reported on the dermal exposure to soluble Pt and Rh of refinery employees, where the exposure could happen by direct or indirect exposure. Employees directly exposed to soluble Pt and Rh in a refinery, experienced dermal exposure to soluble Pt with a geometric mean (GM) of $0.014 \mu\text{g}/\text{cm}^2$ and to soluble Rh GM of $0.011 \mu\text{g}/\text{cm}^2$. Whereas occupations with indirect dermal exposure to soluble Pt and Rh, reported exposure to soluble Pt with a GM of $0.001 \mu\text{g}/\text{cm}^2$ and to soluble Rh GM of $0.001 \mu\text{g}/\text{cm}^2$. Considering the model proposed by Schneider *et al.* (1999) (Figure 2-1), dermal exposure can be a result of contamination directly onto the skin from the air, surface contaminant layer, as well as inner and outer clothing contaminant layer. The study conducted by Maynard *et al.* (1997) found that workers had Pt sensitisation symptoms although respiratory exposure to soluble Pt was below the OEL of $2 \mu\text{g}/\text{m}^3$, except for 2 sites where respiratory protection was utilised and exposure was below the short-term exposure limit (STEL) which is the OEL times three ($6 \mu\text{g}/\text{m}^3$); they subsequently concluded that dermal soluble Pt exposure could contribute to sensitisation.

The model proposed by Schneider *et al.* (1999) explains all the different scenarios of how dermal exposure could occur. The six compartments in Figure 2-1 are: the source of contamination, air, surface contaminant layer, outer clothing contaminant layer, inner clothing contaminant layer and lastly skin contaminant layer. The skin contaminant layer consists of any liquid such as natural skin oil, sweat, contaminants and if applied, barrier cream. The outer and inner clothing contaminant layer and skin contaminant layer are all affected by personal behaviour. Exposure through ingestion is a result of poor personal hygiene, especially if all the control measures are in place and personal protective equipment (PPE) is supplied to the worker. Any activity or process releasing soluble Pt and/or Rh is a source of contamination. While small, and large particles in the air could be inhaled by the worker, as discussed in section 2.3.1, larger particles will likely deposit on a surface where the worker can encounter the soluble Pt and Rh by touching the surface, or directly deposit onto the exposed skin contaminant layer. The mass transferred will depend on the actual contact, be it single pressure or movement along the surface of the skin. The outer and inner layers of clothing act as barriers between the skin and the soluble Pt and Rh on surfaces. Clothing can retain mass ($M_{\text{Reservoir}}$), therefore, the exposure inside clothing is the result of exposure outside clothing – $M_{\text{Reservoir}}$. Permeation is the diffusion of soluble Pt and Rh through clothing or the stratum corneum and penetration is the transport of soluble Pt and Rh

through clothing or the stratum corneum, as a result of external pressure, evaporation, condensation and capillary penetration. The concentration of soluble Pt and Rh is believed to be homogeneously distributed in the air compartment, the surface contaminant layer compartment and the skin contaminant layer. All things considered, the mass in the air, on the surface and on the skin contaminant layer can be assessed and identified.

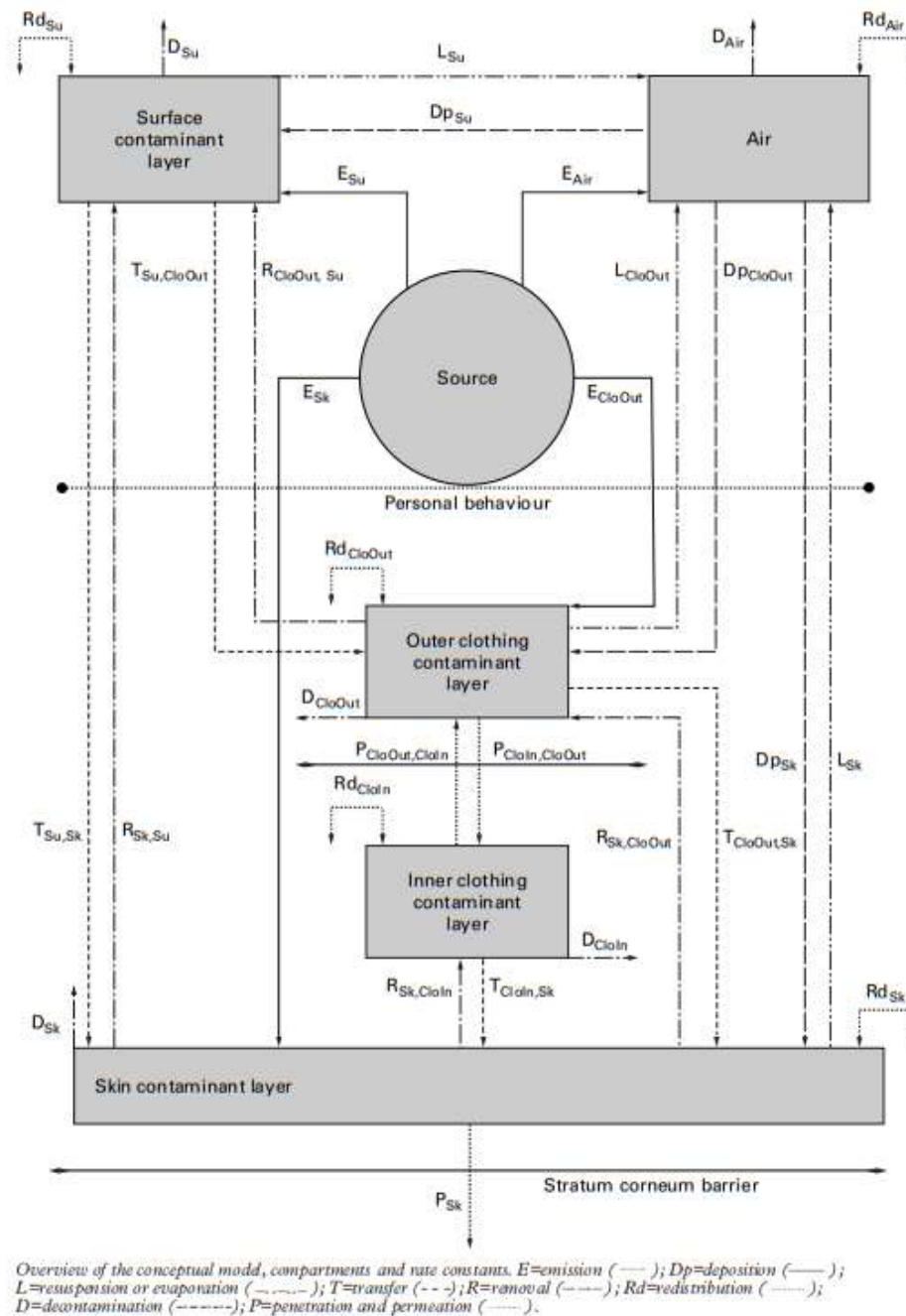


Figure 2-1: Skin exposure to contaminants through different compartments and cross-contamination (Schneider *et al.*, 1999).

Dermal exposure is sampled using wipes such as, Ghostwipes™. The wipes are individually sealed and pre-moistened with deionised water. The wipes are used to sample metal contents on skin surfaces. The initial wipe used to clean the anatomical area is discarded, and the employee is asked to continue with their routine; however, they should not be washing the anatomical area which was wiped. One wipe is used to wipe the surface for a total of four times, each time folding the wipe inward and following an S-motion changing the direction between wiping actions. The same method is used for each anatomical area that is wiped (du Plessis *et al.*, 2013; Linde *et al.*, 2018).

2.5.2.1 Permeation of Pt and Rh

In two separate studies done by Franken *et al.* (2014, 2015), the conclusion was made that both Pt and Rh permeated through intact Caucasian skin, and that Pt permeated through intact African skin (Rh not tested on African skin). The results indicated that African skin is more permeable to Pt exposure in comparison to Caucasian skin. However, both African and Caucasian skin had significantly higher permeation results at 24 hours compared to the 8-hour results. Although Pt and Rh particles had a relatively similar size (9.7 ± 0.7 nm for Pt and 9.6 ± 0.9 nm for Rh), their rate of permeation differed (Franken *et al.*, 2015). In conclusion, the urinary excretion of these metals are not solely due to inhalation exposure, but could also be from dermal exposure.

2.5.3 Ingestion exposure

Ingestion is a possible route of Pt and Rh exposure; however, it is of less significance compared to inhalation of particulates containing PGMs (Linde *et al.*, 2017). There is a lack of information regarding determinants of ingestion due to inadvertent occupational exposure (Gorman Ng *et al.*, 2017). Gorman Ng *et al.* (2017) conducted exposure monitoring in 2012 at different sites, which included a precious metals smelter, engine repair shop, engine fan casing coating area, sheet metal plating workshop and a steel plant. Perioral exposure was assessed using wipes as a substitute for inadvertent ingestion exposure, and eight metals were included in the analysis. Perioral wipe samples were collected before, during and after workers' shifts on both hands and the perioral area with moist patented wipes. The group as a whole had an average of 3.8 hand washes reported during their shift, with a standard deviation of 1.7 hand washes. At the precious metal's smelter, two job groups were included in the study: namely, smelting and precious metal content evaluation. The twelve workers included in this area had a soluble Pt exposure range of 0.001–0.248 $\mu\text{g}/\text{cm}^2$ on their right hand, and a soluble Pt exposure range of < 0.0006–0.191 $\mu\text{g}/\text{cm}^2$ on their left hand, and lastly soluble Pt exposure of < 0.008–0.235 $\mu\text{g}/\text{cm}^2$ on their perioral

area. Although Pt and Rh were not among the eight metals included in this study, there is evidence that ingestion is a possible route of exposure.

2.6 Biomonitoring

The two most important functions of the kidneys are, firstly, excretion of waste materials either produced or ingested, and secondly, to regulate the volume of fluid and electrolytes in the body to maintain an equilibrium. Homeostasis is important for the body's cells to achieve various activities, such as excretion of foreign chemicals like Pt and Rh. Waste materials are transported to the kidneys via the renal blood supply. The renal artery connects to the hilum inside the kidney, where it branches out into different arteries and arterioles and where filtration occurs (Hall, 2016).

Urinary excretion of Pt and Rh serves as a reliable biomarker for assessing exposure to these metals through the various exposure routes (Iavicoli *et al.*, 2007; Petrucci *et al.*, 2004). Biomonitoring exposure of urinary Pt has been reported in Germany, Italy, the United Kingdom and South Africa. However, urinary Rh has only been reported by studies in Italy. Occupations included in the studies for biomonitoring of Pt and Rh are streetcar operators (range = 0.22–27.61 ng Pt/g creatinine; range = 2.54–48.81 ng Rh/g creatinine) and waste-incineration plant workers (mean = 7.21 ng Pt/l; 20.26 ng Rh/l). Additionally, Pt biomonitoring included Pt-catalyst production (range = 16–6270 ng Pt/g creatinine) and recycling (range = 20–630 ng Pt/l), processing of Pt nozzles (range = 10–2900 ng Pt/l), hospital workers (range = <1.8–34.4 ng Pt/l), dental technicians (range = 0.8–167.8 ng Pt/l), road construction workers (range = 0.2–4.4 ng Pt/l), bus drivers (range = 1.0–40 ng Pt/l), TÜV testers (range = 0.5–21.0 ng Pt/l), motorway-maintenance workers (range = <0.1–6.6 ng Pt/g creatinine), taxi drivers (range = 1.0–28 ng Pt/l) and PMR workers (range = 23–9200 ng Pt/l) which was the highest exposed occupation (Michalke *et al.*, 2024). Refinery workers have reported allergic responses of the skin and airways due to occupational exposure to soluble Pt (Hunter *et al.*, 1945; Baker *et al.*, 1990; Calverley *et al.*, 1995; Heederik *et al.*, 2016). Refinery workers directly exposed to soluble Pt were reported to have a GM urinary Pt excretion of 0.29 µg Pt/g creatinine for samples collected over three consecutive days whereas employees who were indirectly exposed had a GM urinary Pt excretion of 0.09 µg Pt/g creatinine over the three consecutive days. Notably, occupational exposure groups who had higher respiratory soluble Pt inhalation exposure were the groups with the higher urinary Pt excretion values (Linde *et al.*, 2018).

Many studies have reported Pt exposure and urinary Pt excretion for industry workers; however limited studies report soluble Rh exposure and the urinary excretion of Rh (Michalke *et al.*, 2024); additionally, Pt in the blood and serum were also reported for industry workers (Kiilunen *et al.*,

2015). The United States Centers for Disease Control (US CDC) reported Pt-industry and PGM workers had 1000 times higher urinary Pt excretion when compared to the general population. The main exposure route is inhalation, with less exposure through the dermal and oral routes (IPA, 2022b). Platinum is absorbed through the inhalation of the soluble Pt particles, and gastrointestinal tract after ingesting Pt. The absorption from the gastrointestinal tract is slower than the diffusion of soluble Pt particles from the respiratory tract. Within 24 hours after exposing rats to soluble Pt through respiratory exposure, 41% of the original load was retained systematically and after 10 days only 1% of the original load was retained. Whereas the gastrointestinal tract absorbed only 1% of the administered dose over 3 days (Czerczak *et al.*, 2012).

Information on Rh absorption, metabolism and excretion is very rare. Rhodium is absorbed in the gastrointestinal tract after ingestion of Rh and the inhalation of soluble Rh particles. Studies on rats injected with soluble Rh and dogs exposed to soluble Rh through inhalation exposure reported that the Rh was stored in the rat's kidneys, heart and spleen, and most of the Rh remained in the dog's lungs with some distribution to the lymph nodes. Almost half (45%) of urinary Rh excretion happens during the first 24 hours after exposure, with a second stage gradually slower. Platinum (IV) chloride has the ability to cause mutagenic activity after exposure, which was demonstrated in both *in vivo* and *in vitro* tests. Platinum (IV) chloride and Rh chloride seem to react with DNA and RNA, causing DNA oxidative damage (Czerczak *et al.*, 2012).

To use biomonitoring effectively as a tool in the industry, it is important to understand key factors that influence biomarker concentrations other than external exposure. Some of these key factors are chemical characteristics, physiological characteristics, route of exposure and frequency of exposure. The intraindividual variation for urinary excretion concentrations are affected by the elimination half-life of chemicals, time between exposure intervals, as well as the difference in urinary flow rate. The sampling time, time of exposure and physiological variation affecting urinary flow or excretion of creatinine (dilution of urine) for different individuals with different metabolic rate and body mass indexes or additional factors affecting the absorption or excretion rate, could add to the variation in results (Aylward *et al.*, 2014; Smolders *et al.*, 2014; Yen *et al.*, 2022). There are differences between individuals and also variations within a single individual, such as water consumption, food, and physiological differences that need to be accounted for when the sampling strategy is designed (Aylward *et al.*, 2014).

The hydration status of workers and the level of dilution of urine samples could affect the concentration of metals found in the samples. The level of dilution of urine is evaluated by measuring the creatinine concentration in the urine and urinary excretion of chemicals is normally

corrected for dilution level by reporting concentration in $\mu\text{g/g}$ creatinine. Urine which is concentrated would have a higher creatinine concentration (less water) as well as higher concentrations of a compound excreted in urine such as Pt and Rh, compared to urine which is diluted (lower creatinine concentration and more water) and would therefore have lower Pt and Rh concentrations. Creatinine excretion is considered more constant than urinary flow rate (Aylward *et al.*, 2014). The guidelines for creatinine excretion concentrations are between 0.30 and 3 g/L (Ampath, 2023). However, creatinine excretion rate changes with age; for instance, children have a lower creatinine excretion rate per kilogram (kg) body weight when compared to adults. Additionally, women also have a lower rate of creatinine excretion per kg body weight compared to men, and the creatinine excretion rate decreases as the person ages. Furthermore, creatinine and body mass do not have a linear growth pattern; there are systemic differences which could also affect the creatinine levels (Aylward *et al.*, 2014). The level of urine dilution is important for biomonitoring studies because a higher level of dilution can lead to concentrations of urinary Pt or Rh that are below the limit of detection of the analytical method. For example, two samples where the concentration of the metal in the urine ($\mu\text{g/g}$ creatinine) is identical, the Pt or Rh in the one sample that is normally diluted can be detected and the other one which is highly diluted might not be detected because the concentration in $\mu\text{g/L}$ is too low.

2.7 Retrospective studies in PGM refineries

Workplaces like refineries do not necessarily have the time, capacity or resources to do in-depth data analysis. Retrospective studies collect information from the past and are non-interventional (Powell and Sweeting, 2015; de Sanctis *et al.*, 2022). Retrospective studies are investigative where past and present conditions are compared to form a trend analysis (Powell and Sweeting, 2015). Methods used by previous retrospective studies included five Pt refineries, where one refinery was in South Africa, one in the United States, and three in the United Kingdom. The one was a primary refinery, three were secondary refineries, and the last refinery was a mixed refinery between primary and secondary refining. The refineries tested the respiratory exposure of soluble Pt for legal compliance and exposure management, and the following studies analysed the generated data for trends (Heederik *et al.*, 2016; Smit *et al.*, 2023; Smit *et al.*, 2025). Heederik *et al.* (2016) used retrospective data for the timeframe of 11 years to investigate the relationship between exposure to soluble Pt and Pt salt sensitisation (1 January 2000–31 December 2010). Smit *et al.* (2023) used the data from the Heederik *et al.* (2016) study and went back to the same

refineries to collect additional information on job descriptions and collected the information for the additional timeframe of 6 years, resulting in 17 years of information (1 January 2000–31 December 2016). Smit *et al.* (2025) added additional information reported by Heederik *et al.* (2016)

for 5 additional years (2011–2015). Smit *et al.* (2025) reported that new employees at a refinery exposed to low exposure of soluble Pt developed platinum salt sensitisation. Heederik *et al.* (2016) reported that one of the limitations of the study was that refineries only selected the highest exposed workers when doing air monitoring, which restricted their ability to do a more advanced comparison on the average exposure levels across different job descriptions in the refineries. Another limitation reported was that smoking habits of employees were not recorded yearly with the air monitoring results, and the smoking status of the employee could have changed, likely resulting in a diluted association. However, new important insights were provided by the results of the exposure response analysis. Smit *et al.* (2023) reported a decline of 10% annually in exposure to soluble Pt in two of the five refineries included in their study. A limitation found by Smit *et al.* (2023, 2025) is that not all recorded data collected by the refineries during the years are stored for the purpose of future studies. Additionally, limited air monitoring results for some job titles may result in an incorrect assumption made by the study. The study contributed to the evidence suggesting that the OEL of 2 µg/m³ is not low enough, and that exposure below the OEL might still result in Pt salt sensitisation. This retrospective study will contribute to the knowledge of the relationship between respiratory exposure of soluble Pt and Rh and the urinary excretion of these metals in workers occupationally exposed to soluble Pt and Rh. As this is the first study to report on the pre- and post-shift urinary excretion of both Pt and Rh in PMR employees who are occupationally exposed to soluble Pt and Rh.

2.8 Conclusion

This literature study explained the history of Pt and Rh, the occupations exposed to soluble Pt and Rh, and reviewed the exposure routes along with the concentrations of soluble Pt and Rh reported by previous studies. Additionally, the use of biomonitoring within the occupational setting as an indicator for occupational exposure to soluble Pt and Rh was discussed. There is limited knowledge regarding the absorption, metabolism and excretion of soluble Pt and Rh. There are various factors that could influence the urinary excretion of Pt and Rh. Therefore, more studies must be conducted regarding this topic.

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CHAPTER 3: ARTICLE

Guide for authors

The *International Journal of Hygiene and Environmental Health* serves as a multidisciplinary forum for reports on exposure assessment as well as reactions to and consequences of human exposure to the biological, chemical, and physical environment.

Abstract: You are required to provide a concise and factual abstract which does not exceed 250 words. The abstract should briefly state the purpose of your research, principal results and major conclusions. Some guidelines:

- Abstracts must be able to stand alone as abstracts are often presented separately from the article.
- Avoid references. If any are essential to include, ensure that you cite the author(s) and year(s).
- Avoid non-standard or uncommon abbreviations. If any are essential to include, ensure they are defined within your abstract at first mention.

Keywords: The author is required to provide 1 to 7 keywords for indexing purposes. Keywords should be written in English. Avoid keywords consisting of multiple words (using "and" or "of"). It is recommended that the author only use abbreviations in keywords if they are firmly established in the field.

Structure of article: Divide the manuscript into clearly defined sections covering all essential elements using headings. Provide definitions of field-specific terms used in the article, in a separate list.

References: Any references cited within the article should also be present in the reference list and vice versa. References cited in the article must be given in full. Do not include personal communications in the reference list, though you may mention them in the text of your article. Any personal communications included in the reference list must follow the standard reference style of the journal. In substitution of the publication date add "personal communication.". The use of Digital Object Identifiers (DOIs) as reference links is encouraged as they provide a permanent link to the electronic article referenced.

Citations can be made directly (or parenthetically). Groups of references can be listed either first alphabetically, then chronologically, or vice versa. Examples: "as demonstrated (Allan, 2020a,

2020b; Allan and Jones, 2019)" or "as demonstrated (Jones, 2019; Allan, 2020). Kramer *et al.* (2023) have recently shown".

The list of references should be arranged alphabetically and then chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

Examples:

Van der Geer, J., Handgraaf, T., Lupton, R.A., 2020. The art of writing a scientific article. *J. Sci. Commun.* 163, 51–59. <https://doi.org/10.1016/j.sc.2020.00372>.

Van der Geer, J., Handgraaf, T., Lupton, R.A., 2022. The art of writing a scientific article. *Heliyon*. 19, e00205. <https://doi.org/10.1016/j.heliyon.2022.e00205>.

Strunk Jr., W., White, E.B., 2000. *The Elements of Style*, fourth ed. Longman, New York.

Mettam, G.R., Adams, L.B., 2023. How to prepare an electronic version of your article, in: Jones, B.S., Smith, R.Z. (Eds.), *Introduction to the Electronic Age*. E–Publishing Inc., New York, pp. 281–304.

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**Respiratory exposure and urinary excretion of both soluble platinum and rhodium at a
precious metals refinery**

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Abstract

Background: Although occupational exposure to soluble platinum (Pt) and urinary Pt excretion have been reported, there is a lack of information on soluble rhodium (Rh) exposure and the urinary excretion of Rh. Additionally, there is a knowledge gap regarding the optimal time for conducting urinary biological monitoring of Pt and Rh.

Objective: The aim of the retrospective study was to evaluate the association between respiratory exposure and urinary excretion among workers exposed to soluble Pt and Rh at a precious metals refinery (PMR) in South Africa and to determine the optimal time for performing urinary biological monitoring.

Method: The sampling strategy was designed by the refinery and included six PMR workers. Respiratory Pt and Rh exposure were monitored for five consecutive shifts (Monday to Friday), and urine samples were collected during the same week for six consecutive pre-shifts and five consecutive post-shifts (Monday morning to Saturday morning). Each urine sample was analysed for Pt, Rh and creatinine.

Results: Three participants had detectable concentrations of urinary Pt excretion and two participants had detectable concentrations of urinary Rh excretion, which could be associated with high respiratory exposure and high exposure activities performed by these participants. There was no significant correlation between respiratory exposure and excretion of Pt or Rh on an individual level; however, there was a significant positive correlation for the results on a group level for Pt ($r = 0.487$; $p = 0.006$) and Rh ($r = 0.691$; $p < 0.0001$). There was no significant difference between pre-shift and post-shift urinary metal excretion results.

Conclusion: Workers in areas with higher soluble Pt or Rh respiratory exposure had higher urinary excretion of the metals compared to participants who worked in low-exposure areas. The optimal time to perform urinary biological monitoring could not be determined.

Word count: 288 words

Key words: Soluble platinum, soluble rhodium, platinum group metals, urinary platinum, urinary rhodium, biological monitoring, MDHS 46/2.

3.1 Introduction

Precious metals refineries extract a variety of precious metals from mined ore (Rao and Reddi, 2000). Platinum (Pt), rhodium (Rh), palladium (Pd), ruthenium (Ru), osmium (Os) and iridium (Ir) are the six recyclable silvery white metals in the platinum group metals (PGMs) (IPA, 2022). Due to Pt and Rh's distinctive physical and chemical properties, they play a key role in the fields of technology and industry (Rao and Reddi, 2000). Both Pt and Rh continue to be in high demand in various industries such as the jewellery manufacturing industry, in automotive catalytic converters and many similar industrial processes (Johnson Matthey, 2025). The PMR involved in this study not only extracts Pt and Rh from mine ore, but also Pd, Ru, Ir and gold (Au).

Inhalation is the main route of exposure to soluble Pt and Rh; additionally, dermal exposure could be a possible route of exposure (Maynard *et al.*, 1997). Soluble Pt and Rh are both capable of causing dermal hypersensitivity reactions; additionally, soluble Pt is capable of causing respiratory hypersensitivity reaction, where fewer studies have reported soluble Rh dermal sensitising reactions (Bedello *et al.*, 1987; De La Cuadra and Grau-Massanéés, 1991; Goossens *et al.*, 2011; Santonen *et al.*, 2022; Santucci *et al.*, 2000). Inhalation of soluble Pt can cause irreversible allergic reactions of the respiratory system, resulting in medical conditions such as allergic asthma, dyspnoea (shortness of breath), bronchial constriction and chronic coughing (Santonen *et al.*, 2022; University of Cambridge, 2025). Dermal exposure to soluble Pt or Rh may cause allergic contact dermatitis and irritation of the skin and eyes. After sensitisation to either soluble Pt or Rh, future exposure can trigger a hypersensitivity reaction (Tsui *et al.*, 2020). Therefore, exposure to soluble Pt and Rh should be controlled within the refinery to protect the workers (Bedello *et al.*, 1987; De La Cuadra and Grau-Massanéés, 1991; Santucci *et al.*, 2000; Goossens *et al.*, 2011; Santonen *et al.*, 2022).

The level of soluble Pt and Rh workers were exposed to is influenced by several factors, including the effectiveness of engineering controls, the procedures and controls used during high exposure activities, and lastly the use of personal protective equipment (PPE). Studies have shown that the correct use of appropriate PPE, such as respirators, disposable coveralls, and gloves, can considerably lower dermal exposure and urinary excretion even when ambient airborne concentrations remain the same (Linde *et al.*, 2021). Linde *et al.* (2018) reported a statistically significant positive correlation between respiratory and dermal exposure to Pt and the urinary Pt excretion of refinery workers. Furthermore, dermal exposure may contribute to delayed absorption and excretion of Pt and Rh, as it has been found that Pt and Rh are retained inside the layers of the skin, causing the formation of a reservoir (Franken *et al.*, 2015). The aim of the retrospective study was to assess and evaluate the association between respiratory exposure and

urinary excretion of workers exposed to soluble Pt and Rh at a PMR in South Africa, and to determine the optimal time for performing urinary biological monitoring.

3.2 Methods

The sampling strategy was designed by the refinery's health and safety team and was based on the method followed by Linde *et al.* (2018) as well as questions raised by the International Platinum Group Metals Association's (IPA) Health and Environmental Science Committee (HESCom). The refinery recruited six PMR workers, three of whom were anticipated to be mainly exposed to soluble Pt and the other three were anticipated to be mainly exposed to soluble Rh. One employee from the clinic was monitored as a control for this study. Utilising the MDHS Method 46/2 (HSE, 1996) and the IPA Harmonised Methodology (IPA, 2016), air monitoring was conducted for both soluble Pt and Rh. The refinery's occupational hygiene officer placed the air sampling train on the workers at the entrance of the refinery and removed it before they left the refinery at the end of their shift. The method followed for the respiratory exposure monitoring is described in detail in Section 3.2.2. The personal air monitoring was conducted over 5 consecutive days (Monday to Friday), with each monitoring period exceeding 80% of the shift. The urine samples were collected at the refinery's clinic by the clinic staff according to the Good Practice Guidance on Pt biomonitoring document of the IPA HESCom. The method followed for the biomonitoring exposure is described in detail in Section 3.2.3. The urine samples were collected during the same week as air monitoring, from Monday (morning) to Saturday (morning), before and after their shifts. Each urine sample was divided into two sterile urine sample cups by the participant, as the analysis for Pt and Rh was done at a laboratory using the "Trace determination of Pt and Rh in human urine using ICP-MS" method by Crespo-Alonso *et al.* (2015). The creatinine was analysed at a separate pathology laboratory using an internal method, based on the Kinetic Jaffe method (Delanghe and Speeckaert, 2011).

3.2.1 Description of workplace

In this retrospective study, the refinery included the highest exposed work areas, where employees are anticipated to be directly exposed to Pt and Rh. The work areas included: PGM separation area, Pt purification and Rh purification. At the PGM separation area, the PGM concentrate is mixed with acids to be dissolved, separating the metals from the concentrate mixture to form a precipitate, which needs to be purified. Thereafter, Pt and Rh precipitates are sent to be purified in their respective purification departments (Pt purification and Rh purification). Platinum and Pd are purified within the same department, while Rh, Ir, Ru and Os are also purified within the same department, but at a different location than Pt and Pd. The acid solutions used to

separate the PGMs cause the metals to form a precipitate (chlorinated salts), which are then removed by using filter presses and glove boxes at the Pt purification and Rh purification departments. Table 3-1 below contains more information about PPE used by participants, and Table 3-2 below elaborates on the daily activities the participants performed during the study.

Table 3-1: Job information for each participant in this study.

		Male / Female	Work area	Years employed (up to 2024)		Personal Protective Equipment					
				At refinery (±)	In section (±)	Safety shoes	Safety glasses	Overalls	Respirator*	Gloves	Other
Employee number	Control	Male	Reception at the clinic	1	1	No	No	No	No	No	No
	Pt #1	Female	Pt purification	11	1	Yes	No	Yes	Full face	Disposable	Disposable overalls
	Pt #2	Female	Pt purification	14	1	Yes	No	Yes	Full face	Disposable	Disposable PVC apron
	Pt #3	Male	Pt purification	16	16	Yes	Yes	Yes	Full face	AI / Latex	No
	Rh #1	Male	PGM separation area	33	33	Yes	No	Yes	Half face	Rubber	No
	Rh #2	Female	Rh purification	32	32	Yes	Yes	Yes	Dräger	Surgical	No
	Rh #3	Female	Rh purification	17	13	Yes	Yes	Yes	Full face	Surgical	Hard hat

* Respirators were fitted with ABEK1 P3 cartridges. Yes - Indicated the PPE each employee was using at the time of Pt and Rh personal air monitoring. No – Indicated that the employees were not using the PPE at the time of Pt and Rh personal air monitoring.

Table 3-2: Activities each participant performed before sampling started, and their daily activities during the study.

Day	Participants						
	Control	Pt #1	Pt #2	Pt #3	Rh #1	Rh #2	Rh #3
Three weeks prior to study	Normal duty	Low production	Low production	Low production	Low production	Stocktaking and cleaning of filters	Stocktaking and cleaning of filters
Sunday prior to study	No activities	Normal production work (packing of Pt salt into paper bags)	Housekeeping and sampling	Hydrolysis of batches to clean them of impurities	Filter Rh–Ir solution, drop solids and dissolve	Stocktaking, normal production	Transfer batch to ignition, dug off the batch (Rh)
1 (Monday)	Conducted chest X-rays in the clinic	Normal production work (packing of Pt salt into paper bags)	Housekeeping and sampling	Hydrolysis of batches to clean, dewatering the Pt salts	Filter the Rh–Ir solution, drop solids and dissolve	Cleaning plant (a lot of dust), normal production	Transfer batch to ignition, dug off the batch (Rh)
2 (Tuesday)	Not monitored	Normal production work (packing of Pt salt into paper bags)	Housekeeping and sampling	Dewatering the Pt salts, cleaning the centrifuge	Filter the Rh–Ir solution, drop the solids and transfer Rh–Ir back	Lots of dust from painters, normal production	Transfer batch to ignition, dug off the batch (Rh)
3 (Wednesday)	Not monitored	Normal production work (packing of Pt salt into paper bags)	Sampling, bromate hydrolysis	Dewatering the Pt salts	Filter bro mud solutions, dissolve transfer to Catix	Dust from painters, normal production	Transfer batch to ignition, dug off the batch (Rh)

Table 3-3: continued

Day	Participants						
	Control	Pt #1	Pt #2	Pt #3	Rh #1	Rh #2	Rh #3
4 (Thursday)	Not monitored	Normal production work (packing of Pt salt into paper bags)	Bromate hydrolysis, sodium bicarbonate make-up	Dewatering the Pt salts	Clean the section	Dust from painters, plant cleaning	Transfer batch to ignition
5 (Friday)	Not monitored	Normal production work (packing of Pt salt into paper bags)	Bromate hydrolysis, sodium bicarbonate make-up, NH_4Cl precipitation	Dewatering the Pt salts	Filter the Rh-Ir batch and dissolve	Dust from production	Transfer batch to ignition

3.2.2 Respiratory exposure

The inhalable soluble Pt and Rh exposure samples were collected using the MDHS 46/2 method. The South African National Accreditation System (SANAS)-accredited laboratory that analysed the samples, supplied the PMR with pre-weighed and pre-labelled Institute of Occupational Medicine (IOM) samples with their own unique sample numbers. For the sampling train, a Gilian GilAir 3 pump was connected to the IOM sampler, which was fitted with a 25 mm mixed cellulose ester (MCE) filter. The sampling pump was calibrated with a Gilibrator 2 calibrator at a constant air flow of 2 L/min. Calibration of sampling pumps was conducted daily for each pump before and after sampling, ensuring that the difference between the pre-calibration and post sampling flow rate was not more than 5%. The IOM sampling head was connected without the respirable MultiDust foam, resulting in the collection of the inhalable fraction. The pump was attached to the employee by using a belt around the employee's waist, and the sampling head was placed on the employee's collar inside his/her breathing zone (IPA, 2016). The pump was switched on as the employee started his/her shift, and it was switched off and removed only at the end of the shift. Filters were transported inside the IOM cassettes in travel cases to a SANAS-accredited laboratory where they were analysed for soluble Pt and Rh using inductively coupled plasma-mass spectrometry (ICP-MS). The limit of detection (LOD) for Pt was 0.0002 µg/m³, and for Rh, the LOD was 0.0003 µg/m³. The method uncertainties for Pt were 1.6% and for Rh 0.84% (L. Lightfoot personal communication). For all respiratory exposure results, the time-weighted average (TWA) was calculated using Equation 3.2-1, and the time of the shift that was not measured was presumed to be negligible.

Equation 3.2-1: Formula for calculating the time-weighted average for HCAs (Department of Employment and Labour 2021).

$$TWA = \frac{C_1T_1 + C_2T_2 + \dots + C_nT_n}{8}$$

Where:

TWA = Time-weighted average (µg/m³)
C_n = Concentration measured (µg/m³)
T_n = Time of measurement (h)

3.2.3 Biological monitoring

The urine samples were collected at the refinery's clinic according to the Good Practice Guidance on Pt biomonitoring document of the IPA HESCom. The analysis of the urine samples was done by two different laboratories; one laboratory analysed for Pt and Rh, whereas the other laboratory analysed for creatinine. Participants were given a large, clean, metal-free plastic cup to urinate

into. They were instructed to decant the sample into two urine sample cups, where there was a line indicating the volume needed. The urine sample cups were pre-marked with unique identification numbers. The samples were placed in the fridge where the average temperature over the 5 days was 8°C.

The analysis of creatinine was done by a SANAS-accredited laboratory, which applied the alkaline picrate method of isotope dilution mass spectrometry (IDMS) standardised to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) to analyse the creatinine in the urine samples. The Beckman AU5800 instrument was used for analysis of samples. This method has a LOD of 0.088 mmol/L and an LOQ of 44.2 mmol/L – if samples were diluted. The uncertainty of measurement for this method is reportedly 5% (Y. du Preez, personal communication).

The analysis of the metals in the urine was done by a different SANAS-accredited laboratory. The method used to analyse for urinary Pt and Rh is not a commercial method used by a pathology laboratory, but a method reported in literature by Crespo-Alonso *et al.* (2015) (“A simple, sensitive analytical method for platinum trace determination in human urine”) using ICP-MS. The laboratory thawed the samples at room temperature and then homogenised them by shaking and ultrasonic bath treatment only for samples with abundant sediment. To obtain homogeneous mixtures, this procedure was repeated for the different samples. An 8 mL aliquot was subsampled from the original urine samples and treated with 65% HNO₃ (4 mL, 50% v/v) and 37% HCl (0.8 mL, 10% v/v) in rinsed (1% HNO₃ and, subsequently, high purity water) polypropylene tubes (15 mL). In the same tubes, to minimise contamination, samples were sonicated for 2 h at 60 °C and subsequently centrifuged for 30 minutes to separate any solid residues. One mL aliquots from these treated samples were finally diluted to a ratio of 1:5 in rinsed polypropylene tubes for Pt determination by high resolution inductively coupled plasma-mass spectrometry (HR-ICP-MS). The Thermo Scientific Element 2 instrument was used. This method had a LOD of 0.19 µg/L for Pt and 0.31 µg/L for Rh and a limit of quantification (LOQ) of 1.52 µg/L for Pt and 2.48 µg/L for Rh (W. Wepener, personal communication).

3.3 Statistical analysis

The statistical analyses for the study were performed by the NWU research team following receipt of the anonymised dataset from the health and safety team of the refinery. The dataset contained the results for soluble Pt and Rh respiratory exposure, and the urinary excretion of Pt, Rh and creatinine. The following analyses were performed on the dataset:

- All the data for the project were analysed and graphically represented using GraphPad Prism 10 (GraphPad® software).
- All results that were below the LOD for their respective methods were substituted using β -substitution. This method was proposed by Ganser and Hewitt (2010) and was reported to be superior to other methods, such as LOD/2 or LOD/ $\sqrt{2}$. Table 3-3 and 3-4 show that a significant number of urine metal concentrations were below the LOD and subsequently substituted using β -substitution. These substituted values were used to calculate concentrations in $\mu\text{g/g}$ creatinine to be used in the data analysis.
- The distribution of the data was tested and was found to be log-normally distributed according to the D'Agostino and Pearson test. Subsequently, the data were log-transformed before statistical analysis.
- Pearson correlations were used to investigate the relationship between respiratory exposure and urinary Pt and Rh excretion, as well as the relationship between creatinine concentration in urine and urinary Pt and Rh concentrations.
- Paired t-tests were performed on the data to compare pre-shift and post-shift urinary Pt and Rh excretion results.
- Spearman correlations were used to investigate the relationship between the IOM results and respectively the difference in pre- and post-shift urinary Pt and Rh excretion.
- The significance threshold of a relationship tested was compared to $p < 0.001$.

The results obtained from the analyses are summarised in Table 3-5.

3.4 Ethics approval

This study was approved by the Health Research Ethics Committee (HREC) of the North-West University (NWU) Potchefstroom Campus (ethics number: NWU-00167-24-A1).

3.5 Results

The detailed Pt and Rh results of the study are shown in Table 3-3 and Table 3-4, respectively, and include soluble Pt and Rh respiratory exposure concentrations as well as all the results from the urine analysis for pre- and post-shift samples, namely, Pt or Rh concentration ($\mu\text{g/L}$), creatinine (g/L), creatinine corrected Pt or Rh concentration ($\mu\text{g/g}$ creatinine) and the difference between pre- and post-shift samples Pt or Rh concentrations ($\mu\text{g/L}$ and $\mu\text{g/g}$ creatinine). All these parameters are included for completeness, and the meanings of these parameters are summarised below:

- Urinary Pt or Rh concentration ($\mu\text{g/L}$): Uncorrected Pt or Rh concentration in urine (pre- and post-shift).
- Creatinine (g/L): Creatinine concentration in urine (pre- and post-shift).
- Urinary Pt or Rh concentration ($\mu\text{g/g}$ creatinine): Creatinine corrected Pt or Rh concentration in urine (pre- and post-shift).
- Difference: Pt or Rh post-shift pre-shift ($\mu\text{g/L}$): Difference between post- and pre-shift samples of Pt or Rh concentrations.
- Difference: Pt or Rh post-shift pre-shift ($\mu\text{g/g}$ creatinine): Difference between creatinine corrected post- and pre-shift samples of Pt or Rh concentrations.

Note that many of the results were below the LOD and that the β -substitution values are shown in table 3-3 and 3-4, and marked with a superscript letter.

For Pt, participants Pt #1 (range: 8.250 to 33.698 $\mu\text{g/m}^3$) and Pt #3 (range: 11.201 to 99.224 $\mu\text{g/m}^3$) experienced significant respiratory exposure to soluble Pt exceeding the OEL-RL of 2 $\mu\text{g/m}^3$ during all five shifts in the Pt purification department while conducting normal production activities (packing of Pt salt into paper bags), and hydrolysis of batches to clean, and dewatering the Pt salt. Participant Rh #1 (10.695 $\mu\text{g/L}$) had the highest urinary Pt excretion reported in table 3-3, while conducting activities such as filtering the Rh–Ir solution, drop solids, dissolve and other activities listed in table 3-2. Participants Pt #1 and Pt #3 used full face respirators fitted with ABEK1 P3 cartridges, whereas Rh #1 only used a half face respirator fitted with ABEK1 P3 cartridges. All three participants used gloves, and only participant Pt #1 used disposable overalls.

For Rh, the OEL-RL of 20 $\mu\text{g/m}^3$ for soluble Rh was not exceeded during the week, but participants Rh #2 (range: 0.334 to 3.841 $\mu\text{g/m}^3$) and Rh #3 (range: 0.345 to 6.782 $\mu\text{g/m}^3$) experienced the highest respiratory exposure to soluble Rh and were the only participants to have urinary Rh excretion above the detection limit reported in Table 3-4. Participant Rh #2 conducted normal

production activities or cleaned plant and other activities listed in table 3-2 which liberated dust, participant Rh #3 transferred the batch to ignition and dug off the Rh batch. Both participants used respirators (Rh #2 – Dräger, Rh #3 – Full face) fitted with ABEK1 P3 cartridges and both participants used surgical gloves.

The samples where the creatinine concentrations did not comply with the range of 0.3–3 g/L are also indicated with a superscript letter. This indicated that these samples were either very diluted or very concentrated.

Table 3-4 Respiratory exposure to soluble Pt and urinary Pt excretion for all participants during the study.

Participant and day	TWA respiratory exposure to soluble Pt ($\mu\text{g}/\text{m}^3$)	Urinary Pt pre-shift ($\mu\text{g}/\text{L}$)	Urinary Pt post-shift ($\mu\text{g}/\text{L}$)	Urinary creatinine pre-shift (g/L)	Urinary creatinine post-shift (g/L)	Urinary Pt pre-shift ($\mu\text{g}/\text{g}$ creatinine)	Urinary Pt post-shift ($\mu\text{g}/\text{g}$ creatinine)	Difference: Pt post-shift - pre-shift ($\mu\text{g}/\text{L}$)	Difference: Pt post shift - pre-shift ($\mu\text{g}/\text{g}$ creatinine)
Pt #1 D1	19.293	3.997	6.517	2.113	2.780	1.891	2.344	2.520	0.453
Pt #1 D2	24.106	3.613	3.801	1.729	1.718	2.090	2.213	0.188	0.123
Pt #1 D3	30.102	2.165	1.053 ^a	0.802	0.396	2.698	2.662 ^a	-1.111	-0.035
Pt #1 D4	33.698	2.864	1.053 ^a	1.650	0.565	1.736	1.864 ^a	-1.811	0.129
Pt #1 D5	8.250	1.674	1.053 ^a	0.825	0.712	2.030	1.479 ^a	-0.621	-0.550
Pt #1 D6		2.486		1.706		1.457			
Pt #2 D1	0.311	2.629	0.543 ^a	1.639	0.825	1.604	0.658 ^a	-2.085	-0.946
Pt #2 D2	0.286	0.543 ^a	0.543 ^a	0.305	0.136 ^b	1.780 ^a	4.004 ^a	0.000	2.226
Pt #2 D3	0.077	0.543 ^a	0.543 ^a	0.576	0.441	0.942 ^a	1.232 ^a	0.000	0.290
Pt #2 D4	0.627	0.543 ^a	0.543 ^a	0.339	0.486	1.602 ^a	1.118 ^a	0.000	-0.485
Pt #2 D5	0.053	0.543 ^a	0.543 ^a	0.237 ^b	0.384	2.288 ^a	1.413 ^a	0.000	-0.875
Pt #2 D6		0.543 ^a		0.780		0.696 ^a			
Pt #3 D1	11.219	1.718	5.442	1.401	2.328	1.226	2.338	3.724	1.112
Pt #3 D2	99.224	2.909	5.597	1.040	1.209	2.798	4.629	2.688	1.831
Pt #3 D3	11.760	0.781 ^a	0.781 ^a	0.283 ^b	0.316	2.765 ^a	2.468 ^a	0.000	-0.296
Pt #3 D4	11.201	0.781 ^a	4.486	0.384	1.220	2.033 ^a	3.676	3.705	1.643
Pt #3 D5	25.103	0.781 ^a	4.564	0.271 ^b	0.927	2.880 ^a	4.926	3.783	2.045
Pt #3 D6		0.781 ^a		0.192 ^b		4.066 ^a			
Rh #1 D1	1.454	0.786 ^a	2.339	0.113 ^b	0.429	6.956 ^a	5.448	1.571	-1.353
Rh #1 D2	0.605	0.786 ^a	10.445	0.350	1.650	2.244 ^a	6.331	9.676	4.137
Rh #1 D3	1.040	4.807	10.332	0.712	1.526	6.753	6.773	5.525	0.020
Rh #1 D4	0.907	2.894	10.695	0.418	1.503	6.921	7.116	7.802	0.196
Rh #1 D5	6.382	2.129	0.786 ^a	0.328	0.136 ^b	6.496	5.796 ^a	-1.360	-0.829
Rh #1 D6		0.786 ^a		0.486		1.618 ^a			
Rh #2 D1	0.094	0.543 ^a	0.543 ^a	0.441	1.865	1.323 ^a	0.291 ^a	0.000	-0.941
Rh #2 D2	0.029	0.543 ^a	0.543 ^a	0.305	1.435	1.780 ^a	0.378 ^a	0.000	-1.402
Rh #2 D3	0.019	0.543 ^a	0.543 ^a	0.339	1.842	1.602 ^a	0.295 ^a	0.000	-1.308
Rh #2 D4	0.034	0.543 ^a	0.543 ^a	0.283 ^b	1.571	1.922 ^a	0.346 ^a	0.000	-1.577
Rh #2 D5	0.015	0.543 ^a	0.543 ^a	0.283 ^b	1.424	1.922 ^a	0.381 ^a	0.000	-1.542
Rh #2 D6		0.543 ^a		0.599		0.907 ^a			

Table 3-5: Continued

Participant and day	TWA respiratory exposure to soluble Pt ($\mu\text{g}/\text{m}^3$)	Urinary Pt pre-shift ($\mu\text{g}/\text{L}$)	Urinary Pt post-shift ($\mu\text{g}/\text{L}$)	Urinary creatinine pre-shift (g/L)	Urinary creatinine post-shift (g/L)	Urinary Pt pre-shift ($\mu\text{g}/\text{g}$ creatinine)	Urinary Pt post-shift ($\mu\text{g}/\text{g}$ creatinine)	Difference: Pt post-shift - pre-shift ($\mu\text{g}/\text{L}$)	Difference: Pt post-shift - pre-shift ($\mu\text{g}/\text{g}$ creatinine)
Rh #3 D1	0.107	0.543 ^a	0.543 ^a	1.379	0.136 ^b	0.394 ^a	4.004 ^a	0.000	3.613
Rh #3 D2	0.142	0.543 ^a	0.543 ^a	1.311	0.373	0.414 ^a	1.456 ^a	0.000	1.043
Rh #3 D3	0.028	0.543 ^a	0.543 ^a	1.537	0.373	0.353 ^a	1.456 ^a	0.000	1.103
Rh #3 D4	0.236	0.543 ^a	0.543 ^a	1.537	0.158 ^b	0.353 ^a	3.432 ^a	0.000	3.081
Rh #3 D5	0.023	0.543 ^a	0.543 ^a	1.175	1.288	0.462 ^a	0.422 ^a	0.000	-0.041
Rh #3 D6		0.543 ^a		1.582		0.343 ^a			
Control	0.001 ^a	0.543 ^a	0.543 ^a	3.006 ^b	3.153 ^b	0.506 ^a	0.482 ^a	0.000	-0.008

TWA – Time-weighted average; ^a – Results were below the limit of detection for the method. The metal concentration ($\mu\text{g}/\text{L}$) results below the detection limit were substituted using β -substitution and divided by the sample's creatinine concentration to obtain a substituted metal concentration in $\mu\text{g}/\text{g}$ creatinine.; ^b – Creatinine concentration did not comply with the guideline of 0.3–3 g/L. D – indicates the day of the study, i.e., D3 = Wednesday. **Bold**-printed values in the TWA respiratory exposure to soluble Pt column indicated that the OEL of 2 $\mu\text{g}/\text{m}^3$ was exceeded. Blank spaces next to day 6 information, indicates no monitoring data.

Table 3-6: Respiratory exposure to soluble Rh and urinary Rh excretion for all participants during the study.

Participant and day	TWA Respiratory exposure to soluble Rh ($\mu\text{g}/\text{m}^3$)	Urinary Rh pre-shift ($\mu\text{g}/\text{L}$)	Urinary Rh post shift ($\mu\text{g}/\text{L}$)	Urinary Creatinine pre-shift (g/L)	Urinary Creatinine post-shift (g/L)	Urinary Rh pre-shift ($\mu\text{g}/\text{g}$ Creatinine)	Urinary Rh post-shift ($\mu\text{g}/\text{g}$ Creatinine)	Difference: Rh post-shift - pre-shift ($\mu\text{g}/\text{L}$)	Difference: Rh post-shift - pre-shift ($\mu\text{g}/\text{g}$ Creatinine)
Pt #1 D1	0.292	0.949 ^a	0.949 ^a	2.113	2.780	0.449 ^a	0.341 ^a	0.000	-0.108
Pt #1 D2	0.152	0.949 ^a	0.949 ^a	1.729	1.718	0.549 ^a	0.553 ^a	0.000	0.004
Pt #1 D3	0.086	0.949 ^a	0.949 ^a	0.802	0.396	1.183 ^a	2.399 ^a	0.000	1.216
Pt #1 D4	0.071	0.949 ^a	0.949 ^a	1.650	0.565	0.575 ^a	1.680 ^a	0.000	1.104
Pt #1 D5	0.015	0.949 ^a	0.949 ^a	0.825	0.712	1.150 ^a	1.333 ^a	0.000	0.183
Pt #1 D6		0.949 ^a		1.706		0.556 ^a			
Pt #2 D1	0.009	0.949 ^a	0.949 ^a	1.639	0.825	0.579 ^a	1.150 ^a	0.000	0.571
Pt #2 D2	0.019	0.949 ^a	0.949 ^a	0.305	0.136 ^b	3.110 ^a	6.999 ^a	0.000	3.886
Pt #2 D3	0.001 ^a	0.949 ^a	0.949 ^a	0.576	0.441	1.647 ^a	2.153 ^a	0.000	0.506
Pt #2 D4	0.011	0.949 ^a	0.949 ^a	0.339	0.486	2.799 ^a	1.953 ^a	0.000	-0.846
Pt #2 D5	0.001 ^a	0.949 ^a	0.949 ^a	0.237 ^b	0.384	3.999 ^a	2.470 ^a	0.000	-1.528
Pt #2 D6		0.949 ^a		0.780		1.217 ^a			
Pt #3 D1	0.081	0.949 ^a	0.949 ^a	1.401	2.328	0.677 ^a	0.408 ^a	0.000	-0.269
Pt #3 D2	0.020	0.949 ^a	0.949 ^a	1.040	1.209	0.913 ^a	0.785 ^a	0.000	-0.128
Pt #3 D3	0.100	0.949 ^a	0.949 ^a	0.283 ^b	0.316	3.359 ^a	2.999 ^a	0.000	-0.360
Pt #3 D4	0.033	0.949 ^a	0.949 ^a	0.384	1.220	2.470 ^a	0.778 ^a	0.000	-1.692
Pt #3 D5	0.026	0.949 ^a	0.949 ^a	0.271 ^b	0.927	3.499 ^a	1.024 ^a	0.000	-2.474
Pt #3 D6		0.949 ^a		0.192 ^b		4.940 ^a			
Rh #1 D1	0.518	0.949 ^a	0.949 ^a	0.113 ^b	0.429	8.398 ^a	2.210 ^a	0.000	-6.185
Rh #1 D2	0.122	0.949 ^a	0.949 ^a	0.350	1.650	2.709 ^a	0.575 ^a	0.000	-2.133
Rh #1 D3	1.121	0.949 ^a	0.949 ^a	0.712	1.526	1.333 ^a	0.622 ^a	0.000	-0.711
Rh #1 D4	0.347	0.949 ^a	0.949 ^a	0.418	1.503	2.270 ^a	0.631 ^a	0.000	-1.638
Rh #1 D5	0.782	0.949 ^a	0.949 ^a	0.328	0.136 ^b	2.896 ^a	6.999 ^a	0.000	4.101
Rh #1 D6		0.949 ^a		0.486		1.953 ^a			
Rh #2 D1	3.841	1.217 ^a	6.920	0.441	1.865	2.762 ^a	3.711	5.703	0.950
Rh #2 D2	1.462	1.217 ^a	4.757	0.305	1.435	3.989 ^a	3.188	3.358	-0.801
Rh #2 D3	0.334	1.217 ^a	6.059	0.339	1.842	3.590 ^a	3.290	4.842	-0.300
Rh #2 D4	2.332	1.217 ^a	5.975	0.283 ^b	1.571	4.308 ^a	3.804	4.758	-0.504
Rh #2 D5	0.533	1.217 ^a	4.516	0.283 ^b	1.424	4.308 ^a	3.172	3.299	-1.136
Rh #2 D6		1.217 ^a		0.599		2.032 ^a			

Table 3-7: Continued

Participant and day	TWA Respiratory exposure to soluble Rh ($\mu\text{g}/\text{m}^3$)	Urinary Rh pre-shift ($\mu\text{g}/\text{L}$)	Urinary Rh post-shift ($\mu\text{g}/\text{L}$)	Urinary creatinine pre-shift (g/L)	Urinary creatinine post-shift (g/L)	Urinary Rh pre-shift ($\mu\text{g}/\text{g}$ creatinine)	Urinary Rh post-shift ($\mu\text{g}/\text{g}$ creatinine)	Difference: Rh post-shift - pre-shift ($\mu\text{g}/\text{L}$)	Difference: Rh post shift - pre-shift ($\mu\text{g}/\text{g}$ creatinine)
Rh #3 D1	6.782	5.331	1.315 ^a	1.379	0.136 ^b	3.867	9.698 ^a	-4.016	5.831
Rh #3 D2	5.672	5.414	1.315 ^a	1.311	0.373	4.130	3.526 ^a	-4.099	-0.603
Rh #3 D3	2.473	6.386	1.315 ^a	1.537	0.373	4.155	3.526 ^a	-5.071	-0.628
Rh #3 D4	6.642	6.649	1.315 ^a	1.537	0.158 ^b	4.326	8.312 ^a	-5.334	3.987
Rh #3 D5	0.345	1.315 ^a	6.435	1.175	1.288	1.119 ^a	4.995	3.955	2.885
Rh #3 D6		5.414		1.582		3.422			
Control	0.001 ^a	0.949 ^a	0.949 ^a	3.006	3.153	0.825 ^a	0.787 ^a	0.000	-0.015

TWA – Time-weighted average; ^a – Results were below the limit of detection for the method. The metal concentration ($\mu\text{g}/\text{L}$) results below the detection limit were substituted using β -substitution and divided by the sample's creatinine concentration to obtain a substituted metal concentration in $\mu\text{g}/\text{g}$ creatinine.; ^b – Creatinine concentration did not comply with the guideline of 0.3–3 g/L. D – indicates the day of the study, i.e., D3 = Wednesday. Blank spaces next to day 6 information, indicates no monitoring data.

Figure 3-1 illustrates the differences in urinary Pt and Rh excretion for the individual participants. In the figure, the participants whose Pt and Rh excretion results were mostly above the detection limit are indicated. The metal concentration ($\mu\text{g/L}$) results below the detection limit were substituted using β -substitution and divided by the sample's creatinine concentration to obtain a substituted metal concentration in $\mu\text{g/g}$ creatinine. These substituted concentrations are also shown in the figure.

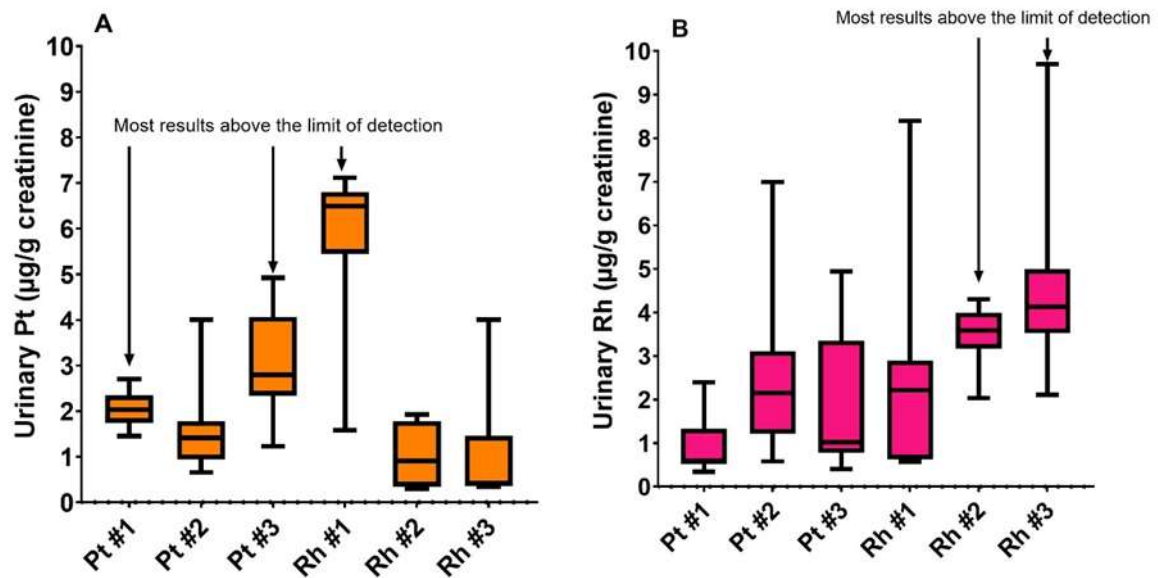


Figure 3-1: Box and whisker plot showing the difference in A) urinary Pt excretion and B) urinary Rh excretion for the individual participants. Note that the metal concentrations below the limit of detection were substituted using β -substitution. For A) urinary Pt excretion, participant Pt #1, Pt #3 and Rh #1 had urinary Pt excretion mostly above the detection limit, while for B) urinary Rh excretion, participant Rh #2 and Rh #3 had urinary Rh excretion mostly above the detection limit. The box indicates the 25th and 75th percentiles, the line in the middle of the box indicates the median and the whisker lines show the minimum and maximum. The participants whose Pt and Rh excretion results were mostly above the detection limit are indicated with arrows.

Figures 3-2 and 3-3 illustrate the relationship between inhalation exposure and urinary Pt and Rh excretion for individual participants over the course of the work week. The participants whose Pt and Rh excretion results were mostly above the detection limit (Pt: Pt #1; Pt #3; Rh #1 and Rh: #2; Rh #3) were included in the figures. The individual results that were below the LOD and substituted using β -substitution are also shown in the figures.

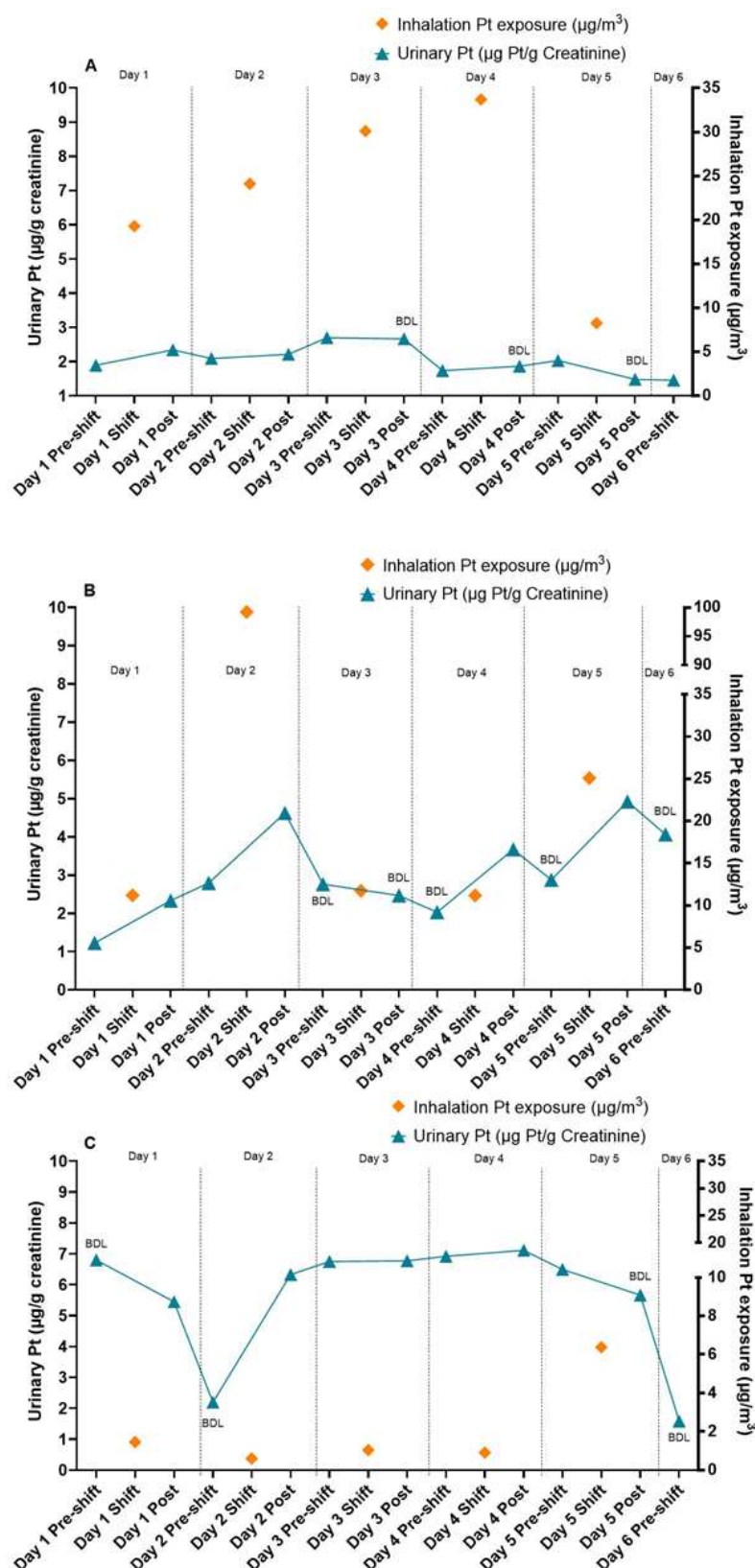


Figure 3-2: Relationship between urinary Pt excretion and soluble Pt inhalation exposure for individual participants over the course of the work week (Day 1–6). A = Pt #1; B = Pt #3; C = Rh #1. Note that the figure does not include participants whose results were predominantly below the limit of detection for urinary Pt. BDL – below detection limit.

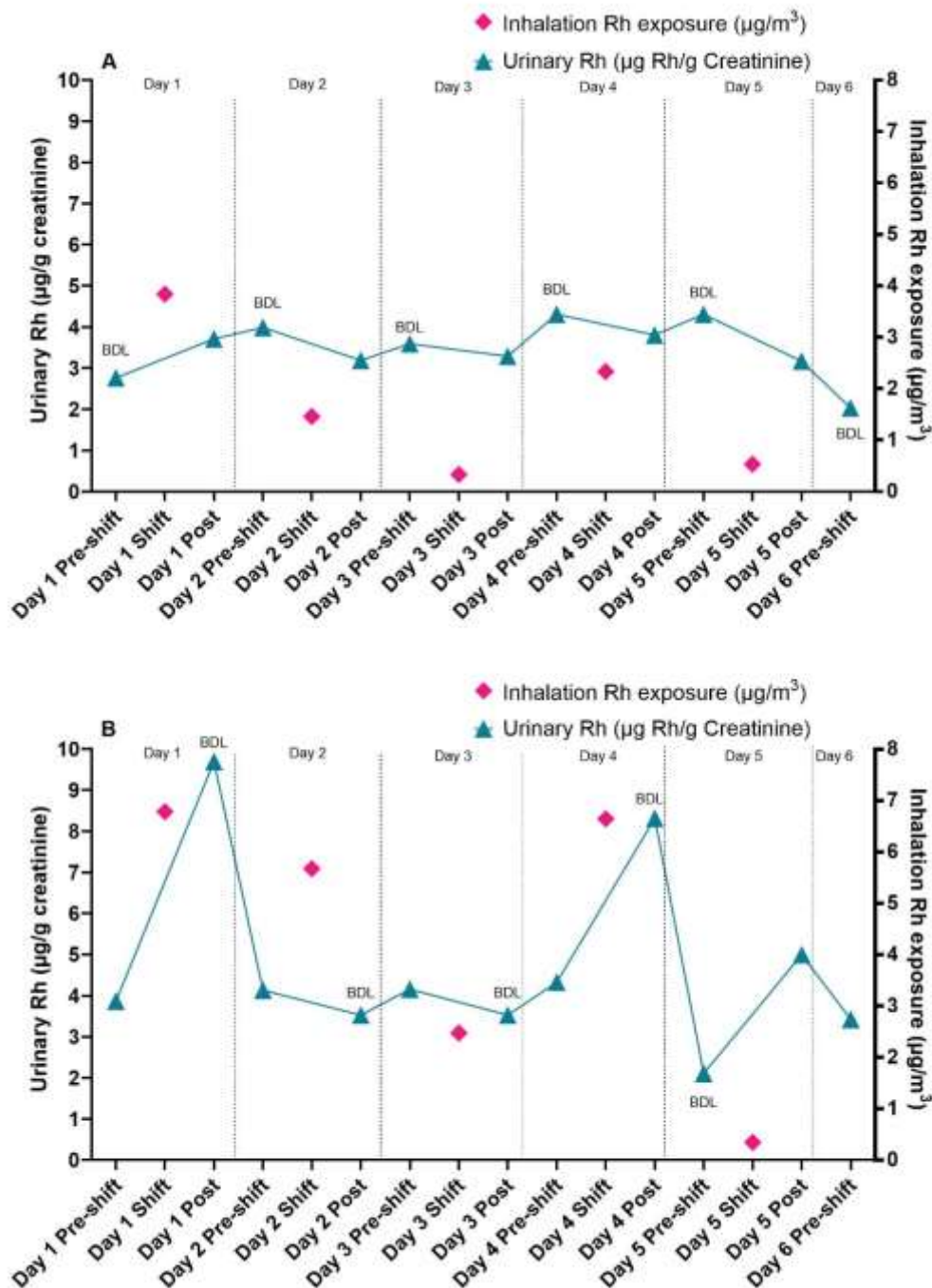


Figure 3-3: Relationship between urinary Rh excretion and soluble Rh inhalation exposure for individual participants over the course of the work week (Day 1–6). A = Rh #2; B = Rh #3. Note that the figure does not include participants whose results were predominantly below the limit of detection for urinary Rh. BDL – below detection limit.

Table 3-5 summarises the results of the statistical tests performed on the dataset. These included Pearson and Spearman correlations and paired t-tests.

Table 3-8: Summary of the results from the statistical tests performed on the dataset

Topic of investigation	Pt	Rh
	<i>Respiratory exposure vs urinary excretion</i>	
Relationship between exposure and urinary excretion	Pearson correlation showed that respiratory exposure was positive significantly correlated with both pre- and post-shift µg/g creatinine concentrations for the entire group of six participants for both Pt and Rh.	
	Pre-shift (r = 0.554; p = 0.001) Post-shift (r = 0.679; p < 0.0001)	Pre-shift (r = 0.451; p = 0.011) Post-shift (r = 0.443; p = 0.013)
	Pearson correlation between respiratory exposure and excretion of the metal in urine (µg/g creatinine) had no significant correlation for individual participants who had detectable concentrations of metal in their urine.	
	Participants working in areas with higher respiratory exposure had higher urinary excretion of the metals compared to participants who worked in low-exposure areas. Both pre- and post-shift results were increased with these participants. Therefore, there was a significant relationship for the entire group of six participants (high and low exposed). However, on the individual level, there was no significant correlation between respiratory exposure and urinary metal excretion. There was more variation in the results on an individual level.	
Relationship between urinary metal concentration and creatinine	Pearson correlation between all pre- and post-shift excretion of the metal in urine (µg/L) was positive moderately correlated with creatinine in urine for the entire group of six participants.	
	(r = 0.404; p = 0.0006).	(r = 0.353; p = 0.0032).
	Pearson correlation between excretion of the metal (pre- and post-shift) in urine (µg/L) and creatinine was significantly correlated for individual participants who had detectable concentrations of metal in their urine.	
	Pt #1 (r = 0.945; p < 0.00001) Pt # 3 (r = 0.894; p = 0.0002) Rh #1 (r = 0.887; p = 0.0003)	Rh #2 (r = 0.964; p < 0.0001) Rh #3 (r = 0.906; p = 0.0001)
	The more concentrated the urine was, as indicated by creatinine concentrations, the higher the metal concentrations typically were. Especially for individual participants, there were high correlations. Therefore, the samples that had metal concentrations below the limit of detection also had relatively low creatinine concentrations, which could mean that they were underestimated due to diluted urine and a relatively high detection limit of the ICP-MS method.	
	Pt	Rh
	<i>Timing of urine collection</i>	
Relationship between pre- and post-shift urinary excretion	Paired t-tests between pre- and post-shift urinary metal excretion found no significant difference between pre- and post-shift urinary metal excretion.	
	Pre- and post-shift µg/g creatinine results were correlated significantly with one another for the entire group of six participants for both Pt and Rh.	
	(r = 0.487; p = 0.006)	(r = 0.691; p < 0.0001)
	For the entire group of participants (low and high exposed), there were no significant difference between pre- and post-shift results and both pre- and post-shift results were increased in participants with higher exposure. Therefore, there was no significant trend indicating whether results from pre- or post-shift urine samples correlated better with respiratory exposure concentrations.	

3.6 Discussion

This retrospective study aimed to evaluate the relationship between respiratory exposure of soluble Pt and Rh and the urinary excretion of these metals in workers occupationally exposed to soluble Pt and Rh. Respiratory samples were collected over five consecutive days (Monday to Friday). Urinary samples were collected for six consecutive days (Monday pre-shift to Saturday pre-shift) during the same week as the collection of respiratory exposure samples. Based on the results reported by Linde *et al.* (2018) the relationship between soluble Pt and Rh exposure compared to the urinary excretion of the metal was anticipated to be statistically significant and positively correlated. Additionally, the study aimed to determine the optimal time for performing urinary biological monitoring. Schierl *et al.* (1998) reported that the maximum urinary Pt excretion was 10 hours post-exposure to soluble Pt, with the first half-life at 50 hours and the second half-life at 24 days after the initial exposure to soluble Pt. Linde *et al.* (2018) found no significant variation between urine samples collected from refinery workers before their shifts over three consecutive mornings and it was anticipated that the optimal time for biological monitoring would be in the morning before the shift, following a previous day of respiratory exposure to soluble Pt and Rh. The following discussion will therefore address the exposure to soluble Pt and Rh within three different departments of the refinery and the urinary Pt and Rh excretion (pre-shift and post-shift) of those workers. Although soluble Pt and Rh exposure, and urinary Pt excretion of PMR workers in South Africa have been reported, this is the first study to report on the Rh excretion of PMR workers and; additionally, the first to report on the pre- and post-shift urinary Pt and Rh excretion of PMR workers in South Africa, which is the largest supplier of Pt and Rh in the world (Johnson Matthey, 2025).

3.6.1 Correlation between respiratory exposure and urinary excretion

The participants were included in the study because their exposure to soluble Pt or Rh was anticipated to be the highest based on their area of work (Table 3-1). The workers with detectable concentrations of Pt and Rh in their urine were the workers who also experienced higher respiratory exposure to soluble Pt and Rh. However, on the individual level, there is no visible trend showing that high respiratory exposure during a shift leads to high post-shift urinary excretion of the metal. Therefore, individuals had no significant relationship between respiratory exposure and urinary excretion of Pt and Rh.

Soluble Pt exposure and the urinary excretion of Pt (Table 3-3 and Figure 3-2):

As reported in Table 3-3, all six participants had soluble Pt exposure, with three of the participants

(Pt #1, Pt #3 and Rh #1) exceeding the OEL-RL of 2 µg/m³ during the study; additionally, those three participants had detectable urinary Pt excretion. Participant Pt #1 conducted the same work activity daily which was packing of Pt salt into paper bags. Participant Pt #3 conducted different daily work activities which included hydrolysis of batches to clean them of impurities and dewatering of Pt salts, cleaning of the centrifuge. Participant Rh #1 also conducted different daily work activities which included filtering of Rh–Ir solution, drop solids, dissolve, transfer Rh–Ir back, transfer to Catix and clean the section. This study encountered significantly higher soluble Pt exposure (range: 0.015 to 99.224 µg/m³) compared to the concentrations found in similar work areas of a PMR by Linde *et al.* (2018) (range: 0.015 to 21.320 µg/m³). These concentrations were not reported in the manuscript and were obtained from the authors upon request. The urinary Pt excretion for this study (range: BDL to 7.116 µg/g creatinine) was also higher compared to similar areas reported by Linde *et al.* (2018) (range: BDL to 3.000 µg/g creatinine). These concentrations were not reported in the manuscript and were obtained from the authors upon request. Exposure to soluble Pt reported in this study was positively significantly correlated with both post-shift ($r = 0.679$; $p < 0.0001$) and the following day pre-shift ($r = 0.554$; $p = 0.001$) urinary Pt excretion for the entire group (all six participants) and a similar positive correlation was also seen for similar work areas reported by Linde *et al.* (2018) ($r = 0.561$; $p = 0.003$). These concentrations were not reported in the manuscript and were obtained from the authors upon request. Therefore, this study found higher respiratory exposure to soluble Pt but revealed the same correlation between respiratory exposure and urinary Pt excretion for similar work areas at a PMR.

Soluble Rh exposure and the urinary excretion of Rh (Table 3-4 and Figure 3-3):

This is the only study to report urinary Rh excretion of PMR workers and, therefore, cannot be compared to other studies. However, other studies reported the respiratory soluble Rh exposure of refinery workers, which can be compared to this study. This study reported soluble Rh exposure between BDL and 6.782 µg/m³, whereas Linde *et al.* (2021) reported soluble Rh exposure between 0.002 and 47.752 µg/m³. These concentrations were not reported in the manuscript and were obtained from the authors upon request. Two participants (Rh #2 and Rh #3) had detectable urinary Rh excretion. Participant Rh #2 conducted activities such as stocktaking, normal production and cleaning (liberating dust). Rh #3 conducted transferring of batch to ignition and dug off the Rh batch. Therefore, this study found lower soluble Rh exposure compared to Linde *et al.* (2021) for similar work areas. Exposure to soluble Rh reported in this study was positively significantly correlated with both pre-shift ($r = 0.451$; $p = 0.011$) and post-shift ($r = 0.443$; $p = 0.013$) µg/g creatinine concentrations for the entire group (all six participants).

3.6.2 Influence of detection limits and urine dilution

The IPA HESCom recommends an LOD of 0.01 µg/L for Pt analysis. However, due to the dilution factor prescribed in the method of Crespo-Alonso *et al.* (2015), urinary Pt analysis had a LOD of 1.52 µg/L and urinary Rh analysis had a LOD of 2.48 µg/L, which is relatively high compared to the IPA HESCom's recommended value and the LOD reported by Linde *et al.* (2018) of 0.1 µg/L for Pt. Linde *et al.* (2018) reported 32 samples out of 118 samples BDL (27%), which included 29 samples from indirectly exposed workers. Indirectly exposed workers were expected to have low exposure to soluble Pt, and also low urinary Pt excretion. Therefore, employees directly exposed to soluble Pt had only three urinary Pt excretion samples BDL from 80 samples analysed (2%). The lower LOD reported by Linde *et al.* (2018) resulted in the detection of Pt in urine samples which may be diluted or have low Pt concentrations.

Considerably different to Linde *et al.* (2018), this study reported a large number of the urine samples analysed for Pt and Rh as below the detection limit, with 67% of Pt samples BDL (Table 3-3) and 83% of Rh samples BDL (Table 3-4). The acceptable range for creatinine levels is between 0.3–3 g/L (Ampath, 2023). From the 66 urine samples, 11 samples had a creatinine concentration level below 0.3 g/L, indicating that participants were very hydrated. Those 11 samples had corresponding BDL levels of urinary Pt and Rh excretion. However, the higher the creatinine levels (more concentrated urine), the more urinary Pt and Rh levels were reported. Three participants (Pt #1, Pt #3 and Rh #1) had soluble Pt exposure that was elevated or exceeded the OEL-RL of 2 µg/m³, Pt #3 had the highest respiratory exposure of up to 49 times the OEL-RL. The three participants had eight to 11 samples each that fell within the acceptable range for creatinine levels, and as a result had detectable urinary Pt excretion (Table 3-3). Two participants (Rh #2 and Rh #3) had elevated soluble Rh exposure that was still below the OEL-RL of 20 µg/m³, and also had nine urine samples each that fell within the acceptable range for creatinine levels; as a result, they had detectable urinary Rh excretion (Table 3-4). In conclusion, the high LOD for urinary Pt and Rh may have resulted in the underestimation of exposure to soluble Pt and Rh, because lower levels of Pt and Rh excretion could not be detected in the urine. However, it did allow for the identification of participants with higher soluble Pt and Rh respiratory exposure and, therefore, detectable urinary Pt and Rh excretion. The creatinine levels of participants also had an influence on the results, as the samples with creatinine levels below 0.3 g/L (less concentrated urine) were diluted even more for analysis and consequently had BDL results. The LOD reported in this study corresponds with the recommendations put forward by the IPA HESCom.

3.6.3 Optimal time to collect urine samples for Pt or Rh exposure monitoring

One of the study objectives was to identify the optimal time to do biological monitoring of employees exposed to Pt and Rh. The optimal sampling time could not be determined as the urinary excretion varied across the sampling days and pre-shift vs post-shift. The exact time of exposure to soluble Pt and Rh during the shift could play a vital role in the timing of the urinary excretion of the metal. Soluble Pt has a maximum excretion 10 hours after exposure (Schierl *et al.*, 1998). Therefore, if exposure took place in the morning at 10 am, the maximum excretion would be at 8 pm, when the employee is at home, and the other way around, if exposure took place at 4 pm, the maximum Pt excretion would be excreted at 6 am. The results from this study support the statement as three participants with Pt excretion had varying pre- and post-shift urinary Pt excretion levels that were detectable. Their combined detectable soluble Pt exposures were 11 out of 18 pre-shift and 10 out of 15 post-shifts. For urinary Rh excretion, Rh #2 had consistent urinary Rh excretion levels that were BDL pre-shift during the six consecutive days, and Rh #3 had urinary Rh excretion levels that were BDL post-shift for the first four days and on the fifth day, she had urinary Rh excretion that was BDL pre-shift like Rh #2.

For all the participants with detectable urinary Pt or Rh excretion, the last collected sample on the morning of day 6 was either below the LOD or one of the lowest detected concentrations of the week. This suggests that the Saturday morning following a week of soluble Pt and Rh exposure is not the best time to collect the sample, and that the urinary Pt or Rh excretion might return to a type of baseline concentration following the week. However, this needs to be confirmed by future studies.

3.7 Conclusion

Although the analytical method to determine the concentrations of Pt and Rh used in this study had a high LOD for both urinary excretion of Pt and Rh, it allowed for the identification of three participants with detectable levels of urinary Pt excretion and two participants with detectable levels of urinary Rh excretion. The urinary excretion of Pt and Rh results in Table 3-3 and Table 3-4 could be linked to their respiratory exposure and work activities such as packing of Pt salt into paper bags, dewatering of Pt salts, cleaning of the centrifuge and filtering and dissolving of Rh-Ir batch, stocktaking, cleaning plant, transferring batch to ignition and dug of the Rh batch. Although there was a positive and significant correlation for all six participants between both soluble Pt and Rh exposure with both pre- and post-shift creatinine concentrations for the entire group-level analysis, the individual-level comparisons did not show a significant correlation on the day-to-day results. There was no significant relationship between respiratory exposure and

urinary excretion of Pt and Rh of the individuals. This means that differences between low and high exposed workers could be identified using urinary metal concentrations but that differences between low and high exposure days could not be identified for individual participants. Furthermore, the specific days of peak exposure or the optimal time of sampling could not be determined. This method needs to be adjusted for possible future use by the refinery and specific times of exposure should be incorporated into the analysis.

3.8 References

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CHAPTER 4: CONCLUDING CHAPTER

In this retrospective study, the association between respiratory exposure and urinary excretion of workers exposed to soluble platinum (Pt) and soluble rhodium (Rh) at a precious metals refinery (PMR) in South Africa was evaluated. Furthermore, the study aimed to identify the optimal time for performing urinary biological monitoring. This chapter summarises the key findings and addresses the objectives and hypotheses as stated in Chapter 1. Additionally, the chapter discusses limitations that were encountered during this study and provides recommendations to the industry and also recommendations for future research on respiratory exposure and urinary excretion of Pt and Rh.

4.1 Key findings

This is the first study to report on the pre- and post-shift urinary excretion of both Pt and Rh in PMR employees who are occupationally exposed to soluble Pt and Rh. The methods followed during this study allowed for the identification of three participants who had detectable concentrations of urinary Pt excretion and two participants who had detectable concentrations of urinary Rh excretion. These results could be linked to respiratory exposure and the activities performed by these participants such as packing of Pt salt into paper bags, dewatering of Pt salts, cleaning of the centrifuge and filtering and dissolving of Rh–Ir batch, stocktaking, cleaning plant, transferring batch to ignition and dug of the Rh batch. The participants who had detectable levels of Pt in their urine worked in the Pt purification had respiratory exposure to soluble Pt [range: 8.250 to 99.224 $\mu\text{g}/\text{m}^3$ time-weighted average (TWA)], and PGM separation department where participants were anticipated to be mainly exposed to soluble Rh had respiratory exposure to soluble Pt (range: 0.605 to 6.382 $\mu\text{g}/\text{m}^3$ TWA). The participants who had detectable levels of Rh in their urine worked in the Rh purification and had respiratory exposure to soluble Rh (range: 0.334 to 6.782 $\mu\text{g}/\text{m}^3$ TWA). However, the biological monitoring results were not able to identify the specific day of the high exposure to soluble Pt and Rh. The study was limited by the high limit of detection (LOD) used in the method to analyse Pt and Rh in urine, which did not allow for the determination of metal concentrations from relatively diluted urine samples. Therefore, one biological monitoring sample per participant would not be sufficient in future studies. It is necessary to refine the method of biological monitoring with regard to urine collection and analysis methods for future use.

4.2 Objectives

Objective 1:

The first objective was to correlate workers' respiratory exposure to soluble Pt in the PMR to the urinary excretion of Pt obtained from urine collected pre- and post-shift. Three participants (Pt #1, Pt #3 and Rh #1) had detectable levels of Pt in their urinary excretion. The three participants had inhalation exposure exceeding the occupational exposure limit-restricted limit level (OEL-RL) of $2 \mu\text{g}/\text{m}^3$ up to 49 times, during some of the sampling days monitored (Table 3-3). The first objective was achieved as the Pearson correlation between respiratory Pt exposure and the urinary Pt excretion ($\mu\text{g}/\text{g}$ creatinine) results for the entire group of participants was found to be significantly positive. The entire group had respiratory exposure that was significantly positively correlated with pre-shift μg Pt/g creatinine concentrations ($r = 0.554$; $p = 0.001$). Furthermore, the respiratory exposure of the group had a stronger positive correlation with post-shift μg Pt/g creatinine concentrations ($r = 0.679$; $p < 0.0001$). None of the six participants had a significant correlation on an individual level between their respiratory Pt exposure and urinary Pt excretion (μg Pt/g creatinine).

Hypothesis 1a stated *"that the retrospective data from the PMR shows a statistically significant positive correlation between respiratory exposure and urinary excretion for Pt."* was partially accepted, as there was a statistically significant positive correlation found at the group level but not on the individual level, where there was no correlation found between the daily inhalation exposure levels and urinary excretion of Pt.

Objective 2:

The second objective was to correlate workers' respiratory exposure to Rh in the PMR to the concentration of urinary Rh obtained from urine collected before and after their shift. Two participants (Table 3-4) had detectable levels of Rh in their urinary excretion. Both participants had inhalation exposure, which was below the OEL-RL of $20 \mu\text{g}/\text{m}^3$. Although Rh #3 had higher soluble Rh respiratory exposure compared to Rh #2, both participants had similar urinary Rh excretion levels. This objective was achieved as the Pearson correlation between respiratory Rh exposure and the urinary Rh excretion (μg Rh/g creatinine) results for the entire group of participants was found to be significantly positive. The entire group had respiratory Rh exposure that was significantly positively correlated with pre-shift ($r = 0.451$; $p = 0.011$) and post-shift ($r = 0.443$; $p = 0.013$) μg Rh/g creatinine concentrations. Unlike the pre- and post-shift correlations in objective one, the post μg Rh/g creatinine concentrations were slightly lower than the pre-shift μg

Rh/g creatinine concentrations. None of the six participants had a positive correlation on an individual level between their respiratory Rh exposure and urinary Rh excretion ($\mu\text{g Rh/g creatinine}$).

Hypothesis 1b stated *“that the retrospective data from the PMR shows a statistically significant positive correlation between respiratory exposure and urinary excretion for Rh.”* and was partially accepted, as there was a statistically-significant positive correlation found at the group level but on the individual level, where there was no correlation found between the daily inhalation exposure levels and urinary excretion of Rh.

Objective 3:

The third objective was to describe how workers' urinary Pt and Rh excretion fluctuated over the sampling period. The results indicated that all participants had urinary Pt and Rh excretion which varied between pre- and post-shift excretion values during the week of sampling. The pre- and post-shift variation over the week for urinary Pt excretion had a coefficient of variation (CV) value of -322.44. Whereas, the pre- and post-shift variation over the week for urinary Rh excretion had a CV value of 933.72. Although the CV results are not reported elsewhere in this dissertation, they support the overall conclusion that an excretion pattern could not be determined between pre- and post-shift urinary excretion of these metals. Coefficient of variation values closer to zero indicate very little variation within a dataset, whereas values more than 100 indicate significant variation within the dataset. Therefore, this objective was not achieved.

Objective 4:

The fourth objective was to determine if there is an optimal time to collect urine samples for Pt or Rh biological monitoring. There was no consistent excretion pattern of Pt and Rh, and the specific days of peak exposure could be determined by the respiratory exposure results; however, the urinary excretion of the metal did not correlate with the respiratory results on an individual level. The paired t-test between pre- and post-shift urinary excretion of Pt and Rh reported no significant difference. Additionally, the pre- and post-shift $\mu\text{g/g creatinine}$ results were correlated significantly with one another for the entire group of six participants for both Pt and Rh which shows that they typically increased and decreased together indicating urine samples can either be collected pre- or post-shift for biomonitoring purposes. Therefore, this objective was achieved.

Hypothesis 2a stated *“that the optimal time to take urine samples will be in the morning before their shift, following exposure to soluble Pt the previous day. Morning urine samples are expected to be the most concentrated and therefore provide the most accurate measure of Pt exposure.”*

Additionally, hypothesis 2b stated *“that the optimal time to take urine samples will be in the morning before their shift, following exposure to soluble Rh the previous day. Morning urine samples are expected to be the most concentrated and therefore provide the most accurate measure of Rh exposure.”* Both hypotheses, 2a and 2b, were rejected, as the optimal time to conduct urinary biological monitoring of Pt and Rh could not be determined and it is therefore required to collect urine samples pre- and post-shift. Diluted urine, high LOD for Pt and Rh analysis in urine and the peak time of exposure to soluble Pt and Rh could have affected the number of urinary metal concentrations that were BDL.

4.3 Recommendations

The recommendations are based on the information received by the refinery for the purpose of this retrospective study. The main focus of the recommendations is placed on the biological monitoring of Pt and Rh, with less focus on the hierarchy of controls (elimination, substitution, engineering, administrative and PPE). Recommendations 1 and 2 are recommendations for future biomonitoring of Pt and Rh, and recommendations 3, 4 and 5 are recommendations for the PMR.

Recommendation 1:

Urinary creatinine concentrations varied between all the participants; 11 of the 66 urine samples had creatinine concentrations that did not fall into the acceptable range for creatinine (0.3–3 g/L). Urine samples with creatinine below 0.3 g/L were more diluted compared to the urine samples with creatinine levels above 0.3 g/L. The analysis method also required further dilution of samples, and contributed to the number of samples with BDL for Pt and Rh. Therefore, it is recommended that the method used for biological monitoring should be refined to account for the high detection limit of this analysis method, to be able to detect urinary Pt and Rh excretion with lower concentrations. Laboratories should be compared in order to use the laboratory using analytical methods and analytical instruments with the lowest LOD for urinary Pt and Rh. Additionally, workers can also be requested not to drink high volumes of fluids before giving the urine samples.

Recommendation 2:

The pre- and post-shift urinary excretion of Pt and Rh differed among individuals and within individuals. The half-life of Pt and Rh could have contributed to the variation in urinary excretion of pre- and post-shift values of Pt and Rh, as it has been reported by Schierl *et al.* (1998) that the maximum Pt excretion happens 10 hours after exposure. The exact time of exposure could not be determined, as activities were recorded once per day with no time indication of when the activities took place. Therefore, it is recommended that employees report hourly and include more

detail, such as specific tasks. Additionally, the use of a personal direct reading optical particle counter can be used to identify the exact time when exposure takes place.

Recommendation 3:

The employees who were anticipated to be mainly exposed to Pt had higher urinary Pt excretion (Table 3-3) when compared to employees who were in Rh departments. The employees mainly exposed to soluble Pt in this study was at the Pt purification and PGM separation areas, and employees mainly exposed to soluble Rh were at the Rh purification area. Employees from the Pt purification area had respiratory exposure to soluble Pt exceeding the OEL-RL of 2 µg/m³ by up to 49 times (99.224 µg/m³), and the employee from the PGM separation area had exposure to soluble Pt exceeding the OEL-RL of 2 µg/m³ by 3 times (6.382 µg/m³). On the other hand, employees who were in areas anticipated to be mainly exposed to soluble Rh had respiratory exposure to soluble Rh well below the OEL-RL of 20 µg/m³. Participants in Pt purification area, PGM separation area and Rh purification area used personal protective equipment (PPE) such as half-face or full-face respirators with ABEK1 P3 cartridges, amongst other PPE (Table 3-1). The employees who conducted tasks where soluble Pt exposure occurred also had detectable urinary Pt and Rh excretion levels, whereas employees at the Rh purification area had lower soluble Pt and Rh exposure, and had mostly urinary Pt or Rh excretion, which were BDL or, in a few cases, very low urinary Pt or Rh excretion levels. It is therefore recommended that when a risk assessment is done or control measures are implemented, focus should be on reducing the exposure of the employees who handle soluble Pt/Rh first. Additionally, it is recommended that the risk assessment be reviewed to include employees in the PGM separation area, for Pt exposure.

Recommendation 4:

Although recommendation 1 emphasises the need to focus on reducing the exposure of the employees who handle soluble Pt or Rh during their shift, the employees who do not handle soluble Pt or Rh during their shift should still be included in the risk assessment, medical surveillance, and implementation of control measures. These would be employees who do not handle soluble Pt or Rh during their shift work in areas such as the health clinic, security, laundry and laboratory. The motivation for inclusion is that the health clinic staff examine the PMR workers, and therefore may come into contact with contaminated PPE; security staff may come into contact with contaminated PPE when PMR workers are searched, and laundry workers handle contaminated PPE by discarding the disposable PPE or washing contaminated overalls.

Recommendation 5:

The ability of soluble Pt and Rh to cause a sensitisation reaction can happen at any level of exposure, even below the OEL-RL. Therefore, concern is raised in the Pt-purification department within the refinery as the maximum inhalation exposure of Pt #3 exceeded the OEL-RL of Pt up to 49 times, and Pt #1 had exposure 16 times more than the OEL-RL. Inhalation and dermal exposure should be prevented or kept as low as reasonably practicable in the PMR. This is a retrospective study; therefore, all the controls (engineering, administrative and PPE) currently in place might not have been included in the information received from the refinery. Therefore, the following general recommendations could be considered, and the controls currently followed in the refinery should be reconsidered. It is recommended that the hierarchy of control be followed in order to reduce the exposure to soluble Pt and Rh within the PMR. First of all, engineering controls are recommended, secondly administrative controls, and lastly, PPE are recommended to reduce exposure to soluble Pt and Rh within the PMR. An example of engineering control would be to install extraction fans at the source of exposure, thereby reducing the exposure of soluble Pt and Rh to the employee at the source of exposure and also any employee working in the area or passing through the area. Administrative controls would be limiting the number of employees in high risk areas (Pt purification, PGM separation and Rh purification), training employees on the health effects of soluble Pt and Rh exposure, training employees on how to properly use, store and clean their PPE, training employees on not positioning themselves between the source of exposure and the extraction fan, encourage employees to give their full co-operation during medical surveillance or future studies, and lastly provide employees with the appropriate PPE for the job. The refinery supplied the employees with half- or full-face respirators fitted with ABEK1 P3 cartridges (Table 3-1). The protection factor of the cartridges should be reconsidered to ensure that the protection factor would protect workers with soluble Pt exposure of almost 50 times the OEL-RL (99.224 $\mu\text{g}/\text{m}^3$). The use of disposable coveralls and gloves covering the wrist of the coverall could aid in preventing dermal exposure to soluble Pt and Rh.

4.4 Limitations

This study was limited by the following factors:

Limitation 1:

This is a retrospective study. Therefore, the PMR chose the laboratories used for analyses of the samples and approved the methods used for analyses. The PMR's reasons for approving the laboratories and methods could be for cost effectiveness or for convenience. The method used

by the SANAS-accredited laboratory to analyse the metal concentrations in the urine samples had a high LOD for both Pt and Rh. Additionally, participants had different creatinine levels in their urine, indicating different hydration levels among the participants. The metal excretion of participants significantly correlated with creatinine in their urine ($r = 0.404$; $p = 0.0006$ for Pt; $r = 0.353$; $p = 0.0032$ for Rh) (Table 3-5). Therefore, urine samples with lower creatinine levels contributed to the reporting of BDL for participants who had lower Pt or Rh urinary excretion concentrations.

Participants with lower levels of creatinine and lower urinary Pt or Rh concentrations contributed to the underestimation of Pt and Rh exposure. Additionally, meaningful correlations could have been missed between the inhalation exposure and urinary excretion of the metal. The laboratory should investigate whether it is necessary to dilute the urine sample to the level reported by Crespo-Alonso *et al.* (2015). The use of this non-commercial method limited the study to a large degree.

Limitation 2:

As reported by Schierl *et al.* (1998), Pt has a first half-life of 50 hours and a second half-life of 24 days, with maximum Pt excretion taking place 10 hours after exposure. The activities reported in this study were reported on a daily basis, and no time reference for when exposure activities took place was provided, which could have contributed to the variation in the pre- and post-shift urinary excretion of these metals. If the activities were reported hourly, or if a direct-reading optical particle counter was used, the peak exposure time would have been recorded and that could have explained the variation in urinary excretion of these metals. If peak exposure happens in the morning, higher urinary excretion could be expected at the end of the shift, whereas if the peak exposure took place in the afternoon, the higher urinary excretion would likely be reported during the next morning's pre-shift sampling. Therefore, a more definitive relationship between the exposure results and the excretion of these metals could have been formed. As this was not the case, an optimal time to do biomonitoring could not be determined.

Limitation 3:

The small sample population of six participants had many variabilities within the group and could have had an influence on the results. The participants were both male and female, the duration of employment varied between one year and 33 years, they were chosen from three different departments working with Pt and Rh in different forms, and also not one participant had the same daily activities during the week of the study.

Limitation 4:

Limited information was reported in connection to how employees used and stored their PPE. Not all participants used the same PPE, and it is unlikely that all employees utilised the PPE correctly as intended. Human error can influence the various results related to exposure and excretion.

4.5 Future studies

Future studies should consult with refineries well in advance to be informed about the procedure to be followed when reporting employees' exposure. Such refineries could be advised to implement reporting on activities hourly instead of daily. The use of a personal direct reading optical particle counter to identify peak exposure could assist in the reporting of the exact time peak exposure takes place. Increasing the number of participants included in future studies especially female participants to enable meaningful gender-specific statistical analyses. The method used for analysing urinary Pt and Rh excretion should be adjusted, or changed to a method which has a significantly lower LOD for urinary excretion of Pt and Rh. Additional samples per person (e.g., extending sampling days), more participants and limiting the volume of liquid consumed before giving a urine sample, should be implemented to ensure that a clear relationship between soluble Pt and Rh exposure and urinary excretion of Pt and Rh can be detected.

4.6 References

Crespo-Alonso, M. C., Rigoldi, A., Ibba, A., Zicca, L., Deplano, P., Mercuri, M. L., Cocco, P., Serpe, A., 2015. A simple, sensitive analytical method for platinum trace determination in human urine. *Microchem. J.* 122, 1–4. <https://doi.org/10.1016/j.microc.2015.03.016>.

Schierl, R., Fries, H., van de Weyer, C., Fruhmman, G., 1998. Urinary excretion of platinum industry workers. *Occup. Environ. Medicine.* 55, 138–140. <https://doi.org/10.1136/oem.55.2.138>.

APPENDIX A:



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**North-West University Health Research Ethics
Committee (NWU-HREC)**

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studies)

27 November 2024

ETHICS APPROVAL LETTER OF STUDY

Based on approval by the North-West University Health Research Ethics Committee (NWU-HREC) on 27/11/2024, the NWU-HREC hereby approves your study as indicated below. This implies that the NWU-HREC grants its permission that, provided the general and specific conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Association between respiratory exposure and urinary excretion of both soluble platinum and rhodium at a precious metals refinery

Principal Investigator/Study Supervisor/Researcher: Dr SJL Linde

Student: S Smit - 29970555

Ethics number:

N	W	U	-	0	0	1	6	7	-	2	4	-	A	1
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Institution Study Number Year Status
Status: S = Submission; R = Re-Submission; P = Provisional Authorisation;
A = Authorisation

Application Type: Single study

Commencement date: 27/11/2024

Expiry date: 30/11/2025

Risk:

Minimal

Approval of the study is provided for a year, after which continuation of the study is dependent on receipt and review of an annual monitoring report and the concomitant issuing of a letter of continuation. A monitoring report is due at the end of November annually until completion of the study.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, the following general terms and conditions will apply:

- The principal investigator/study supervisor/researcher must report in the prescribed format to the NWU-HREC:
 - Annually on the monitoring of the study, whereby a letter of continuation will be provided annually, and upon completion of the study; and
 - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.
- The approval applies strictly to the proposal as stipulated in the application form. Should any amendments to the proposal be deemed necessary during the course of the study, the principal investigator/study supervisor/researcher must apply for approval of these amendments at the NWU-HREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- Annually a number of studies may be randomly selected for active monitoring.
- The date of approval indicates the first date that the study may be started.

- In the interest of ethical responsibility, the NWU-HREC reserves the right to:
 - request access to any information or data at any time during the course or after completion of the study;
 - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;
 - withdraw or postpone approval if:
 - any unethical principles or practices of the study are revealed or suspected;
 - it becomes apparent that any relevant information was withheld from the NWU-HREC or that information has been false or misrepresented;
 - submission of the annual monitoring report, the required amendments, or reporting of adverse events or incidents was not done in a timely manner and accurately; and/or
 - new institutional rules, national legislation or international conventions deem it necessary.
- NWU-HREC can be contacted for further information via Ethics-HRECApply@nwu.ac.za or 018 299 1206

Special in process conditions of the research for approval (if applicable):

- Please provide the NWU-HREC with a copy of the proof of attendance of the Integrated Research Integrity Management System (IRIMS) training course for Dr SJL Linde and Prof A Franken, as soon as they receive it, after attending the first IRIMS training opportunity presented in 2025. Please note that failure to submit this document timeously will result in the termination of the ethics approval of the current study.

As the study progresses the aforementioned conditions should be submitted to Ethics-HRECProcess@nwu.ac.za with a cover letter with a specific subject title indicating "Outstanding documents for approval: NWU-XXXXX-XX-XX." The letter should include the title of the approved study, the names of the researchers involved, that the documents are being submitted as part of the conditions of the approval set by the NWU-HREC, the nature of the document i.e. which condition is being fulfilled and any further explanation to clarify the submission.

The *e-mail*, to which you attach the documents that you send, should have a *specific subject line* indicating the nature of the submission e.g. "Outstanding documents for approval: NWU-XXXXX-XX-XX". The e-mail should indicate the nature of the document being sent. This submission will be handled via the expedited process.

The NWU-HREC would like to remain at your service and wishes you well with your study. Please do not hesitate to contact the NWU-HREC for any further enquiries or requests for assistance.

Yours sincerely,

pp



Chairperson NWU-HREC

Current details: (23239522) G:\My Drive\8. Research and Postgraduate Education\9.1.5.4 Templates\9.1.5.4.2_NWU-HREC_EAL.docm
20 August 2019
File Reference: 9.1.5.4.2

APPENDIX B:



14 November 2025

LANGUAGE EDITING STATEMENT

I, Jannetje Levina De Kock, hereby declare that the dissertation

Association between respiratory exposure and urinary excretion of both soluble platinum and rhodium at a precious metals refinery

by

Stephanie Smit
29970555

in fulfilment of the requirements for the degree
Master of Health Science in Occupational Hygiene
at the North-West University,

- has been edited for language correctness and spelling.
- has been edited for consistency (repetition, long sentences, logical flow)

No changes have been made to the document's substance and structure (nature of academic content and argument in the discipline, chapter and section structure, and headings, order and balance of content, referencing style and quality).

J L DE KOCK

APPENDIX C:

Turnitin showed 12% similarity with internet sources, and the AI detection score was < 20%. Below is a screenshot of the summary of the report.

The screenshot displays the Turnitin interface for a document review. At the top, the Turnitin logo is on the left, followed by a 'Go to New View' button. The document title 'STEFAN LINDE' and a file path '20686641/2025_OHHRIL_PG_S_Smit_2025-11-20.docx' are shown in the center. On the right, navigation arrows and a '1 of 1' indicator are present. The main content area features a purple header with the NWU logo and the document title: 'Association between respiratory exposure and urinary excretion of both soluble platinum and rhodium at a precious metals refinery'. Below the title, the author's name 'Stephanie Smit' is listed, along with an ORCID iD link: 'orcid.org/ 0009-0003-1860-1939'. On the right side of the document preview, a red bar indicates a similarity score of '12'. Below this, a vertical toolbar contains icons for document actions, including a download icon, an information icon, and an 'AI' detection score indicator showing '*%'. The document preview itself is partially obscured by a grey overlay on the right side.