INTERNATIONAL PLATINUM GROUP METALS ASSOCIATION

Biomonitoring of platinum in urine of workers:

Guidance on good practice

Disclaimer

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Table of Contents

1 Glossary of terms and abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
EHS	Environment, Health and Safety
ICP-MS	Inductively Coupled-Mass Spectrometry
IH	Industrial Hygiene
IPA	International Platinum Group Metals Association
OEL	Occupational Exposure Limit
OH	Occupational Health
LOD	Limit of Detection
LOQ	Limit of Quantification
PGM	Platinum Group Metals
PPE	Personal Protective Equipment
PSS	Platinum Salt Sensitisation
RPE	Respiratory Protective Equipment
SEG	Similar Exposure Group
WHO	World Health Organization

2 Introduction

Companies have legal and ethical obligations to protect the health of their workers, including through minimising the potential for ill health from occupational exposure to chemical substances. Various containment and exposure control measures may be put in place to prevent or limit exposure to chemical substances and to comply with regulatory limits (Occupational Exposure Limits, OELs) or to ensure exposure levels are minimised as far as reasonably practicable. Attempts to verify exposure levels traditionally involve sampling and analysis of workplace air, sometimes supplemented with wipe sampling of surfaces and/or skin. These measurements provide insight into levels of a particular contaminant in the workplace, i.e. the external environment experienced by workers. But they do not measure the actual exposure of a worker, since this will be affected by the use of personal protective equipment (PPE) including especially respiratory protective equipment (RPE), organisational effects and controls such as how long workers spend in particular areas, unplanned events such as spills, as well as individual physiological and behavioural differences between workers.

Exposure biomonitoring measures the levels of chemical contaminants within biological tissues, such as urine, blood, or hair. It therefore provides information on the total exposure – through all routes (inhalation, ingestion, skin contact) – of an individual worker.

As well as providing information on each worker's total individual exposure, comparisons of biomonitoring results of workers within and between Similar Exposure Groups (SEGs) can provide indications of what the cause of any higher-than-expected exposure levels might be. If the results for an SEG are broadly consistently higher than those for another SEG, it indicates that the difference is likely to be organisational; for example, differences in the levels of contaminant in the working environment, differences in how long workers spend in particular work areas or performing particular tasks, or differences in assigned PPE. Conversely, if a minority of workers within an SEG show markedly higher biomonitoring results than the other workers in that SEG, it can indicate that those workers have had a longer career working with the chemical, if that chemical accumulates in the body over time, or it can be suggestive of lapses in individual workplace behaviours, such as not wearing PPE correctly at all times.

Within platinum group metals (PGM) refining and processing where the formation of chloroplatinate intermediates is unavoidable, the industry has made great efforts to contain processes and reduce levels of chloroplatinates in the workplace to which workers may become exposed. Incidences of platinum salt sensitivity (PSS) have drastically reduced over the years, but cases do still occasionally occur. Conducting biomonitoring is an additional tool by which greater insight can be gained into worker exposures that can help inform further appropriately targeted exposure reduction initiatives. Biomonitoring workers before and after a change in control measures (e.g. installation of a new engineering control, implementation of new organisational exposure control measures, or provision of new PPE) can empirically demonstrate the impact of the new measure.

Chemical analysis of chloroplatinates within biological tissues is not currently possible; only measurement of total Pt content is feasible. Platinum that is absorbed into the body is subsequently excreted predominantly in the urine. Pt-urine levels are a reflection of both chronic and recent exposure and use of urine avoids the need for drawing blood. Consequently, almost all occupational and general population biomonitoring data available for platinum are measurements of total Pt in urine.

This document provides good practice guidance on the occupational biomonitoring of total Pt in urine.

Measurement of Pt-urine levels is informative only for understanding workplace exposure at an individual level. It does not provide any information about or insight into the health status of the individual and whether or not the platinum has or might have any effect on the individual's health.

Urine biomonitoring measures the *concentration* of the chemical of interest in urine. This will be affected not only by the amount of exposure to the chemical of interest but also by the hydration status of the individual and their frequency of urination and the volume of urine voided on each occasion. Urine biomonitoring results can be 'normalised' by additionally measuring in the urine the concentration of creatinine (a natural metabolic waste product that is excreted from the body in the urine at reasonably constant rate over time) and reporting biomonitoring results of the chemical relative to creatinine, e.g. nanograms of platinum per gram of creatinine (ng Pt/g creatinine).

3 Good Practice Guidance on Pt biomonitoring

What is/are the objectives of the biomonitoring?

- Before embarking on a targeted biomonitoring campaign or implementing a programme of routine biomonitoring, it is important to agree and document its objectives and then design the biomonitoring to meet those objectives.
- Common objectives of occupational biomonitoring include one or more of the following:
    - To meet a legal obligation – in which case the biomonitoring programme must be designed to the legislated requirements, but it may be possible to fulfil additional objectives within the same biomonitoring programme
    - To gain a basic understanding of the (range of) tissue concentrations of the target substance (e.g. Pt-urine levels) within the workforce – either as a one-off or as a regular (e.g. annual) snapshot to broadly track levels over time
    - To better understand the levels of exposure associated with specific tasks or job roles
    - To help identify where either workplace exposure controls may not be working as expected, or where worker behaviour and adherence to safety requirements and procedures may not be as expected
    - To confirm the effect on worker exposures of a new containment or other exposure control system
    - To understand the magnitude of exposure experienced by workers present during a spill

- In addition to the above, biomonitoring can be used as a research tool – for example to better understand the kinetics of different forms of platinum in the body and how quickly or slowly they are excreted – but where human biomonitoring is used for research purposes, there may be additional requirements that must be complied with, including ethical approvals. The design and conduct of scientific research studies is beyond the scope of this guidance document.

- Whatever the specific objectives identified at the time for a routine biomonitoring program or individual campaign, consideration should be given to maximizing the utility of the results. If air sampling, dermal sampling and/or surface wipe sampling for platinum are also conducted at a site, consideration should be given to coordinating the sampling to allow linking of results and gaining greater insights than would be possible if each type of sampling was performed in isolation. In all cases, data should be recorded in such a way that they can be linked to other exposure data or health data either at the time or in the future. The ability to link the data to other salient information, such as time-relevant records of job tasks, exposure controls and their performance, and even weather conditions, is also recommended.

Who should undergo Pt biomonitoring?

- Which workers should undergo biomonitoring for platinum will depend on the objective(s) of the biomonitoring programme.
- Routine biomonitoring would typically include all workers that are expected to be exposed to chloroplatinates as part of their work. Hence, it would normally be those workers that are included in routine health surveillance for PSS.

- Additional biomonitoring campaigns may provide further valuable information; for example, prior to and following the introduction of a new exposure control measure (e.g. an engineering control, organisational control, PPE)
- Following a loss of containment (spill) of chloroplatinates, biomonitoring of potentially exposed workers can provide insight into the extent of exposure, and repeated measurements can track how each worker's Pt-urine levels subsequently decrease following the incident.
- In all cases, except where it is legally mandated, consideration should be given to whether participation in biomonitoring should be an obligation of employment and written into worker contracts or if participation should be the decision of each individual worker. Especially where participation is voluntary, explicit written consent should be obtained from each worker (see Appendix A). Early and open engagement with the workforce and labour unions about the intentions of the biomonitoring and the restrictions and protections in place to safeguard worker rights and confidentiality is encouraged.

Who should organise biomonitoring, collect and analyse samples, and have access to the results?

Organisation of biomonitoring

- A biomonitoring coordination team should be established comprising representatives of relevant stakeholder groups, including Occupational Health/Medical Department, Industrial Hygiene, EHS, Labour union or other workforce representation group, and site management.
- The biomonitoring coordination team should agree the objectives of the biomonitoring and develop a suitable programme or campaign of biomonitoring accordingly, while considering opportunities to maximise the value of the results.
- The team should be responsible for:
    - ensuring all relevant laws and legal obligations are understood and adhered to;
    - engaging with the workforce and clearly communicating both the intentions (objectives and benefits) and the limitations of the biomonitoring;
    - ensuring the agreed infrastructure, policies, procedures, and physical and personnel resources are in place (e.g. procurement of suitable urine sample containers; identification and reservation of a location(s) for sample collection suitable for male and female workers; provision of simple and clear instruction sheets for workers to follow when providing a urine sample; identification and contracting of a suitable laboratory to analyse the samples, and means to store and deliver samples to the laboratory in accordance with applicable regulations; systems to identify and anonymise and record samples and results as necessary to meet the agreed level of privacy and data protection; etc).

Sample collection

- Different countries and territories may have different legal or cultural expectations on who may collect urine samples from workers. In some cases, it must be administered by a medical professional (occupational physician or nurse), while in others an Industrial Hygienist or other EHS professional may be tasked with this. In either case, the actual collection of the sample should be unsupervised; the OH or IH professional is there to provide the worker with the instruction sheet and correctly labelled sample container, to provide any further guidance and answer questions, to receive and store the returned sample container once filled, and to assist where necessary in the completion of the questionnaire.

- In all cases, there must be appropriate training, in particular on hygiene and avoiding contamination of the sample.

Sample analysis

- Analysis of urine samples must be conducted by suitably qualified persons working within an approved analytical laboratory.

Access to sample results

- There should be company policies and procedures in place that ensure only those persons approved and agreed by the workforce (i.e. the biomonitored workers) have access to the biomonitoring results. It is common practice that only the medical department should have access to the non-anonymised results and know the Pt-urine level of any individual worker, while anonymised individual results and as grouped by job role or department are made available to the EHS team and facility management.
- In all cases, each worker participating in the biomonitoring programme should be informed of their own results by the medical department and be given appropriate guidance on the meaning of the results and the opportunity to ask questions.
- Where only the medical department have access to the non-anonymised results, the occupational physician or nurse should counsel any worker showing an unexpectedly high Pt-urine level, provide guidance on how to limit exposure, and suggest that the worker shares their result with their supervisor – but it is the worker's decision whether or not they disclose their result.

When should samples be collected?

- When and how often Pt biomonitoring should be performed will also depend on the objectives of the biomonitoring.
- Each worker is likely to have their own 'baseline' Pt-urine level, dictated by their individual physiology and their non-occupational exposure to platinum (e.g. from Pt-containing dental restorations or implanted medical devices and through dietary exposure to Pt in food) as well as their occupational exposure. And this level may change over time.
- There are limited data available on how quickly different platinum compounds are absorbed into and subsequently excreted from the body following exposure. It has been reported in the scientific literature that Pt-urine concentrations are highest approximately 10 hours after exposure, and that Pt-urine levels subsequently halve every 50 hours initially followed by a slower elimination phase. A study published in the literature also reported that workers' urinary Pt excretion did not decrease following two weeks' vacation. But the experience of a major PGM refining and fabricating company that conducts routine Pt-urine biomonitoring of its workforce indicates that the initial elimination half-life may be much shorter than suggested by these limited published studies (see Appendix A for further information on Pt kinetics).
- Therefore, it is recommended that:
    - To understand the current 'baseline' Pt-urine level of an individual worker, workers within an SEG, or the whole potentially-exposed workforce (i.e. typically all workers included in medical surveillance for PSS), urine should be collected pre-shift, ideally after a weekend or other short (couple of days) break from work. Within a routine biomonitoring programme, this should be repeated at least annually. Measurement of Pt-urine level may also be included in the pre-employment medical screening procedure to establish the initial baseline level. Pt-urine level should also be measured whenever a worker included in the

biomonitoring programme ends their current job role, whether it is to start a new role in the company or to leave the company.
  - For understanding the level of occupational exposure associated with a particular task or set of tasks associated with a job role or SEG, urine should be collected pre-shift and again at the end of the shift.
  - For understanding the magnitude of exposure to chloroplatinates resulting from a loss of containment incident (spill), urine should be collected at the end of the shift. If the incident occurred less than four hours before the end of the shift, urine should also be sampled pre-shift the following day.
  - For tracking the subsequent reduction in Pt-urine levels following a peak exposure, urine should be collected at the end of the shift (Day 0), and then pre-shift the following day (Day 1) and pre-shift for the subsequent two days (Day 2 and 3), and weekly thereafter starting on Day 7 until levels have decreased to a plateau.
  - For understanding the impact of a new exposure control measure, urine samples from affected workers or a subset of affected workers should be collected pre-shift and post-shift prior to implementation of the new measure. This should be repeated (i.e. urine sampled pre-shift and post-shift) following implementation of the new measure, ensuring that all other conditions and possibilities for exposure are the same on each occasion.

Where should samples be collected?

- It is vital that all practicable measures are taken to minimise the potential for contamination of samples. Urine samples should be collected in a clean area where no platinum is present. This should be away from the part of the site where platinum is present or contamination might be anticipated.
- If a site has a medical centre or clinic on a different part of the site to where PGM processing occurs, this may be the most appropriate option but does not have to be.
- If the urine sample is being collected pre-shift, the worker should attend and provide the urine sample before entering the part of the site where platinum is present. Hence, they should be in their normal clothing.
- If the urine sample is being collected post-shift, the worker to be sampled should have finished their shift, removed their PPE and work clothes, showered, and be wearing their normal clothing.

How should samples be collected, identified, stored, analysed, and disposed of?

Sample collection

- Avoiding contamination of samples is paramount. Typical Pt-urine levels within the general population are up to around 10 nanograms per litre of urine (*a nanogram is a billionth of a gram, a single grain of table salt is typically around 60,000 nanograms*). Therefore, there is a risk of sample contamination substantially affecting the result if there is platinum in the air or on the skin or clothing of either the worker being sampled or the worker administering the sampling.
- The worker being sampled should have showered, be in normal clothing, and have washed hands.

- The person administering the sampling should not on the day of sampling have been in a work area where platinum is present. They should wear fresh, clean nitrile or latex gloves.
- Standard urine sampling containers may be used to collect the urine. Pt contamination of such containers is not a known concern, and this can be confirmed through the analysis of control samples. The laboratory used to analyse the samples will often provide sample collection containers to be used. The lids of the containers should remain on at all times except when being filled and later when analysed.
- A mid-stream sample should be collected. Alternatively, if preferred, a complete void sample may be collected and a 20 ml sample taken from this if the additional resource requirements are available.

Control samples

- To help confirm procedures and practices are adequate and do not result in contamination of samples, control samples should also occasionally be taken and analysed. A sample container should be filled with water from a tap in the location where workers provide urine samples. Alternatively, a urine sample may be collected from a colleague that has no occupational exposure to platinum. The control sample should be labelled and placed in a sealed bag in the same way as is done for urine samples and sent with the urine samples to the laboratory for analysis.
- On days when numerous urine samples are collected, it is recommended that two control samples are additionally taken: one control sample before the first urine sample is collected, and the second control sample after the last urine sample of the day is collected.

Sample identification

- Prior to the collection of urine samples, a robust system of sample identification and record-keeping must be established that ensures the agreed level of anonymisation while also maximising the utility of the sample result.
- As samples and/or results are anonymised, there must be clear records linking each sample ID to the appropriate individual worker, date and time. Collectively, the systems in place should ensure that different types of data can be correctly linked together, including other exposure data, exposure controls data, job history information, and medical surveillance data. This is especially important when other forms of exposure measurement (e.g. air sampling, skin sampling, surface wipe sampling) have been undertaken in parallel.
- The system should ensure that only those persons approved to see non-anonymised data are able to do so, while the utility of the data is maximised. If only the medical department is permitted to see the non-anonymised results, the system for anonymisation and sample identification should be agreed between the medical department and the wider biomonitoring coordination team.

Sample storage

- Each sample should be kept in its closed sample container until it is ready to be analysed.
- Samples should generally be kept refrigerated, but storage at ambient temperature is acceptable and may be more practicable at times such as during transport.
- Consideration should be given to freezing samples (at -20°C) if they will not be analysed for more than a few weeks following collection.
- The laboratory responsible for analysing the samples may require more conservative storage conditions in accordance with its internal protocols.

Sample analysis

- Analysis of urine samples for total Pt content should be conducted by an accredited laboratory that participates in an appropriate external proficiency testing verification programme, such as the German External Quality Assessment Scheme that is used by laboratories in many countries.
- Samples should be analysed using a method – typically high resolution ICP-MS[1] – with an appropriate limit of detection (LOD) and limit of quantification (LOQ). An LOQ of 1 ng/L should be targeted; it should be no higher than 10 ng/L.
- Samples should additionally be analysed for creatinine content, and results for Pt provided as ng Pt/L urine and as ng Pt/g creatinine.

Sample disposal

- Urine samples may be used only for the purposes intended and approved by the donor; no additional analyses should be conducted.
- Once a urine sample has been successfully analysed for total Pt content and creatinine content it should be disposed of in accordance with the laboratory's standard procedures for clinical waste.

How should results be interpreted, reported, and recorded?

Interpretation of results

- **Pt-urine biomonitoring is a form of exposure biomonitoring; it is a measure of the total exposure of an individual worker to platinum from all sources and via all routes (inhalation, dermal, oral). It is not a measure of effect, harm, or health.**
- Attempts have been made to correlate Pt-urine levels with risk of Pt sensitisation, but no correlation has been found.
- When introducing and implementing a Pt-urine biomonitoring programme, it is important that the purpose and limitations of the biomonitoring are made clear and the workforce understands that their Pt-urine level represents their personal level of exposure, but it provides no information about their health.
- There is not a consensus on whether Pt-urine levels should be normalised to creatinine. It is therefore recommended that results are given both as ng Pt/L urine and as ng Pt/g creatinine.
- Where the concentration of creatinine itself in the urine is particularly high or low – indicating excessive dehydration or hydration – the biomonitoring results for platinum, either as ng Pt/L urine or ng Pt/g creatinine may become spurious. Therefore, criteria should be established to decide whether a result is considered acceptable or not. A creatinine concentration of 0.3-3 g/L as used by WHO and ACGIH is recommended for this purpose (see Acceptability Criteria). Although creatinine is used to normalise urine analysis results due to its relative consistent rate of elimination, the excretion of creatinine does vary and may be affected by factors such as whether an omnivorous versus a vegan diet is consumed (Abraham et al, 2023).
- In considering Pt-urine results, the absolute values may have less significance than their relativity to each other. If, for example, the results for the majority of workers within a Similar Exposure Group (SEG) are higher than expected, this can indicate an exposure control (e.g. containment system or ventilation system) may be faulty or not be working

[1] If ICP-MS that isn't high-resolution is used it can overestimate results two-three fold

as expected. Alternatively, if within an SEG the results for one or two individual workers are markedly higher than those of the rest of the group, this can suggest they have performed tasks and experienced exposures not typical of their SEG or that individual worker behaviours may be responsible.

- Outside the workplace, there are limited options for notable exposure to platinum; hence, within an occupational biomonitoring programme, Pt-urine levels above 10 ng/L or about 5 nmol Pt/mol creatinine would generally be assumed as representative of occupational exposure (Morton et al, 2014; ACGIH, 2024).
- Non-occupational exposure to platinum can occur, though, and should be considered. Individuals that have received platinum-based chemotherapy for cancer treatment may continue to show significantly elevated Pt-urine levels for years after completion of treatment. Such individuals would therefore not normally be included in an occupational Pt-urine biomonitoring programme. Other causes of elevated Pt-urine levels include Pt-based dental restorations (see Appendix).

Acceptability criteria

- Analysis of control samples should report acceptably low levels of platinum, i.e. concentrations that do not compromise the interpretation of the urine sample results. Very low concentrations of platinum may be present in the tap water itself, but if the control sample result is greater than 10 ng/l contamination should be suspected.
- Creatinine concentrations should be in the range of 300-3,000 mg/l (2.65-26.5 mmol/l, sometimes rounded to 3-30 mmol/l), the range traditionally used for confirming acceptability of urine samples (Cocker et al, 2011).
- Where the urine analysis shows the creatinine concentration to be outside the acceptable range, the worker should be retested and advised on hydration on the day the urine sample will be taken.

Recording and reporting of results

- While Pt-urine biomonitoring is solely a measure of exposure, it requires donation of a biological sample and each result is personal to the individual. In most territories, therefore, Pt-urine results should be treated as confidential medical data, recorded within workers' medical files to which only the medical department has access, and be known to only the individual worker and the medical department.
- Where an individual worker's Pt-urine level is found to be notably elevated, the occupational physician or nurse may counsel the worker on exposure avoidance and suggest they share the information with their line manager, but ultimately that decision should be solely the right of the individual worker.
- It is useful and appropriate, though, for the medical department to share anonymised and aggregated data, where no individual can be identified, with relevant colleagues, including those from the Industrial Hygiene and EHS departments as well as team supervisors and facility management, in order to understand and track exposures at a facility and identify opportunities for interventions to further reduce exposure. It is also important that these results are shared with all workers participating in the biomonitoring programme.
- In developing a Pt-urine biomonitoring results template, consideration should be given to the importance of recording results in such a way that they can be linked to SEGs, work areas, tasks, PPE, dates & times, and other types of exposure data (air samples, dermal samples, and/or surface wipe samples) that may have been collected concurrently. For pre-shift samples, the time since last exposure will be critical information. Explicitly

recording within the data template, the laboratory used for the analysis, the analytical method, and the LOD/LOQ is also advised. Consideration should also be given to what analyses might be attempted in the future and the template designed to collect the data necessary to so. For example: recording if the last shift worked was a dayshift or a night shift would, once sufficient data were available, enable a comparison to explore if exposures experienced overnight might be different from those during the day. Similarly, recording the number of years employed would enable insight to be gained into how exposures amongst relatively new workers compare against long-serving employees. The collection of any supplementary information must consider maintaining the agreed level of confidentiality and anonymity of the biomonitoring data; hence, perhaps only the medical department would have access to the full template data, but could provide an abridged version to other departments.

4 Training

It is important that all persons involved in the operation of the Pt-urine biomonitoring programme (including the collection, storage, and analysis of urine samples, and the recording and reporting of results) are appropriately trained. In particular the need to avoid sample contamination is critical, including through procurement of sample containers, use of a clean area for sample collection, and individual hygiene. The purpose and limitations of Pt-urine biomonitoring should be included in induction and regular training programmes of all workers expected to participate in Pt-urine biomonitoring.

Appendix A Example consent forms

Note: these example consent forms are for information purposes only. Companies undertaking or considering workplace biomonitoring programmes must ensure compliance with all applicable local regulations and requirements.

A.1 Mandatory biomonitoring

As part of the occupational chemical exposure monitoring programme at [*company*], it is a requirement and condition of your employment that you participate in the platinum urine biomonitoring programme and submit urine samples from time to time for the measurement of platinum.

It is requested that you confirm your understanding and approval of this requirement by signing the declaration below authorizing the testing laboratory to release the results to [*company*] medical department:

Declaration for participation in [company] platinum biomonitoring programme

I, _____

ID number: _____

hereby confirm that:

1. I understand that it is a condition of my employment at [*company*] that I provide a urine sample from time to time for the measurement of platinum.
2. The purpose of the urine sampling has been explained to me and I understand that it will provide information only about my exposure to platinum and will not provide any information about my health.
3. any urine sample that I provide to [*company*] for the purposes of chemical exposure biomonitoring will be my own.
4. I authorize the testing laboratory used by [*company*] to analyse the provided urine samples for quantification of platinum content and creatinine content, and further to disclose to [*company*] medical department the results of the analyses.
5. I understand that only the [*company*] medical department will be able to identify my results as mine and will only disclose my results to me. Only anonymised Pt-urine results will be disclosed by the medical department to others.

Signature

_____

Signed at _____on the___/__/_____

A.2 Voluntary biomonitoring

As part of the chemical exposure monitoring programme at [*company, site*], employees with potential exposure to chloroplatinates are invited to participate in the biological monitoring programme. This involves the measurement of the concentration of platinum in a urine sample. The results will be used to check that your exposure to platinum at work is being adequately controlled.

Biomonitoring of platinum in urine gives useful information about your exposure to platinum. It does not provide any information about your health.

You do not have to take part in this programme. If you decide not to take part, this will not affect your conditions of employment. Similarly, if you do take part, the result of your test will not affect your conditions of employment.

If you choose to participate in the programme, your Pt-urine biomonitoring result will be recorded in your [*company*] medical file, to which only the medical department has access. You will be offered a copy of your results.

The Medical Department will share anonymised biomonitoring results with other EHS teams and with [*company, site*] management to allow those groups to understand how well exposures are being controlled and what further actions may be necessary to decrease exposure levels of specific teams or work areas.

If the Medical Department believe your biomonitoring result is high, they will provide you with advice on how to reduce your exposure. They may recommend that you share your result with your supervisor, but this will be your decision.

If you require more information at any time or have any concerns about the programme or your results, you can contact [*enter name of responsible person*] on [*contact details*].

Section A: To be completed by the employee

The purpose of this biological monitoring programme and the actions which might be taken to control my exposure have been explained to me by [*enter name of responsible person*].

I, [*worker name*], agree to provide a sample of urine for the measurement of platinum under the following conditions:

1. The sample I provide will **only** be analysed for platinum and creatinine.

2. The result of my test will be sent by the laboratory to the Medical Department.

3. The Medical Department will keep my results confidential, and only share anonymised biomonitoring data with other [*company*] groups.

4. I would/would not* like to receive my own result and have it explained to me.

** Delete as appropriate*

Signature of employee: …… Date: ……

Section B: To be completed by the biological monitoring programme champion

I agree to abide by the above conditions.

Signature of biological monitoring programme champion:……..

Name (print)…… Date: ……

Notes

Note: A signed copy of the form should be held by the employer and employee.

Appendix B Example questionnaire

Please complete the questionnaire below either immediately before or after providing the urine sample.

Pt-urine biomonitoring questionnaire

Date _____ Time _____

Is the urine sample provided: pre-shift ☐ post-shift ☐

Information about you

Site _____ Work area _____

Department _____ Team _____

Information about your work activities and exposure to platinum

Please describe the activities / tasks you performed during your last shift.* For each task, list the PGM substances involved, the approximate time spent on the task, and the PPE worn.

** If you are providing a 'post-shift' urine sample, please provide information about the shift you have just finished. If you are providing a 'pre-shift' sample, please provide information about the last shift you worked.*

Date of last shift: _____ Was your last shift: Day ☐ Night ☐

Was your last shift: Weekday ☐ Weekend ☐

Work area	Task	PGM substances used	Approximate duration	PPE worn

Have you been involved with any activity recently (last three weeks) that may have resulted in a higher-than-normal exposure to platinum; for example, a spill or a stock take?

Yes ☐ No ☐

Please provide details:

_____

_____

_____

_____

Other exposure measurements of platinum exposure

Were you wearing a personal air sampler during the shift? Yes ☐ No ☐

Were wipe samples of your skin taken during or at the end of your shift? Yes ☐ No ☐

Were wipe samples of your PPE/RPE taken during or at the end of your shift? Yes ☐ No ☐

Factors that may affect your Pt-urine result

How many dental restorations that may contain platinum do you have? _____

Please provide below information about the type and amount of liquids you have consumed during the last 8 hours.

Approximate Time	Type of drink	Approximate volume consumed

Appendix C Example instruction sheet for providing a midstream urine sample

Introduction

- This instruction sheet provides information about how to provide a urine sample that can be analysed for platinum content. This will give a measure of your level of exposure to platinum from doing your job. It does **not** provide any information about your current or future health.
- Before providing a urine sample:
    1. Read this instruction sheet in full;
    2. If you do not understand anything or have any concerns, ask the person that gave you this sheet. This should be a medical doctor or nurse, or a member of your company's EHS team.
- These instructions are to collect a 'midstream' urine sample. This is a sample of the middle part of the urine flow. You should not collect the first part or the last part of urine flow.
- If you experience difficulty in aiming the flow of urine into the sample bottle, you may ask for a larger sterile container into which you can pass a whole urine sample ('complete void'). The medical doctor/nurse/EHS colleague will then remove a sample of this urine and put it in a urine sample bottle.
- Your privacy should be respected when providing a urine sample.

Equipment

You should have been given:

- A copy of these instructions
- A labelled urine sample bottle
- A labelled plastic bag

Do not open the urine sample bottle until you are ready to provide the urine sample.

Check the label on the urine sample bottle and the label on the plastic bag both have your name or your identification number correctly written. If your name or identification number is not correctly written on the labels, ask the person who gave the bottle and bag to you to correct the labels.

Ensure you know how much urine you should collect in the sample bottle.

Procedure

The steps that should be followed to collect a midstream urine sample are listed below. Please follow them in order.

1) Wash your hands.
2) Remove the lid of the sample bottle. Do not touch the inside of the bottle or the inside of the lid at any time.
3) Begin to pass urine into the toilet as you would normally.
4) After about 2 or 3 seconds, stop and then start to pass urine into the sample bottle. Do not allow the top of the bottle to touch your skin.
5) When there is sufficient urine in the sample bottle, stop and then pass any further urine into the toilet as you would normally.
6) Replace the lid of the sample bottle and tighten.
7) Wash your hands.
8) Place the sample bottle in the plastic bag and seal the bag.
9) Hand the sealed bag containing the sample bottle back to the medical doctor/nurse/EHS colleague.

Appendix D Platinum kinetics and urinary excretion

There are a number of published studies reporting Pt-urine levels of different occupational and general population cohorts. Pt-urine levels in the non-occupationally exposed general population are typically in the single digit ng/L and ng/g creatinine range, with 95th percentile levels up to *circa* 20-30 ng/L. Individuals with Pt-based dental restorations have been found to have higher Pt-urine levels than those without such dental work. Studies of health care workers handling platin chemotherapeutics have reported Pt-urine levels of up to 1,000 ng/L or more, and in cancer patients themselves levels may be several thousand ng/g creatinine. A study of women with silicone implants reported Pt-urine levels of 400-2,950 ng/g creatinine (Lykissa and Mahara, 2006), but significant doubts have been raised about this study (Lane, 2006).

Pt-urine levels of up to several thousand ng/g creatinine have also been reported amongst PGM industry workers directly exposed to Pt compounds, e.g. within refineries. A recent study of PGM refinery workers in South Africa reported a geometric mean level of 420 ng/L in workers directly exposed to Pt compounds, while in the subset of nine workers employed for more than 20 years the geometric mean was 1,900 ng/L or 1,453 ng/g creatinine (Linde et al, 2018a; Linde et al, 2018b). The highest level amongst those nine worker might therefore have been much greater than this average level. Other studies of PGM refinery workers have reported levels of, for example, up to 6,270 ng/g creatinine (Schierl et al, 1998).

With the exception of platin chemotherapeutics, there are very limited data on the kinetics (absorption into, distribution around, and excretion from the body) of platinum substances. A variety of platinum substances may be encountered in the workplaces of PGM refining or manufacturing of PGM-based products. The kinetics of each individual Pt substance may vary depending on factors including particle size, solubility, reactivity, etc. The level of exposure and the route of exposure (inhalation, dermal, or oral) will also affect the kinetics, especially the absorption potential.

For chloroplatinates, the most commonly cited kinetic value is an initial half-life of about 50 hours, i.e. following exposure, the concentration of Pt in the urine will halve every 50 hours. This comes from a study in the 1990s of only two workers (Schierl et al, 1998). The two males handled dry ammonium hexachloroplatinate powder for four hours, at calculated exposure levels of 1,700 and 150 ng/m^3, and all urine samples were collected over the next four days, and then morning samples were collected once a week for six months. Each sample was separately analysed for Pt. Pt-urine levels peaked after around 10 hours, and platinum excretion was found to initially follow an exponential decay with a half-life of around 2 days (50 hours). Subsequently, there was a second slower phase of excretion with a half-life of 24 days. Linde et al (2018) cite a separate study (Weber et al, 1991) that could not be located by IPA in which workers' urinary Pt excretion levels were reported to not decrease following two weeks' vacation.

This additional study of two workers was part of a larger study of Pt-urine excretion of 34 workers: 15 that had current exposure; 4 that previously had occupational exposure but had not been exposed for two-six years due to sensitisation; three workers that were only occasionally exposed; and a control group of 12 workers at the same company with no exposure to platinum.

At each assessment, urine was sampled at the end of a work shift and then again the following morning. Each worker was assessed on one, two or three occasions over a six-month period. The Pt-urine results are presented only in summary form with the maximum and minimum concentration for each worker, but for those assessed only once a comparison of the post-shift (maximum) and next day (minimum) levels is possible. Of the 15 workers with current exposure, seven were assessed only once. The overnight decreases in ng Pt/g creatinine concentrations for these seven ranged between 4% and 48%, with a median of 37%. In the group of three workers with stated occasional low exposure, two were observed on only one occasion. Their P-urine levels as ng Pt/g creatinine decreased 11% and 57% overnight.

Decreases in morning Pt-urine concentrations were also commonly observed in the control group. In those with the higher Pt-urine levels in this group the overnight decreases were small, while for the other control volunteers the absolute levels were so low their interpretation is uncertain – e.g. a decrease from 2 to 1 ng Pt/g creatinine – especially when the "*limits of measurement were 2 ng/L for urine*...".

The paper reported that the subgroup of four workers who formerly would have experienced high occupational exposure to platinum but that had not been exposed to platinum for several years still excreted 25-fold more platinum than the 12-person control group. Hence the authors postulated there may be a long-term platinum pool comparable with that found in patients after cisplatin treatment (Schierl et al, 1998). However, the three of these former platinum workers that were only assessed once showed 25% to over 90% decreases in ng Pt/g creatinine concentrations overnight, despite purportedly not having been exposed to platinum for four to six years.

The morning urine samples were taken at the workers' homes. Whether contamination of the end of shift samples – implied to have been collected at work – might have contributed to the apparent overnight decreases in Pt-urine is unclear. The Methods section of the papers notes "…*possible contamination risks should be detected by comparison of results from sampling at the factory and at home*" but no comment is then made on this in the Results or Discussion.

Occupational Pt-urine biomonitoring has been and continues to be conducted by some companies, mostly in the pharmaceutical sector. And, typically, single urine samples are taken on each occasion. One company is known, though, to have collected urine of some workers at the end of shift and then again prior to their next shift on the following day for several successive work shifts. The data are very limited, but indicate Pt urinary elimination may be, at least in some circumstances, much more rapid than the commonly cited half-life of 50 hours suggested in the scientific literature, with Pt-urine levels returning to pre-shift levels by the following day, indicating an initial half-life of several hours.

The uncertainty over the kinetics and elimination half-life of platinum substances should be considered when designing Pt-urine biomonitoring programmes.

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