CO_2 Capture Mongstad – Project A Establishing sampling and analytical procedures for potentially harmful components from post-combustion amine based CO_2 capture

Task 4: Literature survey of analytical procedures and recommendations

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EXECUTIVE SUMMARY

This report details the results from the literature review undertaken under the protocol of CO_2 Capture Mongstad Project A, Task 4. The objective of this task is to evaluate the scientific literature for analytical methodologies which address the quantitative measurement of specific compounds relevant to the environmental monitoring of the amine based PCC process. Further; to assess the principles and attributes of the various methods, determine their applicability for the relevant process sample types, and to make recommendations as to the analytical strategy required.

It has been determined by the CCM Project that the assessment of the PCC process can be made based on information of contaminant levels from four points in the process. These are the CO_2 rich amine solution from the CO_2 absorber; the CO_2 lean amine solution fed back to the absorber from the CO_2 stripper; the absorber wash water used to cool the treated flue gas and collect compounds escaping to the gas; and the treated flue gas from the emissions stack. These matrices are likely to contain, or have the potential to contain, certain compounds which are derived from the amine and alkanolamine capture solvents, their degradation products and other reaction products. As such, five groups of compounds are relevant to the environmental and health assessment of the PCC process. These are *N*-nitrosamines, alkylamines and ammonia, diamines and alkanolamines (PCC process solvents), amides, and aldehydes. Within these classes certain compounds have been specified for quantitative analytical determination (refer Table 1, Section 1).

Environmental and health agencies around the world regulate certain compounds which have been assessed as possessing a significant potential to adversely impact on the environment and human health. Along with regulation comes the requirement for monitoring of these contaminants in the environmental, industrial, manufacturing and human exposure spheres. Hence standard test methods for their analysis are established by the relevant bodies and this is the one significant area where the literature search has focussed.

The standard methods provide a level of quality assurance but commonly they are somewhat conventional in their approach. The potential of more advanced techniques and current instrumentation to provide a higher level of analytical outcome can only be realised through the development of methodologies which fully exploit these capabilities. This study therefore includes a literature search of current developments in the use and application of these more powerful techniques and their relevance to the analytical strategy required.

The information obtained from the review has been evaluated based on certain criteria which were used to objectively recommend techniques and instrumentation which are considered appropriate in an analytical strategy for the effective assessment of the likelihood of environmental impact from PCC process contaminants. This has enabled the following recommendations to be made regarding methodologies for the quantitative determination of these compounds:

N-Nitrosamines

The standard methods established by international environmental agencies are applicable to the volatile suite of specified nitrosamine compounds (NDMA, NDEA, NMor, NPip) in ambient air and water, and to one non-volatile nitrosamine (NDELA) in ambient air. There are no standard methods established for the determination of NDELA in aqueous samples and the techniques used for volatile nitrosamines would require evaluation and validation for this compound. The specified compounds *N*-nitrosopiperazine and 1,4-dinitrosopiperazine are not addressed by any of the standard methods, however it is considered that these would be applicable for determination under similar principles, after appropriate method development and validation. Gas chromatographic (GC) based methods may not provide the necessary efficiency for these more polar species and liquid chromatography (LC) would be evaluated as a more viable alternative.

The standard methods carry maturity based on their on-going validation through agency protocol and also through their use and verification in various applications as attested by the literature. Hence they are likely to be available at contract laboratories specialising in environmental or food and drug applications. As these methods are applicable to nitrosamines of environmental relevance they apply to the assessment of ambient and workplace environments and to drinking and wastewaters. Hence their applicability to gaseous and liquid samples from the PCC process would require further development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices.

On these bases, the following standard methods are recommended as candidates for the analysis of specified nitrosamines in gaseous and liquid matrices:

- OSHA Method 27 for determination of volatile *N*-nitrosamines in the gas phase.
- OSHA Method 31 for determination of *N*-Nitrosodiethanolamine (NDELA) in the gas phase.
    - These methods use Thermosorb/N sampling cartridges for the collection of volatile nitrosamines and glass fibre filter open faced cassettes for collection of NDELA. Analysis is by GC/TEA and/or HPLC/TEA. The later is considered preferable for NDELA, and where this and the volatile nitrosamines are analysed as a full suite.
    - Procedural MDLs of 0.10 µg/m^3 (0.03 ppbv) of NDMA and 2.0 µg/m^3 (0.37 ppbv) of NDELA are achieved using a 100L nominal gas volume.
- US EPA Method 521 for determination of volatile nitrosamines in the liquid phase.
    - Incorporates solid phase extraction (SPE) for analyte enrichment and analysis by GC/CI-MS/MS. It is recommended that the efficiency of SPE be evaluated using alternate methods such as that based on AWWA Method 6450, or other methods sourced from the literature.
    - A procedural MDL of 0.28 ng/L NDMA is achieved using a 500 mL nominal liquid sample volume.

Non-standard methodologies for the determination of nitrosamines, as drawn from the literature, are also recommended for incorporation into the overall analytical strategy, and are summarised as follows:

The chemiluminescence technique is implemented in standard methods and offers superior selectivity and sensitivity compared with other non-MS GC and LC detection systems, and the literature provides performance information in various applications including the recognition and address of interferences and artifacts. The maturity of the chemiluminescence approach, as exemplified by TEA or NCD, its sensitivity and selectivity and the associated reduction in preparative requirements, makes this technique a valuable tool for quantitative analysis of both liquid and gas phase samples from the PCC process. With incorporation of GC for volatiles and LC for non-volatile compounds, it has particular appeal in screening and group type analytical requirements and will provide adequate performance in speciated analysis where unequivocal confirmation is not a necessity. On this basis the chemiluminescence technique is highly recommended.

GC/MS techniques, using the more advanced systems of analysis such as GC/CI-MS/MS, achieve selectivity based on conformational mass spectral information and ultimate sensitivity. It is recommended that this MS mode, incorporating chemical ionisation and tandem MS functionality be incorporated as standard practice. The technique is limited to volatile nitrosamines, if derivatisation is to be avoided; however volatile analytes are a major portion of the contaminant suite. Its main applicability is to analysis of gas phase samples, due also to the nature of PCC process liquids. GC/CI-MS/MS instrumental procedures would be taken from US EPA Method 521 and it is considered likely the method could be developed to include *N*-nitrosopiperazine. As the principles of the technique are highly mature, its development for this purpose should be within the capacity of contract laboratories dealing in trace level environmental analyses.

The superior performance of LC/MS for the direct, or preconcentrated, analysis of non-volatile, thermally labile and polar compounds in aqueous matrices, and in matrices dominated by amine solvents, makes it a valuable and necessary technique for PCC process monitoring. It is possible that the full suite of volatile and non-volatile nitrosamines could be addressed, including *N*-nitrosodiethanolamine, *N*-nitrosopiperazine and 1,4-dinitrosopiperazine. LC/MS presents significant, but not insurmountable, challenges in attaining quantitative quality particularly for complex samples as would be encountered from the PCC process. As the technique is not mature in this application and no standard methodologies exist, a laboratory more aligned with the advancement of techniques and instrumental capability would be required to perform analyses of this type. The LC/MS technique is recommended for inclusion in the overall analytical strategy for determination of nitrosamine compounds.

Amines and Alkanolamines

The standard methods target the majority of compounds specified for assessment by the CCM project (refer Table 1, Section 1), with the exception of *N*-methyldiethanolamine. It is considered that the inclusion of this compound into the target suite would also be feasible. These methods are all applicable to gas phase collection and limited standard methods exist for their analysis in the liquid phase. If standard methods were given

preference, the methods used for determination of gas phase components would require development for analysis from the liquid phase.

The standard methods are necessarily rugged in nature and will provide adequate results for routine analyses, and are well suited to screening analysis. As they are applicable to amines of environmental relevance their application to gaseous and liquid samples from the PCC process would require significant evaluation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. In particular the relative concentrations of the bulk amines compared with trace amine components and the similarity in their characteristics will influence the performance of the sampling and analytical methods for a particular analyte and this requires attention in the development process.

On the basis described above, the standard methods which are considered as likely to provide highest analytical quality for analysis of specified alkylamines, ammonia, diamines and alkanolamines are:

- OSHA Method 40: Methylamine, Method 36: Ethylamine, Method 34: Dimethylamine, Method 41: Diethylamine in the gas phase.
    - Solid sorbent collection using NBD-Chloride coated XAD-7 sampling tubes and analysis by HPLC-Fluorescence.
    - A procedural MDL in the range 3.5 µg/m^3 (2.8 ppbv) for methylamine to 16.0 µg/m^3 (5.3 ppbv) for diethylamine is achieved using a nominal 100 L gas volume.
- JIS Method K 0099 for the determination of ammonia in flue gas.
    - Impinger collection into boric acid solution and analysis by either absorption spectrophotometry in accordance with JIS K 0115, or ion chromatography (IC) in accordance with JIS K 0127 is used.
    - A procedural MDL of approximately 26 µg/m^3 (38 ppbv) is estimated for both methods for a nominal 100 L gas collection volume.
- OSHA Method ID-188 for determination of ammonia in the gas phase.
    - Solid sorbent collection using carbon bead/sulphuric acid impregnated sampling tubes and analysis by ion chromatography (IC).
    - A procedural MDL of 100 µg/m^3 (140 ppbv) is achieved for a 100 L nominal gas collection volume.
- OSHA Method 60: Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetramine (TETA) in the gas phase.
    - Solid sorbent collection using NITC coated XAD-2 solid sorbent tubes and analysis by HPLC/UV.
    - A procedural MDL for ethylenediamine of 37 µg/m^3 (15 ppbv) is achieved for a 100L nominal gas collection volume. The detection limit for EDA is impacted by the chromatography as evidenced by a 20-fold lower detection limit for diethylenetriamine. Optimisation of chromatographic parameters is

likely to achieve a lower detection limit for EDA. A diode array detector is recommended.

- OSHA in-house method: Piperazine in the gas phase.
    - This method is based on similar principles as Method 60 and hence similar performance would be expected. The method is not validated and would be developed in-house under the protocols of OSHA Method 60.
- OSHA Method PV 2111: Ethanolamine, Method PV 2018: Diethanolamine, Method PV 2145: 2-Amino-2-Methyl-1-Propanol (AMP) in the gas phase.
    - Solid sorbent collection using NITC coated XAD-2 solid sorbent tubes and analysis by HPLC/UV. An alternative detector is diode array (DAD) and this is recommended.
    - A procedural MDL for these alkanolamines of around 15.0 µg/m^3 is achieved (approximately 5.0 ppbv, dependent on compound) for a nominal 100 L gas collection volume.

Note that the NITC derivatising agent used in this method for the alkanolamines is also used in the OSHA methods for diamines under the same sampling and instrumental procedures. OSHA also intends that piperazine be measured in the same way. Dependent on the relative concentrations of these compounds in the sample, careful optimisation of the liquid chromatography may allow separation of all analytes and the use of a characteristic absorbance wavelength to enhance sensitivity for each class would be beneficial. For this reason a diode array detector is considered essential to enable programmed wavelength selection and diode array scans of the analyte peaks in order to improve selectivity, determine peak purity and provide a level of analyte confirmation, where mixed di-amine and alkanolamine analytes are expected.

Non-standard methodologies for determination of amines, as drawn from the literature, are also recommended for incorporation into the overall analytical strategy. The use of more specialist techniques for collection, preparation and instrumental analysis is recommended to take full advantage of the quality information that these methods can provide.

Sorbent collection suitable for direct thermal desorption to an instrument is recommended for investigation, for compounds amenable to gas chromatography. This negates the requirement for solvent extraction and provides associated advantages, and would be applied for analyte introduction to GC/MS. The method would be used for volatile amines in gaseous samples, where the gas has been treated in a manner acceptable for collection onto Tenax or other solid sorbents, and would provide complementary information to that from the standard methods.

Another option for investigation is the use of chemiluminescence for the detection volatile amine compounds. Current TEA systems are available with three modes of analysis enabling the determination of aliphatic amines and ammonia as well as nitrosamines. Thus the development of a suitable sorbent system, for gas phase collection, and suitable solvent extraction system for liquid phase samples would allow the use of GC/TEA for compounds amenable to gas chromatography or LC/TEA as an effective means of routine analysis or screening for these three classes of volatiles, possibly with confirmation using other GC/MS and LC/MS methods.

LC instrumental techniques, including ion chromatography, are powerful tools for the routine analysis of amines and alkanolamines of interest in this study. Where derivatisation is selected, for the collection of volatile amines or to enhance selectivity or sensitivity for example, derivatives for LC determination are more commonplace, as established in standard methods, and the methods hold higher maturity than derivatisation designed for GC analysis. When applied to liquids, derivatisation using polymeric reagents advances the science further and offers significant advantages. As such, HPLC techniques incorporating UV/fluorescence and electrochemical detection are the techniques of choice for routine analysis of amine compounds specified in the CCM project.

LC/MS combines the advantages of HPLC with the sensitivity and selectivity of mass spectrometry, as has been discussed in relation to nitrosamine analysis. If the process solution can be effectively chromatographed without significant pre-treatment, this provides significant advantage in the simultaneous analysis of alkanolamine bulk constituents and alkylamine degradation products. This technique requires a high level expertise in the method development and would be chosen for specialist speciated analyses of gas and liquids from the PCC process.

The maturity of LC methodologies ranks these as the major priority for routine analyses for the specified amine compounds. However a significant level of method development is still required and a number of methods are likely to be needed to cover volatile and non-volatile compounds in gaseous products and in process liquids. Target concentrations will obviously differ between gaseous and liquid samples, and within a sample where there will be large differences in concentration between the amine solvent and the alkylamine degradation products. Dependent on the relative concentrations, and whether these fit to the linear range of the method, more than one analysis may be required to optimise sensitivity to minor components. It is considered that this is not beyond the scope of an advanced analytical contract laboratory.

Amides

The CCM project calls for the assessment of formamide and acetamide. Under ambient air and water quality regulation and monitoring these are not of major priority, nor are they emerging as contaminants of high importance. As such few analytical methods have been established. Methods from OSHA for analysis of formamide and acetamide in the workplace application are not fully validated and use rudimentary collection procedures. GC/NPD is specified, but for PCC process application it is considered that if GC based methods were used, GC/MS would be a preferable detector, although at some cost to sensitivity. The entire method would require development appropriate to the matrices. Overall the standard methods, as they stand, are not recommended.

The literature addresses the analysis of amides largely from a biological and pharmaceutical focus. Smalls amides which have been investigated in the use of solvents and manufacturing applications for example, provide some analytical guidance and may be applicable.

GC analysis is an option for small amides, although their chromatographic resolution is not ideal. Sorbent collection for application to thermal desorption is an attractive option for gas phase samples. MS detection is preferable to other detectors for reasons of

confirmation in mixed amine and amide matrices. Chemiluminescence detection is also a consideration. It should be possible to select for amides using the nitrogen mode of a TEA analyser, if it is possible to optimise preparative and chromatographic methodologies. Unfortunately literature as searched to date has not been able to support this opinion but the authors feel that this is worth investigation.

HPLC is an obvious choice for these compounds given their polarity. LC techniques would be especially suited to liquid phase samples incorporating a form of analyte enrichment and may also be applicable to gas phase samples. LC/MS analysis could also be incorporated into the analytical strategy with a significantly higher investment in method development.

Overall, there are no absolute recommendations for procedures for analysis of formamide and acetamide, due to the lack of mature methods and their limited priority in the literature. Development of methods based on the liquid chromatographic technique is favoured, and a simultaneous method may be possible for analysis of amines and amides if these compounds were to remain a priority.

Aldehydes

The DNPH derivatisation method is recommended for the determination of the specified compounds; formaldehdye and acetaldehyde in PCC process gaseous and liquid samples. The recommended guidances are:

- US EPA Method 0011 and CARB 430 for collection of gas phase samples from stationary source emissions. Sampling uses an impinger charged with the DNPH liquid.
- US EPA Method TO-11A for ambient air. Collection using a DNPH solid sorbent cartridge.
- US EPA Method 8315A for analysis of impinger collected samples by Method 0011.
- US EPA Method 554 for collection and analysis of liquid samples using DNPH treatment and SPE concentration.
    - All methodologies use HPLC analysis with UV detection. A superior detector is diode array (DAD) and this is recommended to provide a level of conformational information.
    - The procedural MDL in the gas phase is expected to be 0.15 µg/m^3 (0.12 ppbv as formaldehdye) using a nominal 100L gas sampling volume; and in the liquid phase; 0.3 µg/L.

All aspects of the gaseous and liquid phase sampling and analytical methodology would required evaluation to ensure that matrix components peculiar to the PCC process do not impact on the efficiency of the carbonyl-DNPH reaction and SPE procedures and on the chromatographic resolution of the target species.

The analytical method is selective and sensitive and readily adaptable to both gaseous and liquid collections. It is mature and would be readily available at environmental contract laboratories. It is also straight-forward and cost effective.

Summary

These recommendations are one part of the analytical strategy and form the backbone to the subsequent method development process and establishment of analytical methods. This practical process will be undertaken in Task 5 and will bring with it further knowledge of the characteristics of the matrices and its effect on the determination of target species. The similarity in characteristics of the analyte suite and the complexity of samples from the PCC process will make this an extensive and evolving process and the approach will necessarily change dependent on the outcomes of the various analytical investigations and before finalising the most efficient and effective methodologies.

1. INTRODUCTION

It is well recognised that the process of post combustion CO_2 capture using amine based solvents will generate, and has the potential to emit, certain compounds which may be harmful to the environment and human health. The occurrence and specific nature of these compounds is of course dependent on many process and material related variables and parameters, and whilst theoretical and experimental amine chemistry has been the subject of numerous and often conclusive investigations over many decades, the science as it relates to the PCC process is in its relative infancy. Broadly, the scientific and engineering focus has concentrated on the variables which impact on CO_2 capture efficiency. As such, characterisation of the solvent, its degradation products and other process related reagents and products have necessarily been qualitative in nature, and the nature of process emissions generally predictive.

The objective of this task is to evaluate the scientific literature for analytical methodologies which address the quantitative measurement of specific compounds relevant to the environmental impact of an amine based PCC process. Further; to assess the principles and attributes of the various methods, determine their applicability for the relevant process sample types, and to make recommendations as to the analytical strategy required.

There will be four main points where samples will be collected from the PCC process, and three different sample types (i.e. matrices). These are:

- the CO_2 rich amine solution from the CO_2 absorber
- the CO_2 lean amine solution fed back to the absorber from the CO_2 stripper
- the absorber wash water used to cool the treated flue gas and collect various compounds escaping to the gas
- the treated flue gas from the emissions stack

These matrices are likely to contain, or have the potential to contain, certain compounds which are derived from the amine and alkanolamine capture solvents, their degradation products and other reaction products. As such, five groups of compounds are relevant to the environmental and health assessment of the PCC process:

- *N*-Nitrosamines
- Alkylamines and Ammonia
- Amines and Alkanolamines (PCC process solvents)
- Amides
- Aldehydes

Within each group, individual compounds have been specified for assessment by the CCM Project and these are listed in Table 1. These compounds are termed "specified" compounds in this report.

Table 1. Compounds specified for assessment

***N*-Nitrosamines:**
N-Nitrosodimethylamine (NDMA)
N-Nitrosodiethylamine (NDEA)
N-Nitrosomorpholine (NMor)
N-Nitrosopiperidine (NPip)
N-Nitrosodiethanolamine (NDELA)
N-Nitrosopiperazine (NPz)
1,4-Dinitrosopiperazine

Alkylamines and Ammonia:
Methylamine
Ethylamine
Dimethylamine
Diethylamine
Ammonia

Amines and Alkanolamines (PCC Solvents):
Monoethanolamine (MEA) (Aminoethanol)
Diethanolamine (DEA)
Piperazine (PZ) (1,4-Diethylenediamine)
1,2-Diaminoethane (Ethylenediamine, EDA)
2-Amino-2-methyl-1-propanol (AMP)
N-Methyldiethanolamine (MDEA)

Amides:
Formamide
Acetamide

Aldehydes:
Formaldehyde
Acetaldehyde

2. BACKGROUND AND BASIS

In the United States, substances evaluated as hazardous to environmental and human health are regulated by the US Environmental Protection Agency (US EPA) under various Federal government Acts such as the Clean Air Act, Clean Water Act, Safe Drinking Water Act. The only State based regulatory agency in the US is the California Air Resources Board (CARB). Occupational health and safety standards are promulgated by agencies such as Occupational Health and Safety Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH). The US Food and Drug Administration (FDA) is responsible for protecting public health in this area. The International American Society for Testing and Materials is an organisation responsible for ASTM standards for materials, products and systems. US EPA also publishes and updates various procedural compendiums, such as US EPA SW846 for the evaluation of hazardous waste and the Compendium of Methods for the Determination of Toxic Organic Compounds in Air. From an environmental monitoring viewpoint, these provide an invaluable source of information relevant to the determination of hazardous compounds.

European and British agencies also regulate and monitor the environmental and health area. Some organisations pay strong attention to particular areas of importance, such as the International Agency for Research on Cancer (IARC) as part of the World Health Organisation (WHO) and European Union (EU) directives. Environmental regulation is through the European Commission (EC) and certain EN methods are standardised, for example. Individual countries have their own jurisdiction; for example INRS is a French Institute (Institute National de Reserche et de Securite) which publishes methods for the assessment of occupational health. In the case of the United Kingdom, the Health and Safety Executive (HSE) produces methods for the determination of hazardous substances (MDHS). The British Standard Institute (BSi) is a member of the International Standards Organisation (ISO) and both agencies produce methods related to systems and materials (such as determination of nitrosamines in rubber or cosmetic products for example). In the search for methods offering a level of applicability to the compounds and matrix relevant to this study it was found that the European and British organisations often recommended methodologies of US origin, or the methods were based on similar principles. Therefore the US methods tended to be the predominate source of reference.

US EPA national emissions standards for hazardous air pollutants (NESHAPS) lists 190 compounds which have the potential to impact adversely on human health. These standards require emissions reduction to that deemed achievable under the Maximum Achievable Control Technology (MACT) for a source category. The standards are authorised by Section 112 of the Clean Air Act and the regulations are published in 40 CFR (parts 61 and 63). Of the compounds listed, the following are of relevance to those specified in this study: formaldehyde, acetaldehyde, acetamide, diethanolamine, *N*-nitrosodimethylamine and *N*-nitrosomorpholine. As yet, there are no ambient standards or emissions levels set for these compounds. Of these compounds, standard methods for ambient air assessment have been established for formaldehyde, acetaldehyde and NDMA only; acetamide, diethanolamine and the nitrosamines are covered only by standard methods for workplace assessment.

The US EPA regulates 126 priority water pollutants under the US Clean Water Act as listed in 40 CFR Appendix A (Part 423). Of the compounds of interest in this study, only *N*-nitrosodimethylamine (NDMA) is regulated under the Clean Water Act, although no maximum contaminant level has been established for drinking water. *N*-nitrosodi-n-proplyamine (NDPA) and *N*-nitrosodiphenylamine (NDPhA) are also listed as priority compounds. The US EPA describes certain nitrosamines as "emerging contaminants" as they are "*characterised by a perceived, potential or real threat to human health or the environment, or a lack of published health standard. They may also be classified in this way because a new source or pathway to humans has been discovered, or a new detection method or treatment technology has been developed*". As such the unregulated contaminant monitoring rule (UCMR 2, 2010) has been established and six additional nitrosamines are listed for analysis in drinking water. These are: *N*-nitrosodiethylamine (NDEA), *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA), *N*-nitrosopiperidine (NPip) and *N*-nitrosopyrrolidine (NPyr). The State of California has also established requirements for monitoring, and of notification and response levels for these compounds in drinking water. Of relevance to this study are the compounds NDMA, NDEA and NPip. The US EPA has identified Method 521 (Munch and Bassett, 2004) as the method to be used for analysis of these nitrosamines under the requirements of UCMR 2. The American Water Works Association (AWWA) and their affiliates; the Public Health Association (APHA) and Water Environment Federation (WEF) also include nitrosamines in its methodology publication "Standard Methods for the Examination of Water and Wastewater".

Workplace exposure limits have been regulated by the UK Health and Safety Commission (2007) and by the US through OSHA and NIOSH, and monitoring methods from the latter agencies are well established. These methods provide a useful source of analytical reference as they cover the majority of compounds specified in this study, albeit from the ambient collection perspective. From the list of specified compounds, only three are not part of any workplace assessment priority. These are *N*-nitrosopiperazine, 1,4-dinitrosopiperazine and *N*-methyldiethanolamine, although piperazine and formamide are in-house, non-validated methods tendered for assessment by OSHA.

In the context of industrial source emissions, these compounds may escape to the environment through waste emissions to air or water. However there are no regulatory limits on industrial emissions of these compounds, nor is there a requirement for their monitoring as unregulated contaminants in waste and stack emissions. Hence no specific methodologies have been promulgated for the compounds of interest in US methodologies, although guidelines for volatile organic compounds generally are found which include formaldehyde. The Japanese industrial standard (JIS) regulates for the monitoring of ammonia in flue gas.

The US EPA provides procedural documents and standard test methods for the compounds deemed as priority contaminants; the individual subset of compounds being dependent on the area of assessment (water, air, soil, waste, food, drug, material, workplace etc). Certain methods from European origin are also relevant. These standard test methods can provide quite detailed procedures, particularly for the preparative and determinative aspects of the analysis, and associated validation and quality assurance. The guidance on sampling aspects is often more general and certainly does not extend

to the detailed protocols required for sampling of specific compounds or classes, in specific matrices, and under the specific source parameters as would be encountered in industrial process liquids and flue gas emissions. The methods can also be somewhat traditional in analytical and instrumental approach which is, to a large extent, coincident with the time and rigour required in their validation to the level required of a standard on which regulation and enforcement may be based. However, this also imparts a high level of quality assurance which is useful in itself. Overall, a standard method of analysis, in some form, is available for the majority of the compounds of interest, and these can be used as they stand for less complex classes (such as aldehydes and ammonia for example) and as a guide for the other more complex classes. All standard methods that have been discussed in this report are listed under each agency in Appendix 1.

The potential of more advanced techniques and current instrumentation to provide a higher level of analytical outcome can only be realised through the development of methodologies which fully exploit these capabilities. This study therefore includes a literature search of current developments in the use and application of these more powerful techniques and their relevance to the analytical requirements of this study.

3. CRITERIA FOR METHODOLOGY EVALUATION

The literature has been searched and reviewed from two perspectives; firstly to collect analytical methodologies applicable to the quantitative determination of specified compounds likely to be rated as hazardous pollutants from the PCC process, and secondly to evaluate the worth of the methodologies in their application to the requirements of PCC process and emissions monitoring. The specified compounds are those as supplied by the CCM Project (SoW Attachment A1, Appendix D) and listed in Table 1 Section 1, and the matrices for which analytical methodologies must apply are the process liquids (as lean and rich amine solvents, and wash water) and gaseous samples (as condensate or a sampling sorbent). "Standard" methods derived from international regulatory agencies, and "non-standard" methods which encompass more sophisticated techniques and the latest advances in instrumentation, were addressed. The utility of the method towards true quantitative analysis, rather than qualitative identification or compositional characterisation, was also a predominant factor. The collected publications were evaluated for analytical quality alongside their likelihood in satisfying the requirements of PCC process monitoring, and taking into account the sampling and analytical viewpoints.

The subjects considered in the evaluation of both standard and non-standard methodologies and the criteria used to objectively evaluate and recommend methodologies for quantitative analysis are as follows:

- Chemical and physical characteristics of the compound group and specific analytes with respect to efficient collection and analysis.

- Method principle and basis to the analytical technique is discussed for those methods considered to be most relevant. This includes analyte collection, sample preparation, instrumental and detection techniques and overall performance of the method. The basis behind an area of analytical or instrumental approach for existing and more current, non-standard techniques is also described. Note that this report addresses analyte collection as it relates to the analytical outcome as distinct from, but associated with, the sampling of the process stream itself, which is the subject of Task 2 (Azzi *et al.,* 2010).

- Minimum detection limit (MDL). The detection limit can relate to the instrumental technique itself (the instrument MDL) which is a value which basically describes the relationship between noise and the analyte signal and which is determined statistically. It can loosely be termed the sensitivity of the determinative method to a specific analyte, although this is more correctly a determination of the response of the instrument per unit of analyte mass or analyte concentration. The instrument MDL provides information which can be used to compare between particular instrumental and detection choices and the suitability of that choice for the desired or expected analyte levels likely to be encountered in the sample presented for analysis. However, more relevant descriptions of the MDL include the various preparative steps in the analytical procedure (an analytical MDL) or the full sampling and analytical procedure (procedural MDL), where the value describes the analyte concentration in the native sample. In these descriptions an accurate knowledge of all the variables associated with the entire

method must be known in order to accurately calculate MDLs and compare methods based on MDLs. Unfortunately it is rarely the case that this information is fully provided and the published MDL can therefore be on different and sometimes unknown bases. Also, a number of factors may impact on the MDL values obtained under the conditions of actual analysis which can only be determined under the protocols of method validation. For example the detector sensitivity may be impacted by various instrumental effects or by the effect of the sample matrix. It is these factors, along with the parameters associated with actual collection and sample preparation, which account for the large variation in method detection limits stated in the literature for similar analytical methodologies and applications.

To obtain some consistency in the MDL in order to compare standard methods on an MDL basis, these variables were standardised to some extent. Hence, if sufficient information was supplied, a procedural MDL was calculated where all gas samples were standardised at a nominal 100 L collection volume and all liquid samples to a preparative volume of 500 mL, unless these volumes were considered unsuitable for a particular method. This also provides information on the effect of a 10-fold change in the volume of gas collected which is within the constraints of most sampling protocols. For ease of comparison gaseous concentrations are reported in units of $\mu g/m^3$ and ppbv, or mg/m^3 and ppmv.

- Maturity of the method is important in assessing its accessibility and ruggedness. This factor also determines the likelihood that analyses can be contracted out to external contract laboratories or whether dedicated in-house expertise must be established.

- Advantages and disadvantages of the techniques are discussed from the viewpoint of sensitivity and selectivity, maturity and accessibility, and overall applicability to the PCC process liquids and gaseous sample matrices.

From this evaluation follows our recommendations as to the analytical approach or approaches required. Where it is considered that methods are deficient in fulfilling the needs of PCC process monitoring, this reasoning will be discussed and suggestions made as to an analytical approach which may be investigated. Development of the methodologies will be described in general terms. Development of new methods and the optimisation and validation of standard methods will be not be straight forward due to characteristics of the process streams, the complexity of the sample matrices and the extensive suite of analytes required,

Ranking of the methods is not straight forward in applications as complex as this one as so many factors impact on the reasoning. A formal system of ranking normally involves the accumulation of a method score against various criteria that are important in the specific application and requirements of the method. Such criteria would include the analytical performance criteria as described above but would also incorporate process monitoring requirements (such as applicability, complexity, cost, turn-around-time etc). Typically a weighting is then applied to each score dependent on the analytical and/or process related outcome required. This weighting would change dependent on these relative importance of these requirements. For example, under an engineering development or process monitoring requirement where multiple samples are presented and quick turnaround in delivery of data is required, the cost and turnaround time would

be weighted more heavily than perhaps the specificity. Under an environmental emissions requirement aspects of analytical performance (such as MDL, specificity) may be weighted more heavily than cost. This becomes very complicated when the method includes the collection procedure, the sample workup procedures and the instrumental technique, for both gaseous and liquid matrices, all of which must be weighted for different process requirements.

Hence it was considered that at this stage there is insufficient basis on which to implement this level of ranking as the process constraints, the emissions levels and the associated analytical requirements are not well characterised as yet. Additionally the methods are not yet validated for this specific and unique application and it is therefore difficult to provide scores against the various criteria that would be more than just semi-qualitative, until more practical development work has been conducted. Also it may well eventuate that standard methods are not the method of choice as more efficient, selective or sensitive non-standard methods are developed and take precedence. As such it is felt that this level of ranking may not add significantly to the identification of candidate methods beyond the recommendations as provided in the report.

A simple ranking of the methods as a summary of the recommendations has been included in Appendix 1; standard methods reference. The methods have been given the designation R1: Recommended as the most suitable method. R2: Recommended with exceptions or inclusions or as further guidance to the R1 method. R3: Not Recommended on the basis that alternative methods offer higher performance. In some cases the method may also be considered unsuitable for the reasons described in the text.

The outcomes from these evaluations, for each class of pollutant, are the subject of the following sections of this report.

4. LITERATURE REVIEW AND METHODOLOGY EVALUATION

The information obtained from the literature review and the evaluation of analytical methodologies is detailed in the following sections. The discussion begins with an overview of preparative techniques used for enrichment of analytes collected from gaseous and liquid matrices relevant to all classes of compounds specified for assessment in this study. Subsequent sections treat the specified classes, and address the standard methodologies and the non-standard methodologies for that class, in the groupings; *N*-nitrosamines, amines (alkylamines, ammonia, diamines) and alkanolamines, amides and aldehydes.

4.1 Techniques for Analyte Enrichment

Methods used for sampling and analyte collection are predominantly the subject of Task 2 (Azzi *et al.,* 2010), and the enrichment techniques used are described in detail there. The following discussion refers to methods of analyte enrichment as they relate to the analytical aspects of the preparative and determinative process.

4.1.1 Enrichment Techniques for Gaseous Collection

Gaseous collection of polar and reactive compounds, as is the case for most analytes in this study, is most usually performed by concentration and stabilisation onto a solid sorbent, or solid media (such as a filter) which may be coated with some form of chemical stabilisation or a derivatising agent. This media serves to concentrate the analytes from the dilute gas and to stabilise them. The volatility of the compound and the mode of instrumental analysis are determining factors in the choice of collection media. Collection of whole gas samples into canisters or gas sampling bags is not generally appropriate for nitrogen containing or carbonyl species due to their reactivity on surfaces and their polarity, making their efficient or integral removal from the canister unlikely. Collection into a liquid, particularly for highly water soluble compounds can be used, as is commonly the case for sampling of stack emissions where an impinger charged with a suitable liquid media is implemented. However, liquid collection of gases is inconvenient in the field, is limited by flow rate and often requires subsequent analyte enrichment and clean-up procedures.

Sorbent collection is preferable in the field and can eliminate the preparative steps associated with liquid collection. It is the preferred technique where the gas sample is suitable, or is suitably conditioned, to allow sampling and collection efficiency, as discussed in Task 2 (Azzi *et al.,* 2010). Various solid sorbents are used dependent on the characteristics of the analyte and dependent on the intended method of analysis. Woolfenden (2010 i, 2010 ii) has reviewed sorbent selection and techniques for environmental analysis. The sorption process may be purely physical as in the case of molecular sieve material, it may be physical/chemical such as the adsorption onto a Tenax™ polymer, or purely chemical as is the case for derivative coated sorbents. The DNPH derivative coated solid sorbent is a well known chemisorption technique for the collection of aldehydes. NBD-chloride for *in-situ* derivatisation alkylamines and NITC for alkanolamines are other examples of reagent coated sorbents. These are discussed in

detail in the later sections which address the relevant compound classes. Sorbents can be combined in a single cartridge for collection of compounds with differing properties or can incorporate a stabilising agent prior to the sorbent for analyte collection. The desorption of analytes may be by solvent extraction or the analytes may be desorbed thermally as is often but not exclusively the case in the use of Tenax™ adsorbents.

Nitrosamines are commonly sampled onto commercially prepared Thermosorb/N® cartridges which have been specifically designed with the reactivity of their precursors in mind. Amines, in the present of nitrosating agents, will react to form nitrosamines, as has been discussed in Section 4.2.1. The cartridge contains sulfamic acid positioned prior to a Florisil™ adsorbent in a system designed to inhibit in-situ artifactual formation of nitrosamines, as described by Rounbehler *et al.* (1980 (i). Rounbehler *et al.* (1980 (ii) also evaluated various other solid sorbents (activated charcoal, silica gel, Florisil™, Tenax-GC™) and liquid sorbents (KOH solution and phosphate-citrate buffer containing ascorbic acid) for collection of nitrosamines in air containing nitrogen oxides, but limitations with respect to artifact formation and/or collection efficiency were found. The Thermosorb/N® cartridge, has been universally adopted and is currently prescribed in standard test methodologies for collection of nitrosamines from the gas phase. They are not without issue however, as other polar compounds are eluted from the cartridge which can interfere in the analysis. Various methods have been adopted to address this with varying levels of success. For example US EPA Method TO-7 uses pre-extraction with DCM prior to analyte extraction in acetone to minimise interferences but the effect on analyte recovery is not fully addressed. Aubin *et al.* (2009) have adopted dual in-line sulfamic and Florisil™ packed cartridges in order to extract only the Florisil adsorbent as a method to reduce significant interferences experienced in GC/NPD and GC/MS analysis when Thermosorb/N® cartridges were used; a method also adopted by INRS Method 031. Thermosorb/N® also have a relatively moderate sampling capacity (1500 ng/cartridge) however they can be connected in series to increase total capacity of the sampling system.

Thermal desorption is an alternative to solvent desorption and can be advantageous as it is closer to a direct analysis of the collected analytes and possible analyte loss, degradation or reaction in the solvent extraction process can be avoided. For GC introduction it also limits the exposure of thermally labile compounds to temperature as analytes are rapidly removed from the trap to a cold secondary trap or column. Thermal desorption cannot be achieved with Thermosorb/N cartridges as far as is known. Sorbents suitable for thermal desorption are generally porous polymers such as Tenax (in the forms Tenax-TA™ and Tenax-GC™ or Tenax–GR™) and Chromosorb™ (in the forms 102 and 103). Despite criticisms of artifactual formation of nitrosamines on Tenax-GC™ by Rounbehler *et al.* (1980 (ii), these sorbents have been tested by others. Billedeau and Thompson (1987) report only the limitation of lower break-through volumes on Tenax-TA™, particularly for NDMA. Marano *et al.* (1982) did not report nitrosamine artifacts using Tenax-GC™, although it is unlikely that precursor compounds were present in the air sampled. Conversely, Issenberg and Swanson (1980) used Tenax-GC™ to concentrate volatile nitrosamines from air samples and reported that elution using diethylether was used to minimise artifacts which were observed when thermal desorption was employed.

It is not clear from the literature if it is the chemical or physical characteristics of the Tenax itself that may be the issue with artifact formation, or whether other factors are at

play. Certainly amines will be trapped on Tenax and the nitrosamines may be formed in process of collection and/or thermal desorption. However the literature is not clear on the mechanism of formation and whether the graphitised or non-graphitised forms of Tenax influence the degree of formation. The inclusion of an in-line amine trap seems a practical solution to the issue but, from our review, this has not been reported in the literature to date. The development of Thermosorb/N® seemingly reduced the reliance on these sorbent methods for nitrosamine collection, and their application has been directed towards other less reactive volatile organics. Obviously these issues require further investigation if the advantages of thermally desorbable solid collection can be realised.

A more recent application of thermal desorption is reported by (Dye *et al.* 2008) where Tenax-TA™ sorbent has been used for collection of a range of nitrogen containing compounds of relevance to the PCC process (selected amine and alkanolamine solvents, and formamide and acetamide) with analysis using GC/MS. This was supported by collection of these compounds on acid impregnated filters for analysis using LC/ESI-TOFMS. Ventura *et al* 1994 tested three polymeric sorbents suitable for trapping aliphatic amines using thermal desorption-GC and also after conversion to fluorescent derivatives for HPLC analysis. For compounds stable on the adsorbent and amenable to gas chromatography this is considered to be an efficient method of collection and sample introduction for analysis of volatile amines and possibly amides, present in the gas phase.

Solid phase microextraction is another form of thermal desorption which has application to gas phase concentration. This technique involves the partitioning of analytes between the gaseous (or liquid) sample and a polymeric liquid phase coated on a fused silica fibre, followed by thermal desorption of the concentrated analytes to the instrument. GC is commonly used. Dependent on the conditions the method can be less sensitive than sorbent sampling where large volumes of the gas sample can be concentrated. However the technique has been applied in trace level application such as the determination of volatile organic compounds in ambient air. Namieśnik *et al.* (2003) used SPME to trap volatile aliphatic amines in workplace environments, Parreira *et al.* (2006) used SPME for the analysis of amides in air and Wang *et al.* (2010) prepared a novel sorbent based on carbon nanotubes for trapping certain amines and other VOCs for application to ambient air.

The efficacy of the various porous polymers or SPME techniques for thermal desorption of nitrosamines, or other compounds of relevance to the PPC process, must be tested in each application with rigorous attention to all aspects of the method development and stringent validation in order to obtain accuracy in the analysis of these difficult compounds. However, this investment in time may be of worth in the quality of data obtained or the complementary nature of the data with that from other techniques.

Traditional methods of collection would suffice for the preparation of samples for routine analytical applications. However contemporary techniques may provide specialist information in different applications of process assessment.

4.1.2 Aqueous Enrichment Techniques

Amines such as the nitrosamines, alkylamines, ammonia and the alkanolamines of relevance to this project are difficult to extract from the liquid phase due to their polarity and corresponding high solubility in water. The physical properties of these classes of amines are outlined in the relevant sections that follow. In the past enrichment using liquid-liquid extraction was implemented but today preference is given to solid-phase extraction methods due to favourable factors such as reduction in solvent use, improvements in extraction efficiency and/or a lessening in the requirements for contaminant clean-up. Solid phase extraction is now a mature method in certain applications as is also indicated by its inclusion in established standard test methods, such as US EPA Method 521 which uses coconut charcoal, and AWWA Method 6450 which uses Ambersorb 572® for enrichment of nitrosamines from water. There is still the requirement for thorough development and validation as is exemplified by Padhye *et al.* (2010) who found that activated carbon, commonly used in SPE preparation of water samples, promoted the transformation of secondary amines to their associated nitrosamines. The authors are not aware of other publications reporting this effect. It has also been suggested by Mishra *et al.* (2001) that ammonia and aliphatic amines are unsuitable for SPE extraction under methods typically used for enrichment of aromatic amines in waters, requiring the use of derivatisation followed by preconcentration for analysis by GC/MS. Munch and Bassett (2006) report the unsuitability of organic polymers or C_{18} silica based sorbents for nitrosamine extraction from water, and requiring isotope dilution quantitation to overcome the inefficiency of the SPE technique. Jurado-Sánchez *et al.* (2009) evaluated several commonly used sorbents for SPE of amines and nitrosamines from water with the conclusion that the polymers LiChrolut EN® and Oasis HLB® outperformed RP-C_{18}, graphitised carbon black, fullerenes and nanotubes in the retention of these compounds, with greater than 95% recovery from spiked samples. In a previous study Jurado-Sánchez *et al.* (2007) also recommended Ambersorb 572®, a carbonaceous sorbent, over Florisil™, activated carbon and C_{18} for seven nitrosamines using an automated preconcentration system.

The development of SPE techniques and their application is on-going. Reviews on the technique and new generation sorbent materials include; Huck and Bonn (2000) on developments in polymer-based sorbents, Poole (2003) provides an overview of various sorbent systems and applications, Ravelo-Pérez *et al.* (2010) provides a comprehensive review on the application of carbon nano-tubes in SPE and Augusto *et al.* (2010) reports on carbon nanotubes and molecularly imprinted polymers and on new sol-gels for solid-phase microextraction application.

Membrane enrichment as an alternative to solid sorbents is also reported by a number of authors. An interesting example of this technique has been published by Grönberg *et al.* (1992). A sample obtained from gaseous sampling into an impinger solution is used. The sulphuric acid treated liquid sample is passed across a PTFE membrane in a flow system which is directly interfaced to a gas chromatograph for concentration of methyl-, dimethyl-, trimethyl-, diethyl- and triethylamines. Tomkins and Griest (1996) determined NDMA at part-per-trillion concentrations in contaminated groundwaters and drinking waters featuring carbon-based membrane extraction disks. It is possible this method or other newer concepts of separation could also be applied to process liquids and used for enrichment of samples for LC analysis.

More recently solid-phase microextraction has been implemented as a means by which to eliminate the multiple steps often required in SPE techniques. SPME is solvent-free and involves the partitioning of analytes between a liquid or gaseous sample and a polymeric liquid phase coated on a fused silica fibre, followed by thermal desorption of the concentrated analytes to an analytical instrument. GC is commonly used or LC with the incorporation of an appropriate interface. Walles *et al.* (2005) used SPME coupled to electronanospray for LC/MS analysis of peptides. SPME relies on the equilibration of the analytes between the two phases to obtain quantitative results and certain authors have reported on the development and validation of SPME techniques (Passeport *et al.*, 2010).

A number of authors have used SPME for determination of nitrosamines in water, such as Grebel *et al.* (2006) with application GC/NCD, GC/NPD and GC/CI-MS analysis, Hung *et al.* (2010) used SPME and GC/CI-MS/MS and Perera (2006) cites a number of other authors who have used SPME for the concentration of nitrosamines from air and water matrices. Detection limits in the low ng/L range were achieved, comparing favourably with analyses using more conventional SPE techniques.

SPME can also be combined with derivatisation to increase the selectivity and sensitivity of the analysis. Herráez-Hernández *et al.* (2006) reported a new technique using on-fibre derivatisation for the quantitative analysis of aliphatic amines (methylamine, dimethylamine and trimethylamine) from tap, river and waste water for analysis using liquid chromatography. Various extraction and SPME derivatisation techniques were compared to evaluate the performance of the SPME method; with derivatisation on-fibre producing the best results. Cháfer-Pericas *et al.* (2005) presented a SPME method with two-stage derivatisation for the accurate and reproducible analysis of dimethylamine in water and achieved detection limits of 0.3 ng/L by LC/fluorescence, which rivals other methods and liquid derivatisation methods particularly. They also report on the successful application of the method for urine and other complex samples.

Other more complex preparative techniques have been developed for application to polar compounds, such as liquid-phase microextraction (LPME) and liquid-liquid-liquid microextraction (LLLME). A description of these sampling and preparative techniques and instrumental methods of analysis for environmentally important amines is detailed by Pielesz (2006).

Static headspace (HS) preconcentration is also used for GC analysis of volatile compounds in air, water and solids. However few reports are published on the use of this technique for free amines in aqueous samples because of their high polarity and solubility and the associated difficulty in obtaining equilibrium concentrations. Maris *et al* (1999) applied HS to aliphatic amines by chemically forcing the compounds out of solution and Tsukioka *et al.* (1993) also applied the technique to lower aliphatic tertiary amines from river water and sediments by a complex technique of distillation and chemical treatment prior to headspace GC/MS analysis. HS combined with SPME has found particular application to nitrosamine emission, e.g. from cooking or tobacco smoke. Andrade *et el.* (2005) used HS-SPME-GC-TEA for determination of N-nitrosamines emanating from sausages. Gaseous matrices are an obvious application of SPME, as discussed previously.

Overall, these publications indicate that the HS and/or SPME technique, with or without on-fibre derivatisation, may offer potential in the characterisation of process liquids

although significant challenges would be encountered in the achievement of quantitative results. The use of contemporary and emerging analyte enrichment techniques may be beneficial in providing specialist information in certain aspects of PPC process assessment. Even where conventional SPE is used thorough method development, optimisation and validation is essential in achieving qualitative determinations.

4.2 *N*-Nitrosamines

4.2.1 Significance and Properties

In recent decades *N*-nitrosamines compounds, and their precursors amines and nitrites, have been a focus of environmental and health concern with the recognition of their formation in various manufacturing and product treatment processes, and the findings of their toxicity and carcinogenicity. *N*-nitrosodimethylamine and *N*-nitrosodiethylamine have been rated by the International Agency for Research on Cancer (IARC, 2005) as Group 2A probable human carcinogens and *N*-nitrosomorpholine, *N*-nitrosopiperadine and *N*-nitrosodiethanolamine as Group 2B, possible human carcinogens. The formation of nitrosamines is known to occur in both anthropogenic and biological processes and their presence has been determined in products from a wide range of industries. Examples include the food industry, for example in the smoking of meat, pickling processes and beer production, in personal and cosmetic products, in cutting fluids and corrosion inhibitors, in rubber vulcanisation and plastics production, in iron foundries and leather tanneries, in tobacco products and tobacco smoke, in rocket fuel emissions, and from the disinfection of water. They are also formed endogenously from food or drug consumption for example and from microbial activity such their action on fertilisers in soil. Accordingly nitrosamines and often their amine or nitrite precursors are monitored and controlled in affected industries and are monitored as regulated and unregulated contaminants by international environmental and health agencies. From this follows the establishment of standard test methods for nitrosamine analysis of certain nitrosamine compounds, relevant to the area under assessment.

The conditions under which nitrosation of amines occurs and the stability of the formed nitrosamine are important factors in the sampling and analytical context in ensuring that *in-situ* formation of nitrosamine artifacts, or their decomposition, does not occur to affect the integrity of the sample collection or accuracy of the nitrosamine determination. The analysis of reactive substances poses special challenges for the analytical chemist. An analyte which is prone to reaction or decomposition during sampling or analysis has to be determined either by an on-line sampling technique or using suitable treatment to either inhibit the reactant and/or render the product stable. The theory of nitrosamine formation in aqueous systems and their decomposition is briefly reviewed to gain some insight into treatment considerations for samples collected from the PCC process.

The following overview information on the formation of nitrosamines is taken from Perera, 2006, p. 420-422, and references therein. *N-nitrosamines, like all N-nitroso compounds, possess the N-N=O functional group. In the general formation scheme, N-nitrosamines are generated by a chemical reaction between a secondary or a tertiary amine and a nitrosating agent, such as chemicals derived from nitrites and nitrogen oxides. Primary amines react with these nitrosating agents to form unstable N-nitroso derivatives which degrade to olefins and alcohols. The nitrite ion and nitrous acid are not capable of the N-nitrosation themselves, but under moderately acidic conditions they form nitrogen oxides such as dinitrogen trioxide (N_2O_3) which is a strong nitrosating agent and dinitrogen tetroxide (N_2O_4), also an effective agent. Under strongly acidic conditions (pH < 2) nitrous acid forms more powerful agents such as nitrous acidium ion (H_2ONO^+) or the nitrosinium ion (NO^+). N_2O_3 reacts with the unshared pair of electrons on unprotonated secondary amine by a nucleophilic substitution reaction to form*

nitrosamines. The rate of nitrosation of secondary amines in a weakly acidic aqueous solution is proportional to the concentration of the amines and to the square of the nitrite concentration. The concentrations of these two precursors depend on the pH of the medium. While the concentration of unprotonated amines increases when pH increases, the concentration of nitrous acid increases when the pH decreases. Hence the pH rate profile for the nitrosation of amines shows a maximum resulting from the interaction between these two opposite reactions. The optimum pH for the nitrosation of the most secondary amines is between 2.5 and 3.5, depending on the pKa of the amine under consideration. N_2O_3 *and* N_2O_4 *are effective reagents for nitrosation in both neutral and alkaline solutions. Nitrosamines can be formed quite rapidly at basic pH because nitrogen oxides are direct nitrosating agents and do not require an acid medium to be transformed into reagents for nitrosation as is the case for nitrite. The reaction is fast in basic medium because the amines are unprotonated. In the presence of a nucleophilic anion (such as* I^-, Br^-, Cl^-, SCN^-, *acetate or phthalate) nitrous acid can be converted into more active nitrosating species. Inhibition of nitrosation reactions can be effected by compounds such as ascorbic acid, sulfamic acid and a-tocopherol.* It is expected that PCC process samples will be treated with a nitrosation inhibiting or quenching agent although this may be dependent on the physical and chemical properties of the matrix, as is discussed in Task 2 (Azzi *et al.,* 2010) where this is of particular relevance. Keefer and Roller (1973) and Ikeda *et al.* (1990) report the effect of formaldehyde in catalysing the conversion of secondary amines to nitrosamines in neutral and basic solution, up to pH of 10-11. As these are expected to be formed and dependent on the levels and mechanisms of the reaction, the effect of aldehydes is a consideration in the method development.

Once formed, nitrosamines are stable in neutral and strongly basic media in the absence of light. When exposed to UV light they decompose rapidly to form aldehydes, nitrogen and nitrous oxide, or amine and nitrous acid. In acidic media, decomposition via denitrosation occurs slowly, however in the presence of nucleophiles (iodide, thiocyanate, bromide or chloride) the denitrosation can become rapid (Ikeda *et al*., 1990). Their reaction with inorganic acids (such as HCl, HBr and HI) is the basis for the process of denitrosation, such as the decomposition reaction using hydrobromic and in glacial acetic acid. They are sensitive to prolonged thermal treatment. The reduction of the nitroso group to the amino group is a characteristic reaction which can be used as a check for the presence or absence of *N*-nitrosamine compounds. *N*-nitroso derivatives can be readily oxidised to their *N*-nitro analogs and they can be converted into their corresponding *N*-nitramines; a characteristic which has been the basis of various analytical methods.

Most *N*-nitrosamines encountered in the environmental and health setting is alkyl and cyclic nitrosamines and these are classified as volatile, and have been intensively studied. The most commonly encountered non-volatile species are the aryl compounds, hydroxylated compounds and *N*-nitrosated amino acids (Perera, 2006). On this basis, the compounds specified for assessment in this study are classified as volatile with the exception of the hydroxylated compound; *N*-nitrosodiethanolamine, which if found in the gas phase would be present as an aerosol. Nitrosopiperazine is less volatile than the simpler nitrosamines and 1,4-dinitrosopiperazine are considered non-volatile. The nitrosamines are polar compounds and are water soluble or water miscible. In the presence of water, gas phase components will partition readily into the liquid phase and their low water/octanol partition coefficients (NDMA $\log P_{o/w}$ = -0.57 and NDEA 0.48)

make their efficient extraction from water difficult to achieve. These characteristics must be taken into consideration in designing a collection and analytical protocol.

A significant physical property of *N*-nitroso derivatives is the relative ease of dissociation of the N-NO bond and release of the nitric oxide group. For *N*-nitrosamines this is accomplished at temperatures of 400-500ºC. In fact, some decades ago, it was recognised that this property could be used as an effective means by which to analyse for these compounds in the presence of other nitrogen containing species and the thermal energy analyser (TEA) was developed.

4.2.2 Standard Methodologies

International agencies have established standard test procedures for the collection and analysis of certain volatile and non-volatile nitrosamine compounds of environmental and health relevance. These apply to gaseous matrices, mainly in the ambient and workplace assessment applications, to aqueous matrices such as drinking and waste water or to hazardous waste more generally, and are designed for analysis of certain nitrosamines which are prioritised as contaminants or pollutants in the particular area of assessment. Certain other industrial standards have been established but these relate more to specific areas of manufacturing, such as the cosmetics industry for example, and to only one or so analytes, and as such the methods are not as relevant. Where aspects are found useful, these will be included in the section discussing non-standard methods. Of the nitrosamine compounds specified by the CCM Project, an environmental standard method has been established for all except *N*-nitrosopiperazine and 1,4-dinitrosopiperazine, these being specific to the solvents used in the PCC process and of no current regulatory relevance under environmental and health priorities.

The standard test methods sourced from major international environmental and health agencies of relevance to the analysis of nitrosamines, the analytical and instrumental principles on which these are based and relevant performance data are outlined in the following sections for gas and liquid phase matrices. The CCM Project specified compounds are in bold face. All information is taken directly from the procedural documents, except for the sections titled "Comments and Recommendations" which are the authors evaluation of the method and its attributes and limitations, as relevant to the analytical requirements of this study. In all cases where a positive recommendation is made this applies to the sampling and analytical performance of the method in the application for which it was designed. This means it may be applicable as a starting point for application to PCC process samples, but by no means guarantees its performance in that role, and indeed that alternative non-standard methods may be preferable.

Standard Methods for Gas Phase Collection

The following standard test methods apply to the collection and analysis of gas phase samples in the workplace exposure and ambient air applications.

OSHA Method 27: Volatile Nitrosamines Mixture I

Principle and Application: Volatile nitrosamines in ambient and workplace air by GC/TEA and HPLC/TEA.

Method Status: Fully evaluated, 1981

Target analytes: *N*-nitrosodimethyamine (**NDMA**), *N*-nitrosodiethylamine (**NDEA**), *N*-nitrosopyrrolidine (NPyr), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomorpholine (**NMor**), *N*-nitrosopiperidine (**NPip**), *N*-nitrosodi-n-butylamine (NDBA).

Collection: Thermosorb/N™ solid sorbent air sampling cartridges.

Air Sampling Volume and Rate: 75L at 0.2 to 2 L/min.

Storage and Stability: Cartridge stored at freezer temperature. Extracts refrigerated and protected from light.

Preparative: Sample desorbed with 1 mL of 75/25 v/v dichloromethane/methanol.

Analysis: Gas chromatography with Thermal Energy Analyser (GC/TEA). Confirmation using HPLC/TEA.

Instrument MDL (GC/TEA): NDMA 50 pg, NMor 75 pg.

Procedural MDL: NDMA 0.13 µg/m^3 (0.043 ppbv), NMor 0.20 µg/m^3 (0.042 ppbv) (parameters as stated).

Recovery: NDMA 103 ±7%, NMor 94 ±8% from vapour spikes of pure compound onto cartridges.

Interferences: The TEA has been shown to respond to compounds other than *N*-nitrosamines and the HPLC method is therefore required as a confirmatory technique. Confirmation is based on the different order of chromatographic elution for compounds analysed on the two systems, and hence the unlikely event that a target and interfering species will have a coincident retention time.

Artifactual formation of nitrosamines from precursor amines and nitrosating agents has been shown to be eliminated for the compounds NDMA, NPyr, NMor and NDPA, under the conditions of the test, using sulfamic acid treatment which is incorporated into the Thermosorb/N air sampling cartridges.

Comments and Recommendation

TEA offers high sensitivity and selectivity to nitrosamine compounds however it can be prone to interferences from other nitroso compounds holding a chemiluminescence response. The quality of the chromatographic separation is therefore paramount, as is a knowledge of response factors for other nitroso-compounds and the likelihood of their presence. This can be assessed to some degree using the TEA's nitrogen and nitro modes to determined other nitrogen containing species to evaluate the overall sample characteristics and perhaps infer possible nitroso inferences.

Confirmatory techniques such as GC/MS or LC/MS would provide quality assurance, particularly for complex samples of unknown nitroso characteristics.

This method is recommended for the routine analysis of volatile nitrosamines.

NIOSH Method 2522, Issue 2: Nitrosamines

Principle and Application: Volatile nitrosamines in ambient and workplace air by GC/TEA

Method Status: Partially evaluated, 1994

Target analytes: **NDMA**, **NDEA**, NPyr, NDPA, **NMor**, **NPip**, NDBA.

Collection: Thermosorb/N™ solid sorbent air sampling cartridges.

Air Sampling Volume and Rate: 15 to 1000L at 0.2 to 2 L/min.

Storage and Stability: 6 weeks at 20ºC, protected from light.

Preparative: Sample cartridges desorbed with 2 mL of 3:1 v/v dichloromethane/methanol

Analysis: Gas chromatography with a Thermal Energy Detector (GC/TEA).

Instrument MDL (GC/TEA): not stated.

Procedural MDL: 0.05 µg/sample (parameters not stated).

Lower Working Range: 3 $\mu g/m^3$ for 50L air sample (equiv. to 0.15 $\mu g/m^3$ for 1000L)

Recovery: Not determined.

Interferences: Little or no interference due to selectivity and sensitivity of the TEA operated in the nitrosamine mode.

Supporting Information: No further information of relevance.

Comments and Recommendation

A rudimentary method with little procedural detail or specific information as to method requirements in ensuring performance or determining interferences.

Overall, this method is not recommended; OSHA method 27 provides superior guidance for this technique.

US EPA Method TO-7: Method for the Determination of N-Nitrosodimethylamine in Ambient Air using Gas Chromatography (GC/MS)

Principle and Application: NDMA in ambient air by GC/MS

Method Status: Not fully validated, 1986

Target analytes: **NDMA**

May be applicable to other volatile nitrosamines based on in-house validation.

Collection: Thermosorb/N™ solid sorbent air sampling cartridges.

Air Sampling Volume and Rate: 300L maximum at 2 L/min.

Storage and Stability: Cartridge at room temperature under activated charcoal. Extract is protected from light and refrigerated.

Preparative: Cartridge is forward flushed and pre-eluted with 5 mL of dichloromethane, to remove interferences, and purged with nitrogen. Sample is collected using reverse flush with 2 mL of acetone.

Analysis: Gas chromatography with mass spectrometry (GC/MS) using electron impact (EI) in full scan mode. Quantitation of NDMA using extracted ion m/z 74.

Instrument MDL (GC/MS): Not stated (equiv. ~0.15 ng, dependent on inlet parameters).

Procedural MDL: NDMA 1 µg/m^3 (parameters not stated).

Recovery: Not stated.

Interferences: Interferences (as compounds with similar mass spectral characteristics) are removed from the cartridge by pre-eluting with dichloromethane in the same direction as the sample flow. The cartridges are eluted with the acetone in the reverse direction to collect nitrosamine analytes. *Note that there is no analyte recovery information supplied to support the efficiency of this method.*

Compounds having retention times similar to NDMA and yielding detectable m/e 74 ion fragments may interfere. The inclusion of the pre-elution step minimises this. GC columns of differing polarity may be used to confirm identification.

Supporting Information:

The selection of Thermosorb/N adsorbent over Tenax GC was due, in part, to laboratory studies indicating nitrosamine artifact formation on Tenax GC from presence of oxides of nitrogen in the sample matrix.

Comments and Recommendation

Spectra generated from electron impact are not ideal for qualitative determination of NDMA as the fragment ions are not specific enough for identification. They occur in the region of background noise (m/z 42, 43) which adversely impacts on the MDL. The ion specified for NDMA quantitation (m/z 72) is not present in high abundance, which reduces sensitivity of the determination, and may be a common ion to another co-eluting compound present in the sample.

As also suggested in the method, unequivocal determinations require the use of alternative confirmatory techniques. This could be circumvented by the use of more advanced systems of mass spectrometry utilising GC and LC chromatography.

Overall this method is not recommended for the routine or specialist analysis of volatile nitrosamines.

INRS Method 031: N-Nitrosamines volatiles

Principle and Application: Volatile nitrosamines in ambient and workplace air by GC/TEA

Method Status: Fully validated, 2007

Target analytes: **NDMA**, NMEA (*N*-nitrosomethylethylamine), **NDEA**, NPyr, NDPA, **NMor**, **NPip**, NDBA.

Collection: Solid sorbent air sampling cartridges containing Florisil® (magnesium silicate) and a sulfamic acid pre-cartridge or Thermosorb/N™ solid sorbent air sampling cartridges.

Air Sampling Volume and Rate: 250 to 300L at 1 to 4 L/min.

Storage and Stability: Extract solutions stored at freezer temperatures, protected from light.

Preparative: Florisil® cartridge desorbed with 1.5 mL of acetone, Thermosorb™ cartridge desorbed with 75/25 v/v dichloromethane/methanol.

Analysis: Gas chromatography with a Thermal Energy Detector (GC/TEA).

Instrument MDL (GC/TEA): 0.1 – 1 µg/mL (equiv. ~0.1 – 1 ng).

Procedural MDL: 1 µg/m^3 (parameters as stated).

Recovery: Not stated.

Interferences: Not stated.

Supporting Information:

Sulfamic acid used to inhibit in-situ nitrosamine formation.

Comments and Recommendation

Use of dual cartridge system and ability to extract only the Florisil™ sorbent is reported to eliminate interferences experienced with Thermosorb/N®, particularly important for NPD detectors which are sensitive to certain solvents and (Aubin *et al.* 2009).

This extraction technique may make the method more amenable to analysis using alternative detection techniques, such as GC/MS and LC/MS, and may extend the solvent choice to that suitable for LC/MS requirements.

The disadvantage is that these cartridges are not commercially available and must be prepared in house and in a way which ensures that the cartridges will allow the required flow rates used in gas sampling.

This method is recommended for consideration in routine and specialist analysis of volatile nitrosamines.

OSHA Method 31: N-Nitrosodiethanolamine (NDELA)

Principle and Application: Non-volatile nitrosamine in ambient and workplace air by GC/TEA or HPLC/TEA.

Method Status: Fully evaluated, 1981

Target analytes: **NDELA**

Collection: Gelman Type A glass fibre filters (without chemical impregnation) in open faced cassettes.

Air Sampling Volume and Rate: 480L at 2 L/min.

Storage and Stability: Filters stable for 16 days at ambient temperature, protected from light. Freezer storage improves recovery. Extracts stored under refrigeration.

Preparative: Sample treated with Dowex 1-X8 anion exchange resin and extracted with 5 mL of 2-propanol. The resin is added to remove nitrate ions which are detected as an interference by TEA. Note that the resin will also remove a small proportion of NDELA from solution and must therefore be applied to standard solutions in the same quantity and over the same time period.

Analysis: GC/TEA and HPLC/TEA. Confirmation required using both methods.

Screening Analysis: HPLC/UV.

Instrument MDL (GC/TEA): NDELA 0.2 ng.

Procedural MDL: NDELA 0.42 $\mu g/m^3$ (under parameters stated).

Recovery: 97 – 103% from NDELA spiked sampling filters.

Interferences: Nitrites interfere with TEA detection and are removed using anion exchange resin, under the limitations described above.

This method is not validated as artifact free. NDELA can be formed on the air sampling device from chemical reaction of di- and triethanolamine with a suitable nitrosating species such as nitrogen oxides.

Supporting Information:

NDELA is considered non-volatile and if the airborne compound is present it would be contained in an aerosol. Collection efficiency for aerosols on solid sorbents has not been established.

Comments and Recommendation

Substantiation of the efficiency or application of the filter collection method could not be found in the literature and this would required evaluation.

NDELA chromatographs relatively poorly by GC due to its low volatility and its polar nature and it is commonly derivatised prior to GC analysis (Ohshima *et al.* 1979). It is considered that LC would provide improved chromatography resulting in higher sensitivity, selectivity and precision.

The method is recommended if HPLC/TEA technique is implemented. The GC/TEA method is not recommended for the routine analysis of NDELA or other non-volatile nitrosamines.

Standard Methods for Liquid Phase and Universal Collection

The following standard methods apply to the collection and analysis of liquid phase samples from drinking, ground and waste water sources. This section also includes methods which apply to the analysis of a wide range of semivolatile compounds from all types of solid waste matrices, soils, and groundwater and from air sampling media.

US EPA Method 521: Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionisation Tandem Mass Spectrometry (MS/MS)

Principle and Application: Nitrosamines in finished drinking water by GC/CI-MS/MS.

May be applicable to untreated source waters and other water samples, under in-house validation.

Method Status: Fully evaluated, 2004.

Target analytes: **NDMA**, NMEA, **NDEA**, NPyr, NDPA, **NPip**, NDBA.

Collection: Amber glass bottles. Dechlorination with sodium thiosulphate. Note: no other nitrosation inhibitor is used.

Storage and Stability: Transported below 10ºC, stored below 6ºC but not frozen, for up to 14 days. Extracts stored at minus 15ºC for up to 28 days, protected from light.

Preparative: 500 mL sample spiked with isotopically labelled NDMA-d_6 and passed through SPE cartridge containing coconut charcoal. Analytes eluted with dichloromethane. Concentrated under nitrogen to 1 mL.

Analysis: Large volume (20uL) injection (LVI) and programmed temperature vaporising (PTV) inlet system using cool injection temperatures, gas chromatography tandem mass spectrometry (GC/MS/MS) operated in the chemical ionisation mode (CI) using methanol or acetonitrile as the CI reagent. Identification is based on retention time, the MS precursor ion $[M+H]^+$ obtained from CI/MS and the product ion mass spectrum produced in MS/MS by collisionally activated dissociation of the precursor ion. A product ion is selected for quantitation using internal standard technique with isotopically labelled NDEA-d_{10} and NDPA-d_{14}

Instrument MDL (GC/CI-MS/MS): Not stated (equiv. ~3 pg dependent on LVI/PTV inlet conditions).

Procedural MDL: NDMA 0.28 ng/L, NPip 0.66 ng/L (parameters as stated).

Recovery: NDMA 87%, NPip 83% Recovery of NDMA validated using isotopically labelled NDMA-d_6 surrogate spiked into the water sample prior to extraction.

Interferences: Contaminants from polypropylene cartridges and SPE sorbents should not be at a level which precludes MS identification and quantitation. Nitrosamines are present in rubber products and use of PTFE coated rubber septa should be avoided.

Supporting Information:

Applicable to those nitrosamines that are efficiently partitioned from the water onto a solid phase extraction (SPE) sorbent, and sufficiently volatile and thermally stable for gas chromatography.

Use of a PTV inlet at cool initial injection temperatures reduces or eliminates decomposition of thermally labile compounds.

NMor was evaluated for inclusion but was not validated due to unresolved problems with background contamination.

Comments and Recommendation

SPE sorbent technique appears to provide improved recovery for NDMA and other nitrosamines than methods using liquid-liquid extraction and requiring solvent evaporation and possibly clean-up procedures. The method would require development and validation for more complex liquid matrices.

Method offers optimum performance with advantage of advanced GC inlet systems to reduce effects of inlet on thermal decomposition, and advanced mass spectrometry modes (CI-MS/MS) to provide enhanced qualitative and quantitative performance compared with EI-MS and provides unequalled sensitivity.

However, it is suitable only for volatile nitrosamines and would not allow for the analysis of the complete suite of nitrosamines specified for assessment in PCC process matrices. For this reason, mass spectrometry using LC should be considered.

Overall this method is recommended for the specialist analysis of volatile nitrosamines provided validation is undertaken to ensure nil artifact formation and to ensure the efficiency of the SPE extraction technique for specific process matrices.

AWWA (and Affiliates) Method 6450: Nitrosamines

Principle and Application: Nitrosamines in raw source water, finished water and recycled water by GC/CI-MS/MS.

Method Status: Fully evaluated, 2007.

Target analytes: **NDMA**, NMEA, **NDEA**, NPyr, NDPA, **NMor**, **NPip**, NDBA.

Collection: Amber glass bottles. Addition of sodium sulphite or sodium thiosulphate for sampling of chlorinated or chloraminated waters, to quench residual and minimise additional nitrosamine formation. For potable waters ascorbic acid may be used.

Storage and Stability: Transport < 6ºC, store < 6ºC but not frozen, protected from light, for up to 14 days. Extracts stored at ≤ 10ºC protected from light, for up to 6 months.

Preparative: 500 mL sample spiked with isotopically labelled internal and surrogate standards; NDMA-d_6, NDPA-d_{14}, NDEA-d_{15}. Nitrosamine sorption using Ambersorb 572 carbonaceous adsorbent resin added to sample. Resin is filtered, collected into a vial and extracted with 400 µL of dichloromethane.

Analysis: 8uL injection onto temperature programmable injector using cool injection temperatures, gas chromatography tandem mass spectrometry (GC/MS/MS) operated in the chemical ionisation mode (CI) using methanol or acetonitrile as the CI reagent. Identification based on retention time, the MS precursor ion $[M+H]^+$ obtained from CI/MS and the product ion mass spectrum produced in MS/MS by collisionally activated dissociation of the precursor ion.

Instrument MDL (GC/CI-MS/MS): Not stated (equiv. ~8 pg dependent on inlet conditions).

Procedural MDL: NDMA 0.84 ng/L, NPip 0.74 ng/L (parameters as stated).

Recovery: NDMA 101%, NPip 97%.

Interferences: Contaminants from reagents, glassware etc.

Supporting Information: Use of a PTV inlet at cool initial injection temperatures reduces or eliminates decomposition of thermally labile compounds.

Comments and Recommendation

Major difference between this method and US EPA Method 521 is choice of SPE sorbent and mode of application (i.e. Ambersorb® resin added to sample versus sample through a charcoal cartridge). Ambersorb® resin is a carbonaceous sorbent. Evaluation of the efficiency of these sorbents for application to process liquids is advised.

Method is supported by optimisation and validation from Fields *et al.*, 2004.

Comments made for Method 521 with respect to advantages of SPE and advanced GC and MS modes of operation are relevant to this method also. Method would require development and validation for more complex liquid matrices.

Method suitable only for volatile nitrosamines and would not allow for the analysis of the complete suite of nitrosamines specified for assessment in PCC process matrices. For this reason, mass spectrometry using LC should be considered.

Overall this method is recommended as a support method for US EPA Method 521, for the routine and specialist analysis of specified volatile nitrosamines provided validation is undertaken to ensure nil artifact formation and to ensure the efficiency of the SPE extraction technique for specific process matrices.

US EPA Method 607: Nitrosamines

US EPA Method 8070A: Nitrosamines by Gas Chromatography

Principle and Application: Nitrosamines in municipal and industrial wastewater and in ground water by GC/NPD. Applicable also to GC/TEA and GC/MS.

Method Status: Fully evaluated, 2004.

Target analytes: **NDMA**, NDPA, NDPhA.

Collection: Amber glass bottles. Dechlorination with sodium thiosulphate where presence of chlorine is determined in the field by US EPA methods 330.4, 330.5.

For NDPhA determination, the pH is adjusted to 7-10 with sodium hydroxide solution or sulphuric acid.

Storage and Stability: Transported under ice, refrigerated at 4ºC but not frozen, for up to 7 days. Extracts stored under refrigeration for up to 40 days, protected from light.

Preparative: 1 L sample adjusted to pH 5-9 with NaOH or H_2SO_4 solution and solvent extracted with dichloromethane. The extract is washed with dilute HCl to remove free amines, dried and concentrated to 10mL or less.

For NDPhA determination a Florisil or alumina clean-up is used to eliminate diphenylamine interferences.

For GC/NPD detection the solvent is exchanged to methanol to a final volume of 2mL.

Analysis: GC/NPD (thermionic detector).

Instrument MDL (GC/NPD): Not stated (equiv. 0.3 ng, dependent on injection parameters).

Procedural MDL: NDMA 0.15 µg/L (parameters as stated).

Recovery: NDMA 32%, 37%, NDPA 61%, 96% (single operator using Methods 8070 and 607 respectively)

NDMA 13-109%, NDPA 45-146% (Method 8070 interlaboratory)

Interferences: Quenching agents added at sampling stage relevant only to dechlorination. pH 9 adjustment specified only for NDPhA.

Free amines are removed from the sample extract using dilute hydrochloric acid wash, to aid in nitrosamine detection using GC/NCD.

Florisil and alumina cleanup procedures to separate diphenylamine from nitrosamines and to aid in the elimination of interferences.

Supporting Information:

NDPhA undergoes transnitrosation reactions and care must be exercised in the heating or concentration of this compound in the presence of reactive amines. It will degrade completely in the GC injection port (200 - 250ºC) to diphenylamine and is chromatographed and detected as such, in the knowledge that native diphenylamine has been removed from the sample by the clean-up procedure.

TEA offers highest selectivity of the non-MS detectors and may be used in place of NPD when interferences are encountered.

Confirmation of NDPA or other products using Method 625 Base Neutral and Acids, or Method 8270 Semivolatile Organics, by GC/MS is recommended.

Comments and Recommendation

The method offers good procedural detail for solvent extraction and clean-up, particularly for removal of free amines interferences and removal of diphenylamine for analysis of N-nitrosodiphenylamine. Liquid-liquid extraction has generally been replaced with SPE techniques, however.

The method provides only rudimentary gas chromatographic procedural information and uses packed columns, which do not provide the resolution of capillary columns. It does not address the procedural requirements in the use of NPD detectors (apart from requirement to solvent swap to methanol). The method recommends the use of GC/TEA as offering higher selectivity but does not address procedural requirements of this technique.

Recoveries of NDMA and NDPhA are very low and probably impacted by the rigorous clean-up procedures, and possibly extraction and solvent swap procedures required for NDP analysis (based on the fact that other GC based methods return >90% recoveries for these analytes). This is a major limitation of this method.

Mass spectrometry methods and the use of isotopically labelled surrogate standards would allow an account of losses and may render the method useable, in the case these extraction and clean-up techniques are considered appropriate.

Overall this method is not recommended for routine or specialised analysis of nitrosamines in gaseous or liquid samples.

US EPA Method 1625C: Semivolatile Organic Compounds by Isotope Dilution GC/MS

Principle and Application: Base/neutral and acid extractable semivolatile organic compounds in municipal and industrial waste waters by isotope dilution GC/MS.

Method Status: Partially evaluated, 1991

Target analytes: Multi-analyte semivolatile organics (over 70 components) including nine nitrosamines: **NDMA**, NMEA, **NDEA**, NDPA, **NMor**, **NPip**, NMPhA, NDBA, NDPhA.

Collection: Amber glass bottles. Dechlorination with sodium thiosulphate if required (using Method 330.4, 330.5 field measurement). Note: no other nitrosation inhibitor is used.

Preparative: 1 L sample is spiked with isotopically labelled compounds (NDMA-d_6, NDPA-d_{14}, NDPhA-d_6), pH adjusted to 12-13 with NaOH solution and extracted with dichloromethane using continuous liquid-liquid extraction technique. Concentrated to 1 mL (or 10 mL if GPC clean-up is required).

Storage and Stability: Transport and store 0-4ºC for up to7 days. Extracts stored at 0-4ºC for up to7 days for up to 40 days, protected from light.

Analysis: Gas chromatography with mass spectrometry (GC/MS) using electron impact (EI) in full scan mode with quantitation by extracted ion current profile areas.

Instrument MDL (GC/MS): Not stated (equiv. 0.2 ng).

Procedural MDL: NDMA 16 µg/L, NDPA 46 µg/L (parameters as stated).

Recovery: NDMA 10%, NDPA 100 ±45% Method losses accounted using isotope dilution quantitation.

Interferences: Contaminants from solvents, reagent, glassware.

Supporting Information: No further information of relevance.

Comments and Recommendation

No procedure is recommended to account for thermal lability of nitrosodiphenylamine.

Use of isotope dilution accounts for analyte losses through entire analytical procedure thereby improving accuracy compared with non corrected methods.

Liquid-liquid extraction, concentration and clean-up procedures impact adversely on recovery compared with SPE technique (as per Method 521), particularly for NDMA.

Overall, the method could be considered for routine screening analysis of volatile nitrosamines with the incorporation of SPE extraction to improve analyte recoveries.

US EPA Method 8270D: Semivolatile organic compounds by gas chromatography / mass spectrometry (GC/MS)

Principle and Application: Semivolatile organic compounds in water, solid waste matrices, soils and air sampling media, by GC/MS.

Method Status: Not fully validated for all compounds Note that this method provides detailed analytical determinative procedures but does not provide specific guidance as to sampling protocols, and general guidance only to preparative procedures.

Target analytes: Multiple component analysis of over 200 neutral, acidic and basic organic compounds.

Includes nine nitrosamines: **NDMA**, *N*-nitrosomethylethylamine (NMEA), **NDEA**, NPyr, NDPA, **NMor**, **NPip**, NDBA, *N*-nitrosodiphenylamine (NDPhA).

Collection: Air - Method 0010 air sampling train (impinger and solid sorbent sampling).

Collection: Liquid – not stated.

Air Sampling Volume and Rate: Not stated.

Aqueous Sampling Volume: Not stated.

Storage and Stability: Not stated.

Preparative: Air - Method 3542A separatory funnel liquid-liquid extraction into dichloromethane.

Preparative: Aqueous - Method 3510C separatory funnel liquid-liquid extraction into dichloromethane. Clean-up using Method 3610B (basic alumina) or Method 3620C (Florisil) to remove amines. Method 3640A (gel permeation chromatography) to remove high molecular weight species. Method 3535 solid phase extraction (SPE) into dichloromethane.

Analysis: Gas chromatography with a mass spectrometry (GC/MS) using EI mode and extracted ions as specified for each compound.

Instrument MDL (GC/MS): not stated.

Procedural MDL: Air - not stated.

Procedural MDL: Aqueous – NDMA not stated, NDEA 10µg/L groundwater (parameters not stated).

Recovery: Not stated.

Interferences: Contaminants from equipment and reagents.

Supporting Information:

Method is applicable to compounds which are able to be efficiently extracted into dichloromethane and are capable of being eluted, without derivatisation, as sharp peaks from a gas chromatographic column.

NDMA is difficult to separate from the solvent under the chromatographic conditions described.

N-nitrosodiphenylamine decomposes in the gas chromatographic inlet to diphenylamine and cannot be separated from native diphenylamine. The concentrations are combined and reported as such.

Comments and Recommendation

Method 8270 is a universal semivolatile method, hence there is little specific attention given to the requirements of nitrosamine analytes. Analyte degradation or losses in the sampling and preparative steps may be a consequence of this.

GC/MS analysis using electron impact is not the preferred mode for identification of nitrosamines due to similarity in EI generated mass spectra and presence of lower m/z ions which are not specific enough for identification of lower nitrosamines. Reliance therefore is on chromatographic resolution for closely eluting compounds. Ions in the region of background noise such as m/z 42, 43 are less suitable for quantitation and secondary ions can also reduce method sensitivity.

Overall this method is not recommended for routine or specialised analysis of nitrosamines in gaseous or liquid samples.

4.2.3 Standard Methods Summary Recommendations

The previous section reviewed ten standard test methods considered as possessing attributes most appropriate to the determination of nitrosamines of relevance to this study. Environmental methods were selected due to their applicability in trace level analysis and to matrices similar to the gaseous and liquid matrices to be assessed in this study. The principle, analytical and instrumental requirements and performance of the selected standard methods was outlined and comments have been made as to their attributes and limitations. On this basis a summary of this review and the recommended methods is now presented.

The standard methods are applicable to the priority suite of volatile nitrosamine contaminants and the non-volatile nitrosamine; *N*-nitrosodiethanolamine (NDELA). The target analytes include those compounds specified for assessment by the CCM project (NDMA, NDEA, NMor, NPip, NDELA) apart from *N*-nitrosopiperazine and 1,4-dinitrosopiperazine which are not addressed by any of the standard methods. The latter compound falls towards the non-volatile end of the range and also possesses high polarity. The sorbent cartridge and filter methods would both require evaluation for efficiency of collection of these compounds. Unfortunately substantiation of the filter collection technique used in the standard method for NDELA could not be found in the literature. Additionally the impact of water and bulk amine solvents on the capacity of the cartridge to collect trace levels of nitrosamines will require assessment and validation. There are no standard methods available for NDELA, *N*-nitrosopiperazine and 1,4-dinitrosopiperazine in aqueous samples and validation of the SPE technique used for the volatile nitrosamines would require evaluation and validation. Due to the low volatility of these compounds and of NDELA, GC based methods may not provide the necessary efficiency or chromatographic resolution. This is not addressed in the standard method for NDELA and would also require assessment. It is possible that these compounds are better analysed using liquid chromatography using the LC/TEA option in the standard method, or by alternative methods using derivatisation/HPLC or LC/MS techniques as discussed in the next section.

These methods are applicable to nitrosamines of environmental relevance and apply to ambient, workplace and combustion source assessment for determinations from the gas phase, and to drinking and wastewaters for determinations from the liquid phase. As such their applicability to gaseous and liquid samples from the PCC process would require development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. It may eventuate that the standard method, or aspects of it, may be applicable as a starting point for application to the PCC process, or indeed that alternative non-standard methods may be preferable.

On these bases, a summary of the methods recommended for speciated analysis of specified volatile nitrosamines and *N*-nitrosodiethanolamine in gaseous and liquid matrices is presented. For details of reasoning and attributes and limitations of these methods, please refer to the relevant method in the previous section. The recommendation applies to the sampling and analytical performance of the method in the application for which it was designed but by no means guarantees its performance in its application to PCC process samples.

Gas Phase Methods

- OSHA Method 27: Volatile Nitrosamines Mixture I

Principle: Volatile nitrosamines in ambient and workplace air using Thermosorb/N sampling cartridges and analysis by GC/TEA and HPLC/TEA.

Target analytes: NDMA, NDEA, NPyr, NDPA, NMor, NPip, NDBA.

Procedural MDL: 0.13 µg/m^3 (0.04 ppbv) NDMA using 75L gas sample volume and under method parameters stated. Standardised back to 100L for comparison of methods; equivalent to 0.10 µg/m^3 (0.03 ppbv) NDMA.

- INRS Method 031: N-Nitrosamines volatiles

This method is based on similar principles to OSHA Method 27 but implements a dual cartridge technique which reportedly provides an improvement in the level of interferences and the possible use of solvents favourable to the use of LC/MS as the determinative technique.

- OSHA Method 31: N-Nitrosodiethanolamine (NDELA)

Principle: Non-volatile nitrosamines in ambient and workplace air using glass fibre filters open faced cassettes and analysis by GC/TEA or HPLC/TEA.

Target analyte: NDELA.

Procedural MDL: 0.42 µg/m^3 (0.08 ppbv) NDELA using 480L gas volume and under methods parameters stated. Standardised back to 100L for comparison of methods; equivalent to 2.0 µg/m^3 (0.37 ppbv) NDELA.

GC based method for NDELA would require further evaluation as to its efficiency. HPLC is recommended for this and other non-volatile nitrosamines.

Liquid Phase Methods

- US EPA Method 521: Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionisation Tandem Mass Spectrometry (MS/MS)

Principle: Volatile nitrosamines in finished drinking water using solid phase extraction and analysis by GC/CI-MS/MS.

Target analytes: NDMA, NMEA, NDEA, NPyr, NDPA, NPip, NDBA.

Procedural MDL: 0.28 ng/L NDMA using 500 mL liquid sample.

- AWWA Method 6450: Nitrosamines

This method is based on similar principles to US EPA Method 521 but implements Ambersorb® carbonaceous resin instead of coconut charcoal filled SPE cartridges. An evaluation of the efficiency of these two sorbents and/or an alternative sorbent for application to process liquids is advised.

4.2.4 Non-Standard Methodologies

Almost all analytical methods for nitrosamines utilise some form of chromatographic separation prior to analyte detection. In samples with a simple matrix, the nitrosamines can be determined directly using polarographic and spectrophotometric methods. However, these techniques are subject to interferences and have limited application for low level analysis of complex samples but they can find application as a screening technique in certain applications. Thin layer chromatography (TLC) also finds semi-quantitative application and various methods are used to form fluorescent derivatives or coloured complexes. The TLC methods are easy to use and some have low detection limits but they lack resolution. (OSHA Method 27, background information). A description of these methods can be found by Perera *et al.* 2006.

Gas chromatographic methods originally incorporated conventional detection techniques such as the FID, but this is limited by its lack of sensitivity for nitrogen containing hydrocarbons and sensitivity is accomplished only after derivatisation. Nitrogen-specific detectors can be useful but their non-selectivity to nitrosamines make them mainly useful for routine screening. Non-specific detectors, such as FPD, have also been used but the incorporation of suitable derivatisation step is required to render the nitrosamine detectable. For example, Kataoka *et al*. (1996) reported the determination of seven volatile *N*-nitrosamines in cigarette smoke by GC/FPD. The method is based on the denitrosation with hydrobromic acid to produce the corresponding secondary amines and their subsequent diethylthiophosphorylation. To ensure selectivity, the derivative must accurately target the analyte class of interest. The gas chromatographic analysis of less volatile and polar nitrosamines, such as *N*-nitrosodiethanolamine (NDELA), can be problematic due to adsorption and poor chromatographic resolution and again derivatisation is commonly implemented. Ohshima *et al.* (1979) assessed the efficiency of reagents for derivatisation of hydroxylated nitrosamines and yielded up to 2000-times greater sensitivity in their detection compared with analysis of the compounds in their free form. This was prior to the use of deactivated columns and injector treatments commonly employed today to alleviate these issues but certainly limitations still exist for the direct analysis of compounds of this type.

In the case of liquid chromatographic methods, fluorescence detection is commonly achieved after chemical denitrosation with an acid, such as hydrobromic-glacial acetic acids, to produce secondary amines followed by their derivatisation with dansyl chloride. A few examples only of the many applications of this method to a variety of solid and liquid matrices include Wang *et al.* (1992), Komarova and Velikanov (2001), Cardenes *et al*. (2002). The later author achieved high sensitivity; 10 - 100 pg for certain volatile nitrosamines. Liquid chromatography offers significant advantages in the analysis of the non-volatile nitrosamines and is commonly used for the analysis of NDELA, as will be discussed the following sections.

To overcome the ineffective or cumbersome nature of these methods of detection, the thermal energy analyser (TEA), or nitrogen chemiluminescence detector (NCD) as it is alternatively known, and mass spectrometry (MS) and have become the principle methods for determination of nitrosamines. These two techniques and their application to gas and liquid chromatographic methods will therefore be the focus of the following discussion.

Chemiluminescence Methods

The analytical methodology for the determination of trace levels of nitrosamines using the thermal energy analyser (TEA) was first described by Fine *et al.* in 1975. This method holds its popularity today due to its inherent selectivity to *N*-nitroso compounds and its sensitivity for trace level analysis of complex environmental samples. The TEA can be interfaced to a GC which is generally more practical for determination of volatile nitrosamines or to LC for non-volatile or thermally unstable nitrosamines, such as *N*-nitrosodiphenylamine. The technique is based on the relative ease of dissociation of the N-NO bond in *N*-nitroso compounds and release of the nitric oxide group (denitrosation). In the case of TEA this is followed by chemiluminescence determination of nitric oxide (NO) by measurement of the emission from decay of excited nitrogen dioxide. This is the basis for the selectivity associated with the TEA system for determination of nitrosamines. Determination of the resulting nitrite ion or its amino counterpart can also be implemented and these are measured by means such as spectrometry, fluorescence, chemiluminescence and amperometry. These techniques are described in detail by Perera, 2006. An example of the colorimetric detection of nitrite ion after HPLC and post-column photohydrolysis is found in the publication by Bellec *et al*. (1996) and by amperometry by Richezza *et al*. (1987). The TEA will be emphasised in this report due to its maturity as a technique in many applications.

The GC/TEA interface operates with gaseous analytes, separated previously by GC, which are swept through a catalytic pyrolyser with the carrier gas. All *N*-nitroso compounds are thermally cleaved at the *N*-nitroso bond (N-NO), releasing the nitrosyl radical (·NO). This is separated from organic fragments and other gaseous products by passing through one or more cold traps and/or through a solid state chemical CTR filter cartridge. The NO containing gas is introduced into a reduced pressure reaction chamber where it is oxidised to with ozone to generate electronically excited nitrogen dioxide (NO_2*). The NO_2* instantaneously decays back to its ground state with emission of a characteristic radiation in the near-infrared region of the spectrum (0.6 – 2.8 µm). This is monitored by a photomultiplier tube associated with a red optical filter to eliminate wavelengths shorter than 600 nm. The amplified signal is integrated as being proportional to the amount of *N*-nitroso compound present in the sample (Perera 2006).

The technique has been applied to various environmental and health assessments in air, water and soil matrices by Fine *et al.* (1975 (ii), 1976, 1977) after its introduction in 1975 (Fine *et al.,* 1975 (i)). Roundbehler *et al.* (1980) measured volatile nitrosamines in the cabin of new motor vehicles, Goff *et al.* (1980) measured nitrosamines in diesel engine emissions and also addressed the effect of NO_x on artifact formation and on the requirement for nitrosation inhibitors incorporated into emissions sampling. Freed *et al.* (1977) published a method for preparation of calibrants by direct generation of nitrosamines in the GC inlet for GC/MS and applicable to GC/TEA. Althorpe *et al.* (1970) determined nitrosamines by conversion to their corresponding nitramines. Parees (1979) applied GC/TEA to direct analysis of *N*-nitrosodimethylamine in dimethylamine solution using silica gel isolation technique with confirmation using GC/MS. He also examined the detection of dimethylnitramine formed from photodecomposition of NDMA which he used to propose another method of nitrosamine confirmation, and to elucidate nitramine interferences. Musson and Sternson (1979) analysed nitrosamines in aqueous biological fluids based on measurement of photochemically liberated nitrite. Walker and Castegnaro (1980) determined the TEA response of nitramines and Parees and Prescott

(1981) examined amine matrix effects on the nitrosamine TEA response. Krull *et al.* (1978) published on the limitations of TEA with respect to the possibility of false-positive and negative results and the various aspects which require address in ensuring accuracy of analytical results, and alternative confirmatory methods and Krull *et al.* (1979) determined an analysis scheme to distinguish N-NO compounds from C-NO, O-NO, N-NO_2 (nitramine), C-NO_2, and O-NO_2.

Massey *et al.* (1982) proposed a modification to the technique to allow liquid chromatography to be used as the separation technique particularly for less volatile compounds. Ruhl and Reusch (1985) also worked to overcome the limitations associated with the use of LC/TEA with aqueous LC systems; an issue which is associated with an aspect of the instrument hardware and which can render the technique non-sensitive to nitrosamines. Havery (1990) suggested a post-column reaction scheme to allow the use of LC with TEA. Modern analysers incorporate a selection of interfaces which still require reverse phase techniques but operate on more suitable principles for LC sample introduction. These interfaces use a reaction based mechanism to liberate nitric oxide rather than by pyrolysis.

The application of the technique to exposure and environmental monitoring, and to the monitoring of manufactured products, occurred with the realisation of these compounds health implications and, along with the selectivity and sensitivity of TEA, meant that the technique found wide acceptance, particularly GC/TEA. This is exemplified by the vast number of publications promoting its application to date; the number being too many to record here. The reader is referred to Ikeda *et. al* (1990) who presents a selected listing of around 150 references on the various application of GC/TEA and LC/TEA to the determination of nitrosamines through to 1990. More recent examples include Brunnemann *et al.* (1992) who monitored indoor air for tobacco-specific nitrosamines using a thermal desorption technique to transfer collected analytes to GC/TEA. Oury *et al.* (1997) applied the GC/TEA technique to workplace exposure in the rubber industry and Fadlallah *et al.* (1996) in application to ambient air assessment in metal working factories. Incavo and Schafer (2006) used GC/TEA to determine volatile nitrosamines in rubber vulcanisates. Tomkins *et al.* (1995) determined NDMA at parts-per-trillion (ppt) levels in drinking and ground waters and Grebel and Suffet (2007) compared the performance of NPD and NCD for volatile nitrosamines in water matrices. Ding *et al.* (1998) used the TEA to develop a group-selective method for the determination of total nitrite and total *N*-nitroso compounds in air samples, which may find particular application for determinations of this type for this project. The application of the method has been reported in many other areas, such as food and personal products and in biological contexts. Methods for *N*-nitrosodiethanolamine are particularly relevant to the cosmetic industry. The current European cosmetics association standard (Colipa, 2009) uses chemiluminesence for screening total nitrosamine content, as validated by Challis *et al.* (1995). GC/TEA is used for determination of NDELA accompanied by prior derivatisation to the trimethylsilyl derivative in a method also reported by Sommer and Eisenbrand (1988) and Spiegelhalder and Preussmann (1984). A post column derivatisation HPLC/colorimetric method is also specified in the industry standard (Flower *et al.* 2006) and an LC/MS/MS technique, without derivatisation, is also suggested (Schothorst and Somers, 2005). In gas chromatography, the hydroxylated nitrosamines are commonly derivatised to improve their chromatographic performance however some authors have used direct injection to GC/TEA. Ducos *et al*. (1999) reported GC/TEA analysis of NDELA without derivatisation for evaluation of its presence

in urine from workers exposure to metalworking fluids. Modern columns and treatment of instrument hardware, such as base deactivation can reduce adsorption and improve resolution for certain compounds but this is still a limitation which must be considered in the direct analysis of the free form of these types of compounds.

Modern instruments utilise three modes of operation; the nitrogen mode (which responds to nitroso, nitro and organic nitrogen), the nitro mode (nitroso and nitro compounds) and the nitroso mode, allowing the analysis of nitroso compounds and other nitrogen containing compounds, such as small amines and ammonia (CSi and ACS companies, TEA Model 610). The TEA is highly selective to nitrosamines but other nitroso compounds will also respond such as some organic nitrites, *N*-nitramines, C-nitroso, O-nitroso, nitrate and inorganic nitrite, as discussed previously. The relative response of these compounds is dependent on the pyrolysis temperature and catalyst activity, and the basis of selectivity in the three modes of operation for current analysers.

Chemiluminescence methods have a number of attributes. TEA is very sensitive allowing detection in the 30 - 100 pg range as the instrument detection limit. Compared to GC/NPD and GC/MS the TEA provides approximately 5 to 10-times higher sensitivity. Its main rival for this level of analysis is GC/CI-MS/MS which will deliver approximately 100-times the sensitivity of GC/TEA, although at higher cost and complexity. Combined with its inherent selectivity the TEA can be applied to the analysis of complex samples where the presence of co-eluting compounds would otherwise interfere in the analysis. This also eliminates the need for clean-up procedures and the associated issues of analyte losses and time spent on preparative procedures. As in any chromatographic method, the chemical structure of the nitrosamine, the polarity of the column, column length, diameter and flow rate are important variables to be addressed in order to optimise the chromatographic resolution of the nitrosamines.

One practical disadvantage of TEA instrumentation from a laboratory operations perspective is its relative expense as the entire GC or LC system is likely to be dedicated to samples for analysis of nitrosamine and nitrogen containing species only. Alternative instrumental techniques using GC and LC with more traditional detection systems were outlined in the initial paragraph of this section, but these methods all hold additional complexity in order to achieve the required selectivity or sensitivity, which is an obvious drawback. Compared to the most advanced GC/CI-MS/MS or LC/MS/MS systems the cost of TEA is not high.

The role of the thermal energy analyser and chemiluminesence detection cannot be underrated but its success has tended to be based on its application in areas where products or matrices have known amine and nitrite precursors, and hence known nitrosamine reaction products (such as water disinfection, cosmetics etc), or targeted regulatory levels for certain nitrosamine compounds (such as drinking water or workplace exposure), and in the case of GC/TEA only the volatile and less polar nitrosamines can be determined. In other areas of application where the conditions of nitrosamine formation are more complex, the limitations of TEA techniques become more obvious and the requirement for more advanced methods of nitrosamine characterisation are required. In the context of PCC process assessment, TEA has an obvious role as a selective and sensitive tool for volatile nitrosamine analysis, and modern instruments have the capability to monitor for ammonia and other amines, provided they are amenable to the required sample preparation. For more complex

nitrosamine elucidation tasks, and other products from PCC processes, one would also look to GC and LC mass spectrometry systems, as these offer confirmatory and structural information which cannot be obtained from TEA or other detection systems.

Recommendation – Chemiluminescence Methods

The maturity of the chemiluminescence approach, as exemplified by TEA or NCD, as a determinative method for analysis of nitrosamines (and of amines and ammonia using 2nd generation analysers), including the recognition and in some cases address of interferences and artifacts, its sensitivity and selectivity, and the associated reduction in preparative requirements, makes this technique a valuable tool for quantitative analysis of both liquid and gas phase samples from the PCC process. With incorporation of GC and LC for the non-volatile analytes, it has particular appeal in screening and group type analytical requirements and will provide adequate speciated analysis where unequivocal confirmation is not a necessity, and on this basis the chemiluminescence technique is highly recommended.

Mass Spectrometry Methods

GC/MS Methods

Mass spectrometry based on gas chromatographic separation is an accepted method for detailed analysis of volatile nitrosamines as exemplified by its establishment as a standard technique in environmental applications (specifically US EPA Method 521, AWWA Method 6450). These methods implement the more sophisticated modes of GC/MS where chemical ionisation and tandem mass spectrometry is incorporated (GC/CI-MS/MS), rather than the more commonly used GC/MS techniques which generally use electron impact. The limitation of EI-MS is mainly due to the similarity in the mass spectra obtained from this "hard" ionisation mode which aims to produce a characteristic mass spectrum of the fragmented molecule. For the volatile alkyl-nitrosamines, their structure will produce very similar spectra, and similarly between cyclic-nitrosamines, and these spectra are inadequate in confirming the identity of each analyte. For this reason chemical ionisation (CI) is a more powerful tool as, being a soft ionisation technique, fragmentation of the molecule is limited and a mass spectrum is produced with one significant ion which is used to produce a product ion mass spectrum under a second ionisation (MS/MS mode) by collisionally activated dissociation of the selected precursor ion. This spectrum is then highly characteristic of the specific analyte. CI-MS/MS therefore improves the selectivity of the analysis and is an advantage for trace concentrations in very complex samples.

The GC/CI-MS/MS technique is also very sensitive, achieving instrument detection limits of around 1 - 10 pg under the fairly routine analytical and instrumental parameters specified in standard methods. Under typical liquid preparative and instrumental conditions these methods return a method detection limit of around 0.1 - 1 ng/L in the liquid phase. Under a suitable sorbent collection procedure the GC/CI-MS/MS method would also be used for gas phase samples and would provide a method detection limit of around 1 - 10 ng/m^3 using a 100L gas collection volume. The most advanced MS instruments have optimum sensitivity, and sub-picogram instrument detection limits levels are achievable.

The maturity of the method is demonstrated by the establishment of GC/CI-MS/MS by international agencies as a standard method of analysis. This places the technique in a category where this level of analytical complexity is now seen as commonplace in a trace level analytical laboratory, and is accessible from contract laboratories. As such this method is being developed further under a US and Canadian joint effort for water quality, as reported Fields *et al.* (2004) and based on the method originally developed by Taguchi *et al.* (1994) and reported by Jenkins *et al.* (1995). These use Ambersorb 572™ as an alternative to coconut charcoal solid phase extraction in a method similar to that detailed in AWWA Method 6450. The GC/CI-MS has been applied to water analysis (Mitch *et al.,* 2003) and others, as reviewed by Weinberg (2010). Yurchenko and Mölder (2005) used GC/CI-MS to monitor NDMA in beer. Charrois *et al.* (2004) uses a two component solid phase extraction followed by GC/MS and ammonia positive ion chemical ionisation to determine NDMA and seven other nitrosamines at method detection limits approaching that of MS/MS. The techniques are relatively well established and reviewed in many applications, particularly with respect to water quality (Andrzejewski and Nawrocki, 2005, WHO, 2006, and Richardson, 2010). The many other publications which have reported method modification and application therefore do not require further elaboration here.

The application of the simpler GC/EI-MS system of analysis using electron impact could also be considered for screening style analyses and has also been reported by many authors. More recent examples include Choi and Valentine (2002), Planas *et al.* (2008), Templeton and Chen (2010). Generally these methods apply to simple matrices or a single target analyte (such as US EPA Method TO-7 for NDMA) or are more appropriate to screening level analyses (such as US EPA Method 8270) which is applicable to a wide range of semi-volatile compounds. An improvement in the performance of the method is made using the isotopic dilution technique (as recommended in US EPA Method 6125) which reduces the variability in method and instrument efficiency and ensures accuracy of quantification. Being a less intensive analytical process EI-MS offers this advantage in time and hence cost. The technique may have some application to screening level methodologies where cost is an important factor in the PCC process monitoring protocol. At this level of analytical quality, it is considered that GC-TEA offers similar if not superior performance.

The limitations of MS using GC as the mode of separation mainly relates to the hardware components of the GC itself. The analytes, which are usually concentrated in a solvent or on a sorbent need to be volatilised so they enter the carrier stream in their vapour state. The injected analytes must therefore have vapour pressures that are compatible with the temperature limitations of the injector port, analytical column and detector. Hence nitrosamines with boiling points in excess of 200ºC are least amenable to GC analysis and those with polar substituents even less so, due to their poor chromatographic resolution. In this study, this creates a limitation of GC analysis for *N*-nitrosopiperazine, 1,4-dinitrosopiperazine and *N*-nitrosodiethanolamine. Also, under vapourisation in a hot injector, thermally labile species will decompose or degrade, such as NDPhA (not a specified species in this study), and others are temperature sensitive if exposure is excessive. For this reason most modern systems incorporate injectors which allow cool initial injection temperatures and programmable temperature ramping to minimise temperature effects. In the case of thermal desorption of sorbents the exposure to temperature is also minimised.

A derivatising agent can also be used to improve the volatility or reduce the polarity of the nitrosamine and if implemented *in-situ* can also serve to stabilise reactive analytes. Using an agent which offers specificity to the target analyte class and high detectability to the chosen detection system, derivatisation enhances method performance by providing greater selectivity and higher sensitivity. The disadvantage of post collection derivatisation is that it adds to method complexity compared with analysis of the compound in its free form, and can be prone to losses. The derivatisation technique uses a selected compound (the derivatising agent) which reacts with the analyte to form a new compound (the derivative) which possesses the required attributes. Derivatives applied to GC analysis of NDELA for example, have been prepared by acylation, trifluoracylation, trimethylsilylation and methylation (OSHA Method 31 background information) and Ohshima *et al. (*1979) determined that acylation and trimethylsilylation provided best yield for hydroxyamines. As previously discussed with respect to GC/TEA, derivatisation is routinely used in the cosmetics industry for analysis of NDELA when gas chromatography is implemented (Colipa, 2009 and publications previously cited).

Recommendation – GC/MS Methods

For highly specific analytical requirements and where the characteristics of nitrosamine products are less well known, the use of mass spectrometry provides a more definitive result than other GC detectors. GC based analyses should incorporate chemical ionisation and preferably tandem MS functionality (GC/CI-MS/MS) and the determination is restricted to only the more volatile compounds of interest in this study, unless derivatisation is implemented. For this reason LC/MS, discussed in the next section, is considered preferable if the full suite of nitrosamine analytes are to be measured from a single determination, or complementary if the analysis is split for volatile and non-volatile components.

LC/MS Methods

Mass spectrometry based on liquid chromatographic separation adds another dimension to the power of advanced separation science. The inherent limitations of GC based analysis are overcome using LC chromatographic separation and once again the advantages of MS are attainable for non-volatile, thermally labile and ionic compounds, without the requirement of derivatisation. It also allows the direct analysis of water samples (analyte concentration permitting) which can remove the need to extract the analytes into an organic solvent and enables the direct analysis of highly polar, hydrophilic analytes that are difficult to extract from aqueous matrices. Electrospray ionisation (ESI) and atmospheric pressure chemical ionisation (APCI) are currently the most effective ionisation techniques being used with LC/MS and permitting the lowest detection limits (Richardson, 2002), and can provide greater sensitivity than LC/TEA, by a factor of around 50-times. APCI acts in a manner similar to CI in the ion source of a mass spectrometer, and it does not require that ions are already present in the solution before the ionisation takes place, as in ESI. As ions formed in APCI carry a single charge, the technique is generally not suitable for high molecular weight compounds and is routinely used for analytes such as pesticides, drugs and their metabolites, surfactants, PAHs and many other organic compounds. It is a technique that can be considered complementary to ESI, and both have been applied to the analysis of volatile and non-volatile nitrosamines (as referenced below).

These ionisation modes mostly result in mass spectra with the pseudomolecular ion as the base peak and little or no fragmentation, offering the advantage of molecular weight information as an aid to analyte identification and confirmation. When more information is required tandem mass spectrometry is implemented with triple quadrupoles and ion trap technologies being the most popular choices. Instruments such as time-of-flight (TOF) mass spectrometers possess the capability for accurate mass determinations, where high mass resolution allows unequivocal determination of a molecules elemental composition and hence further improves the accuracy of the identification. These instruments are quickly gaining popularity and are available at a fraction of the cost of high-resolution double focussing instruments, formally used for this level of analysis. Hybrid systems are also used for tandem applications including magnetic sector quadrupole, magnetic sector-TOF, quadrupole-TOF (Q-TOF) and ion trap-TOF. The most successful among these hybrids is the Q-TOF instrument. Nuclear magnetic resonance (NMR) spectroscopy is a widely used method for structural elucidation in organic chemistry and this too has been coupled to LC (Górecki, 2006). Its poor sensitivity (requiring high nanogram analyte levels compared with sub-picogram for mass spectrometry) and other specificities of the technique make it unlikely option for quantitative analysis in this study however.

LC/MS methods have been extensively applied to volatile nitrosamine analysis, particularly NDMA, in drinking water and wastewaters. Many publications provide guidance on LC/MS modes and preparative and quantitative requirements in this application (Reemtsma, 2001 i, 20001 ii, 2003, Hayen and Karst, 2003, Zhao *et al.,* 2006, Plumlee *et al.,* 2008). Sophisticated techniques can be used such described by Zhao *et. al.* (2009) who applied nanoelectrospray ionization high-field asymmetric waveform ion mobility spectrometry with quadrupole time-of-flight mass spectrometry to the analysis of waters and wastewaters.

Of course LC/MS techniques are well suited to non-volatile analytes and has been applied in the environmental, food, tobacco, cosmetics and pharmaceutical areas (e.g. Petrovic *et al.* 2005, Petrovic *et al.* 2010, Wu *et al* 2008, Wagner *et al.* 2005, Malik *et al.* 2010). For the analysis of NDELA in personal care products Colipa (2009) suggest LC/MS/MS as confirmation for their other specified GC and HPLC techniques, although the method is reported to be less sensitive than that achieved using derivatisation. The technique and its application to various personal care products is described by Schothorst and Somers (2005). Ghassempour *et al.* (2008) extended the technique to include ion-pair complex liquid chromatography in order to increase chromatographic retention time, and hence separation, of nitrosamines and other compounds and thereby improve selectivity. The complexation of NDELA and sodium 1-octanesulfonate was confirmed by negative ion ESI-MS and ESI-MS/MS with an instrumental detection limit of 10 ng/mL.

A limitation in LC/MS techniques is the maturity of the method in producing accurate quantitative results. Ion suppression or enhancement of the analyte signal, which is mainly, but not wholly, a result of the effect of the matrix on the generation of ions has been widely reported, and occurs in both ESI and APCI sources (Gosetti *et al.* 2010 and others previously cited). This effect can lead to poor analyte recoveries and decreased accuracy and precision in quantitative analyses. The extent of the effect varies for each analyte and has more or less effect in each ionisation source. APCI suffers ion suppression to a lesser extent for most mixed analytes as it is less sensitive to chemical

structure and the nature of the applied solvents and the consequent effect on response than ESI (Lanina, *et al.*, 2007). The flow of the liquid phase also effects the response, this being of greater issue with ESI, it being concentration dependent, than APCI, it being mass dependent. The concentration dependency of ESI has been addressed by authors such as Asberger *et al.* (2001), and Siegel *et al.* (1998) published on minimising this problem. Many authors have explored the application specific extent of the issue (Souverain *et al.*, 2004, Benijts *et al.*, 2004, van de Steene *et al*., 2006). King *et al*. (2000) took a mechanistic approach to the issue in ESI and Caetano *et al.* (2005) modelled the responses of EIS and APCI techniques based on molecular descriptors.

In some cases the error can be low enough to tolerate, in others many orders of magnitude error can be encountered. This can be expected in the case of PCC process matrices according to Dye *et al.* (2008). However the effect can be accounted to a large extent through the incorporation of isotopically labelled standards, ideally for each and every analyte (Reemtsma, 2001 and others as cited). Of course, even if ^{13}C isotopically labelled standards were available for every compound, this can become a rigorous if not impractical exercise depending on the number of target analytes, and will account for sensitivity loss but cannot avoid loss of sensitivity. The molecular weight of the analytes is an important consideration if ultimate sensitivity is required. Low molecular weight compounds can be difficult to distinguish above the high chemical background inherent in the solvents used with LC-MS. The chemical background is made up of protonated molecular ions of the solvents (in the positive ionisation mode) together with a number of dimers, trimers, and adducts of the solvents and sodium and other ions are present (Richardson, 2001). These factors must be evaluated in the method development and validation and their impact minimised or accounted for as far as is possible.

Recommendation – LC/MS Methods

An analytical method capable of detecting multiple classes of these contaminants from PCC processes would be a significant addition to any process monitoring program. In addition, the necessity to employ a combination of multiple analytical techniques to cover a range contaminant classes can add significantly to the cost of the monitoring program. In many ways LC/MS offers this capability due to its ability to address compounds of differing volatility, size, polarity and thermolability. However, the method suffers from immaturity in this application as there are no validated methods available for each class of compounds, let alone over a number of classes, and the literature addresses only specific applications. A significant drawback of LC/MS is its response variability for different compounds, and for the same compound in different matrices, as has been discussed. New generation ionisation sources may be developed to address this but currently only strict adherence to quality assurance protocols and an acute awareness of the characteristics of the matrices and analytes under test will go some way towards accounting for this issue and towards producing quality quantitative results.

4.2.5 Analytical Strategy for Determination of *N*-Nitrosamines

The standard methods are applicable to the volatile suite of nitrosamine compounds and a separate method is provided for the non-volatile nitrosamine; *N*-nitrosodiethanolamine (NDELA). The target analytes include those compounds specified for assessment by the CCM project (NDMA, NDEA, NMor, NPip, NDELA) apart from *N*-nitrosopiperazine and

1,4-dinitrosopiperazine which are not addressed by any of the standard methods. These compounds fall towards the less volatile and non-volatile end of the range and also possess high polarity. It is considered that both sorbent cartridge and filter collection (as is specified for NDELA), be evaluated for efficiency of collection for these compounds. There are no standard methods available for NDELA in aqueous samples and validation of the SPE technique used for volatile nitrosamines would require evaluation and validation. GC based methods may not provide the necessary efficiency or chromatographic resolution and this also would require assessment. It is possible that the non-volatile compounds are better analysed using liquid chromatography, using LC/TEA as the standard method or LC/MS techniques.

The standard methods are applicable to nitrosamines of environmental relevance and apply to ambient, workplace and combustion source assessment for determinations from the gas phase, and to drinking and wastewaters for determinations from the liquid phase. As such their applicability to gaseous and liquid sampling and analysis from the PCC process would require development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. This means the standard method, or aspects of it, may be applicable as a starting point for application to the PCC process, but by no means guarantees its performance in that role, and indeed that alternative non-standard methods may be preferable.

In the realm of non-standard methods the superior performance of LC/MS for the direct, or preconcentrated, analysis of non-volatile, thermally labile and polar compounds in aqueous matrices makes it a valuable and necessary technique for the PCC project. It is possible that the full suite of volatile and non-volatile nitrosamines could be addressed, including *N*-nitrosodiethanolamine, *N*-nitrosopiperazine and 1,4-dinitrosopiperazine. LC/MS presents significant, but not insurmountable, challenges in attaining quantitative quality particularly for complex samples as would be encountered from PCC process monitoring. As the technique is not mature in this application and no standard methodologies exist, a laboratory more aligned with the advancement of techniques and instrumental capability would be required to perform analyses of this type. On the basis that non-volatile compounds and aqueous matrices are a major requirement of a PCC process monitoring program the LC/MS technique is recommended for inclusion in the overall analytical strategy.

GC/MS techniques, using the more advanced systems of analysis such as GC/CI-MS/MS, achieve selectivity based on conformational mass spectral information and ultimate sensitivity. They are limited to volatile nitrosamines, if derivatisation is to be avoided; however volatile analytes are a major portion of the contaminant suite. US EPA Method 521 is a highly mature method carrying good analytical verification and quality and its establishment as a standard makes it readily available at contract laboratories dealing in trace level environmental analyses. Verification of SPE techniques for process liquids would be required based on Method 521 (sorbent cartridge) or AWWA Method 6450 (solid resin). For gas phase samples Method 521 could be adapted to encompass the GC/CI-MS/MS method after collection based on OSHA Method 27 and INRS Method 031 using Thermosorb/N or dual sorbent cartridges, respectively. These methods could be developed to include *N*-nitrosopiperazine. Overall, it is recommended that this mode of GC/MS analysis be incorporated into the analytical strategy for the determination of volatile nitrosamines.

Chemiluminescence techniques (using TEA or NCD) are also recommended to form an integral part of the analytical strategy for nitrosamine analysis. The technique has superior selectivity and sensitivity compared with other non-MS GC and LC detection systems. In the PCC scenario the awareness of the possibility of interferences, mainly by nitramines, is required and this information could be gathered when GC/MS or LC/MS is part of the analytical strategy. The methods are mature from both their use and verification in the literature and as standard methodologies. OSHA standard Method 27 (volatile nitrosamines) and OSHA Method 31 (*N*-Nitrosodiethanolamine) is likely to be available at contract laboratories specialising in environmental or food and drug applications. For routine analyses or screening of known nitrosamines this method is highly recommended in forming an integral part of the overall analytical strategy.

4.3 Amines and Alkanolamines

4.3.1 Significance and Properties

Amines, in their many forms, are present as contaminants in the environment; often at trace levels and originate mainly from industrial and manufacturing processes. Environmental priority is mainly, but not exclusively, attributed to aromatic amines. Amines are generally toxic in themselves and are reactive, and importantly they can react in the presence of nitrosating agents, to form *N*-nitrosamines which are potentially carcinogenic. This is of interest in the monitoring of PCC processes and one of the reasons secondary alkylamines are specified as contaminants in process assessment.

In the description of standard methodologies the amines specified for assessment will be grouped as follows

- Alkylamines: methylamine, ethylamine, dimethylamine and diethylamine
- Ammonia
- Diamines: 1,2-diaminoethane (ethylenediamine, EDA), piperazine (PZ) (1,4-diethylenediamine)
- Alkanolamines: monoethanolamine (MEA), diethanolamine (DEA), 2-amino-2-methyl-1-propanol (AMP), N-methyldiethanolamine (MDEA)

These compounds are all water soluble or water miscible. They are classed as polar molecules and as relatively weak bases. Ammonia and the smaller alkylamines, apart from diethylamine, are present as a gas at nominal ambient temperature (25ºC). Boiling points range from -33ºC for ammonia through to 55.5ºC for diethylamine, at standard atmospheric pressure. Boiling points of the diamines are 118ºC and 146ºC for EDA and PZ, respectively and alkanolamines through to 268ºC for diethanolamine. Vapour pressure (at 25ºC) ranges from 1001 kPa for ammonia, 353 kPa for methylamine to 32 kPa for diethylamine. Vapour pressure of EDA is 1.6 kPa through to 0.05 for MEA and 2.7×10^{-5} kPa for MDEA Their water solubility is expressed by their octanol/water partition coefficient, log $K_{o/v}$ –0.57 for methylamine and 0.58 diethylamine, and in the region of -1.5 for the diamines and alkanolamines. This property makes their efficient solvent extraction from water difficult to achieve. Their physical properties dictate that in the gas phase they can be collected on suitable sorbent or filter which is usually acidified or chemically treated, as in the case of derivatisation, or solubilised into acidic solution. In the liquid phase the can be extracted and concentrated using liquid extraction or more preferably solid phase extraction (SPE).

The environmental monitoring of certain amines is required under various jurisdictions. The standard test methods established under these protocols are outlined and evaluated in the following sections. In all cases where a positive recommendation is made it is on the basis of sampling and analytical quality and under the understanding that its application to the PCC process will require further investigation and method development.

4.3.2 Standard Methodologies - Alkylamines

Gas Phase Methods

OSHA Method 40: Methylamine

OSHA Method 36: Ethylamine

OSHA Method 34: Dimethylamine

OSHA Method 41: Diethylamine

Principle and Application: Volatile amines in ambient and workplace air by HPLC/Fluorescence

Method Status: Fully evaluated, 1982

Target analytes: Methylamine, Ethylamine, Dimethylamine, Diethylamine (respectively).

Collection: Sampling tube containing XAD-7 resin coated with 10% w/w NBD-Chloride (7-chloro-4-nitrobenzo-2-oxa-1,3-diazole) derivatising agent.

Air Sampling Volume and Rate: 10L at 0.2 L/min.

Storage and Stability: Stable at room temperature for at least 2 weeks.

Preparative: Resin is desorbed with 5% (w/w) NBD chloride in tetrahydrofuran (THF), sodium bicarbonate is added and the solution is heated.

Analysis: HPLC analysis of the amine derivative, using fluorescence (at 465 nm excitation, 525 nm emission). UV detection can also be used (conditions not stated).

Instrument MDL (HPLC/Flu):	Methylamine	1.9 ng
	Ethylamine	1.8 ng
	Dimethylamine	2.8 ng
	Diethylamine	8.7 ng
Procedural MDL:	Methylamine	35 µg/m^3 (28 ppbv)
	Ethylamine	29 µg/m^3 (16 ppbv)
	Dimethylamine	43 µg/m^3 (24 ppbv)
	Diethylamine	160 µg/m^3 (53 ppbv)
		(parameters as stated)

Recovery: 97% methylamine, 87% ethylamine, 93% dimethylamine, 91% diethylamine sampling of a test atmosphere of the pure compound, sampled under parameters stated and a 15 day storage period.

Interferences: Any analyte responding to derivatisation and eluting at the retention time of the analyte.

Supporting Information:

Previous methods used impinger sampling into sulphuric acid solution followed by GC analysis. This method proved cumbersome and GC analysis of low molecular weight free amines is stated as difficult (due to peak tailing, ghosting and column decomposition from injection of aqueous solutions).

This method also provides better performance than does silica gel collection, as used by the current NIOSH Method 2010, as NIOSH have found that low molecular weight amines are not stable after being collected on silica gel and the method also suffers issues with GC analysis as stated above.

Other reagents react with amines to form suitable derivatives, including dansyl chloride and fluorescamine. NBD chloride was chosen because it reacts with both primary and secondary amines, will not react with water, and forms highly coloured and fluorescent derivatives that can easily be analysed by HPLC at high sensitivity.

Sorbents used for coating the derivatising agent have included Gas Chrom R (firebrick) but this resulted in unacceptably low break-through volumes. Silica gel and Florisil™ had high breakthrough volumes but poor recoveries of the extracted derivative, with various solvents. XAD-4 demonstrated high capacity but turned brown when coated with NBD chloride, indicating a possible complicating reaction.

XAD-7 (also known as Amberlite® XAD-7) provided satisfactory breakthrough volumes and high desorption efficiencies using tetrahydrofuran as the desorption solvent and the addition of sodium bicarbonate to the desorption vial provided higher and more consistent recoveries. This is possibly due to the fact that some of the amine may be tied up as hydrochloride salt and the addition of sodium bicarbonate converts the amine salt to free amine which can react with the NBD chloride.

Comments and Recommendation

Derivatisation and HPLC/fluorescence offers improved sampling and analytical performance, than does silica gel collection and GC analysis.

Method supported by Elskamp and Schulitz (1986).

The use of a diode array detector (DAD) is of benefit in that a diode array scan of the peak can determine peak purity which may be helpful in assessing the presence of interferences, and may be helpful in the identification of unknowns.

The OSHA methods are recommended for the analysis of volatile alkylamines.

NIOSH Method 2010, Issue 2: Aliphatic Amines

Principle and Application: Volatile amines in ambient and workplace air by GC/FID

Method Status: Partial Evaluation, 2010

Target analytes: Dimethylamine, Diethylamine.

Collection: Silica gel tube (uncoated).

Air Sampling Volume and Rate: 30L maximum at 0.01 to 1 L/min.

Storage and Stability: Refrigerated. Stability not determined.

Preparative: Silica gel desorbed with dilute hydrochloric acid in 10% (v/v) aqueous methanol, under ultrasonic agitation.

Analysis: Gas chromatography with FID detection (GC/FID).

Instrument MDL (GC/FID): Not stated.

Procedural MDL: 0.02 mg per sample (equivalent to 0.7 mg/m^3 using 30L gas collection volume).

Recovery: 82% dimethylamine, 92% diethylamine.

Interferences: Methanol could interfere in low level analysis

Supporting Information:

NIOSH confirm that this method suffers sampling instability on silica gel and poor chromatographic performance, as described by OSHA, above.

Also that silica gel may have reduced capacity at high humidity.

Comments and Recommendation

The method has not been assessed for primary amines, as required for this study.

This method is not recommended due to issues with sampling instability on silica gel and the detection limits are high and inadequate.

Liquid Phase Methods

US EPA Method 1666: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS

US EPA Method 1671: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID

Principle and Application: Volatile organic compounds in clean water by purge and trap or direct aqueous injection GC/MS, or GC/FID

Method Status: Not stated, Revision A, 1998

Target analytes: VOCs including Methylamine, Dimethylamine, Diethylamine.

Collection: Amber bottle. Dechlorination with sodium thiosulphate where presence of chlorine is determined in the field by US EPA methods 330.4, 330.5.

Sampling Volume: 500 mL.

Storage and Stability: Refrigerated at 0 - 4ºC for 14 days.

Preparative: Addition of isotopically labelled analogs of the compounds of interest.

Analysis: The amines are not applicable to purge and trap and are for direct injection method only. Gas chromatography with MS detection in the electron impact mode (GC/EI-MS). Identification based on agreement between retention time and mass spectrum of authentic standards. Quantitation by extracted ion current profile and isotope dilution technique or internal standard technique as applicable.

Gas chromatography with FID detection (GC/FID). Identification based on agreement between retention time of authentic standards and samples. Quantification by internal standard technique.

Instrument MDL: Not stated.

Procedural MDL: GC/MS 200 mg/L all target amines. GC/FID 50 mg/L all target amines.

Recovery: Approximately 60 - 140% all target amines.

Interferences: Procedural only.

Supporting Information: Method used for surveying and monitoring purposes specific to the pharmaceutical industry.

Comments and Recommendation

Rudimentary method as per requirements of industrial monitoring.

Useful GC/FID and GC/MS guidance for determination of amines.

Under direct injection technique, method detection limits are high and inadequate for trace level analysis. Where lower concentrations are required the development of a solid phase extraction technique for the concentration of analytes would be required.

The target analyte list does not include ethylamine however the method is likely to be suitable for its analysis.

These methods are not recommended for analysis of process liquids due to the basic nature of the liquid and the presence of other non-volatile or highly polar compounds.

4.3.3 Standard Methodologies - Ammonia

Gas Phase Methods

JIS (Japanese Industrial Standard) Method K 0099: Methods for the Determination of Ammonia in Flue Gas

Principle and Application: Ammonia in flue gas by absorption spectrophotometry in accordance with JIS K 0115, or ion chromatography (IC) in accordance with JIS K 0127.

Method Status: Fully evaluated, 2004

Target analytes: Ammonia

Collection: Impinger charged with boric acid solution.

Air Sampling Volume and Rate: 20L nominal at around 1 L/min.

Storage and Stability: Not stated.

Preparative: Spectrophotometric method: addition of sodium phenolpentacyaninitrosylferrate (III) solution and sodium hypochlorite solution to generate indophenol blue.

Analysis: Absorption spectrometry of indophenol blue at 640 nm.

Ammonium ion (NH_4^+) analysed by ion chromatography (IC).

Instrument MDL (IC): Not stated.

Procedural MDL: Not stated.

Working Range: Spectrophotometric method 1.3 to 1200 mg/m^3 (1.9 to 1729 ppmv)

Ion chromatography method: 1.2 to 11.8 mg/m^3 (1.7 to 17 ppmv)

Estimated procedural MDL at nominal 100L volume and based on lower WR of 10x MDL is approximately 26 µg/m^3 (38 ppbv) for both methods.

Recovery: Not stated

Interferences: The spectrophotometric method is affected by coexisting components at the following concentrations (relative to ammonia concentration) 100× NO_2, 10× amines and SO_2 and equivalent volume of H_2S. If these values are exceeded then ion chromatography should be used.

Supporting Information:

Flue gases, by this standard, are those which are generated by combustion, chemical reaction, denitration or other process.

Comments and Recommendation

Ion chromatography must be optimised for the separation of relevant amines and alkanolamines as these may interfere with ammonium ion peak.

This method is recommended for the analysis of ammonia with reference also to OSHA method ID-188 which is also uses ion chromatography.

OSHA Method ID-164: Ammonia in Workplace Atmospheres

Principle and Application: Ammonia in ambient and workplace air by ion specific electrode (ISE)

Method Status: Partial Evaluation, 1988

Target analytes: Ammonia

Collection: Impinger collection into 0.1N sulphuric acid.

Air Sampling Volume and Rate: 120L at 1 L/min.

Storage and Stability: Not stated.

Preparative: Solution made alkaline with NaOH.

Analysis: Ammonia gas sensing ion specific electrode. Quantitation by standard addition.

Instrument MDL (ISE): 2 µg NH_3 in solution.

Procedural MDL: Not stated.

Recovery: Not stated.

Interferences: Not stated.

Supporting Information:

Previous methods used a calorimetric method and the Nessler reagent. This method suffered interferences and was subject to error due to old or contaminated reagent.

Comments and Recommendation

Rudimentary method for high concentration application only. Impinger sampling is inconvenient.

Method does not discriminate between ammonia, amines and alkanolamines.

Method is not recommended for trace analysis in the presence of amines.

OSHA Method ID-188: Ammonia in Workplace Atmospheres – Solid Sorbent

Principle and Application: Ammonia in ambient and workplace air by ion chromatography (IC)

Method Status: Fully validated, 2002

Target analytes: Ammonia

Collection: Sampling tube containing carbon beads impregnated with sulphuric acid (CISA) which converts ammonia to ammonium sulphate.

Air Sampling Volume and Rate: 24L at 0.5 L/min.

Storage and Stability: Ambient temperature (20 to 25ºC) for at least 29 days.

Preparative: Ammonium sulphate desorbed from tubes using deionised water and solution acidified with H_2SO_4.

Analysis: Ammonium ion (NH_4^+) analysed by ion chromatography (IC).

Instrument MDL (IC): 10 µg as ammonia.

Procedural MDL: 0.6 ppm (0.4 mg/m^3) for 24L gas collection volume, under parameters stated.

Recovery: Not stated.

Interferences: Methylamine, dimethylamine, monoethanolamine, diethanolamine, isopropanolamine and propanolamine will produce peaks in the vicinity of the ammonium ion. In particular methylamine and ammonium ion are not well separated. Response of MEA is approximately 50% of ammonia. Mobile phase ion chromatography should be used to separate these compounds to confirm the ammonia result, if these compounds are present. The method suggests an alternative eluant mixture.

Ammonium salts present in air as dust would constitute a positive interference. Glass wool preceding the beads will help prevent this or a filter cassette can be used.

Loss of chromatographic peak resolution due to metal-column binding to separator column. Overcome with equipment as described which minimises contact with metal surfaces.

Peak characteristics change at diluent concentration of 0.1N H_2SO_4. Under normal protocol pH does not affect ammonium peak characteristics however.

Supporting Information:

Method is improvement over Method ID-164 due to use of sorbent tube rather than liquid impinger.

This method is able to discriminate between ammonia and amines.

Ammonia can also be determined by a calorimetric procedure (procedure not given)

Ion chromatography must be optimised for the separation of relevant amines and alkanolamines, as above as these may interfere with ammonium ion peak.

Comments and Recommendation

Method provides detailed guidance and validation criteria.

This method is recommended for the routine analysis of ammonia, provided ion chromatography is optimised to eliminate interference from amines, as stated above.

NIOSH Method 6015, Issue 2: Ammonia

Principle and Application: Ammonia in ambient and workplace air by visible absorption spectrophotometry.

Method Status: Partial Evaluation, 1994

Target analytes: Ammonia

Collection: Sampling tube containing suIphuric acid treated silica gel to form ammonium sulphate on collection of ammonia.

Air Sampling Volume and Rate: 96L maximum at 0.2 – 2 L/min.

Storage and Stability: Not determined.

Preparative: Sorbent extracted with deionised water. pH adjusted to 5.0 – 6.5 with NaOH solution.

Analysis: Sample mixed in the autoanalyser unit with reagents which produce indophenol blue solution which is detected by the colorimeter at the visible absorption wavelength of 630 nm or 660 nm.

Instrument MDL (Spectrophotometer): Not stated.

Procedural MDL: 0.5 µg ammonia per sample (parameters not stated).

Working Range: 0.15 to 300 mg/m^3 (0.2 to 240 ppmv).

Recovery: Not stated.

Interferences: None identified.

Supporting Information: No further information of relevance.

Comments and Recommendation

Rudimentary method for high concentration application only.

Method is not recommended for low level analysis of ammonia.

NIOSH Method 6016, Issue 2: Ammonia by IC

Principle and Application: Ammonia in ambient and workplace air by ion chromatography (IC).

Method Status: Full evaluation, 2003

Target analytes: Ammonia

Collection: Sampling tube containing sulphuric acid treated silica gel (reacts ammonia to ammonium sulphate).

Air Sampling Volume and Rate: 96 L maximum at 0.1 – 0.5 L/min.

Storage and Stability: 5ºC for at least 35 days.

Preparative: Ammonium sulphate desorbed from tubes using deionised water.

Analysis: Ammonium ion (NH_4^+) analysed by ion chromatography (IC).

Instrument MDL (IC): Not stated.

Procedural MDL: 2 µg per sample (parameters not stated)

Working Range: 17 to 68 mg/m^3 (24 to 98 ppmv)

Recovery: Not stated

Interferences: Monoethanolamine, isopropanolamine and propanolamine have retention times similar to ammonium ion. Use of an alternate (weak eluant will aid in separating these. (*Note: OSHA also report interferences for methyl- and dimethylamine*).

Supporting Information:

Ion chromatography must be optimised for the separation of relevant amines and alkanolamines, as above as these may interfere with ammonium ion peak.

Comments and Recommendation

Method provides rudimentary guidance and validation criteria.

This method is not recommended for the analysis of ammonia, rather the use of OSHA's method ID-188 which also uses ion chromatography.

Liquid Phase Methods

No standard test methods for determination of ammonia under regulation of drinking water or wastewaters have been established.

The JIS protocol for determination of ammonia in flue gas, which incorporates collection into solution, could be adapted for liquids analysis.

4.3.4 Standard Methodologies - Diamines

Gas phase methods

OSHA Method 60: Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetramine (TETA)

Principle and Application: Volatile diamines in ambient and workplace air by HPLC/UV

Method Status: Fully evaluated, 1986

Target analytes: Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetramine (TETA).

Collection: Sampling tube containing XAD-2 resin coated with 10% w/w NITC derivatising agent (1-naphthylisothiocyanate).

Air Sampling Volume and Rate: 10L at 0.1 L/min.

Storage and Stability: Stable at room temperature for at least 15 days.

Preparative: Resin is desorbed with 2 mL dimethylformamide (DMF).

Analysis: HPLC analysis of the amine derivatives (naphthylisothioureas), using UV detection at 254 nm.

Instrument MDL (HPLC/UV):	Ethylenediamine	4.6 ng
Procedural MDL:	Ethylenediamine	370 µg/m^3 (150 ppbv)
		(parameters as stated)

The detection limit for EDA is impacted by the fact that it elutes on the tail of DMF, as shown by the MDL for diethylentriamine of 16 µg/m^3 (4 ppbv) as this elutes well after the DMF. Optimisation of chromatographic parameters would achieve a lower detection limit for EDA.

Recovery: 99% ethylenediamine based on desorption of standard liquid spikes to tube.

Interferences: Any analyte responding to derivatisation and eluting at the retention time of the analyte. Sampling times should also be adjusted to account for other amines collected on the sorbent which might impact on its capacity to collect target components.

Supporting Information:

The agent used for derivatisation of monoamines (NBD chloride) does not successfully derivatise polyamines.

The THF solvent commonly used for desorption of NBD-Cl derivatives causes instability of TETA and DMF is therefore used.

Comments and Recommendation

NITC derivatising agent used in this method for the diamines is also used in the OSHA methods for alkanolamines under the same sampling and instrumental procedures. It is also indicated that piperazine is to be measured in the same way (as indicated by in-house OSHA method, over).

OSHA do not mention the possibility of mixed atmospheres or the interference this may cause in the analysis. Careful optimisation of the liquid chromatography may allow

separation of all analytes and the use of a characteristic wavelength to enhance sensitivity for each class would be beneficial.

For this reason a diode array detector is considered essential to enable programmed wavelength selection and diode array scans of the analyte peaks to improve selectivity, determine peak purity and provide a level of analyte confirmation, where mixed di-amine and alkanolamine analytes are expected.

OSHA Method 60 is recommended for the routine analysis of the CCM project specified compound; ethylenediamine, and the target polyamines if required.

OSHA In-house method: Piperazine

Principle and Application: Piperazine in ambient and workplace air by HPLC/UV

Method Status: Not validated, 2001

Target analytes: Piperazine

Collection: Sampling tube containing XAD-2 resin coated with 10% w/w NITC derivatising agent (1-naphthylisothiocyanate).

Air Sampling Volume and Rate: 10L at 0.1 L/min.

Storage and Stability: Not determined.

Preparative: Resin is desorbed with 2 mL dimethylformamide (DMF).

Analysis: HPLC analysis of the amine derivatives (naphthylisothioureas), using UV detection (wavelength not stated).

No further information is provided as the method is referenced as "in-house" and classed as "not validated".

Comments and Recommendation

The method, as provided, appears the same as OSHA methods for alkanolamines and diamines and the implications of this are discussed under Method 60.

This method, developed in-house under the protocols of Method 60, is recommended for the analysis of piperazine.

NIOSH Method 2540, Issue 2: Ethylenediamine

Principle and Application: Volatile diamines in ambient and workplace air by HPLC/UV

Method Status: Unrated, 1994

Target analytes: Ethylenediamine (EDA)

Collection: Sampling tube containing XAD-2 resin coated with 10% w/w NITC derivatising agent (1-naphthylisothiocyanate).

Air Sampling Volume and Rate: 20L (maximum) at 0.01 to 0.1 L/min.

Storage and Stability: Stable at 20ºC for > 30 days.

Preparative: Resin is desorbed with 2 mL dimethylformamide (DMF).

Analysis: HPLC analysis of the amine derivatives (naphthylisothioureas), using UV detection at 254 nm.

Instrument MDL (HPLC/UV): Not stated.

Procedural MDL: 0.9 µg/sample (equivalent to 45 µg/m^3 (18 ppbv) using 20L gas collection volume).

Recovery: Not stated. Bias: -6.6%

Interferences: Other low molecular weight amines.

Sodium and ammonium ions can interfere with MEA.

Other information:

Method supported by Anderson *et al.* (1985)

Comments and Recommendation

Rudimentary method with low level validation and basic analytical and instrumental guidance. OSHA Method 60 is based on similar principles and attains higher level validation.

NIOSH Method 3509 is not recommended for the analysis of volatile alkanolamines.

May be useful as additional guidance to OSHA Method 60.

Liquid Phase Methods

No standard test methods for determination of diamines under regulation of drinking water or wastewaters have been established. Method would require development.

4.3.5 Standard Methodologies - Alkanolamines

Gas phase methods

OSHA Method PV 2111: Ethanolamine

OSHA Method PV 2018: Diethanolamine

OSHA Method PV 2145: 2-Amino-2-Methyl-1-Propanol (AMP)

Principle and Application: Volatile alkanolamines in ambient and workplace air by HPLC/UV

Method Status: Partially evaluated, 1988

Target analytes: Monoethanolamine, Diethanolamine, AMP (respective methods).

Collection: Sampling tube containing XAD-2 resin coated with 10% w/w NITC derivatising agent (1-naphthylisothiocyanate).

Air Sampling Volume and Rate: 10L at 0.1 L/min.

Storage and Stability: Stable at room temperature for at least 16 days.

Preparative: Resin is desorbed with 2 mL dimethylformamide (DMF).

Analysis: HPLC analysis of the amine derivatives (naphthylisothioureas), using UV detection at 254 nm or 280 nm.

Instrument MDL (HPLC/UV):	Monoethanolamine	8.1 ng
	Diethanolamine	15 ng
	AMP	15 ng
Procedural MDL:	Monoethanolamine	150 µg/m^3 (60 ppbv)
	Diethanolamine	172 µg/m^3 (40 ppbv)
	AMP	146 µg/m^3 (40 ppbv)
		(parameters as stated)

Recovery: 99% diethanolamine, 100% AMP as recovery from retention efficiency based on standard liquid spikes to tube and 10L flow of humidified air.

Interferences: Any analyte responding to derivatisation and eluting at the retention time of the analyte. Sampling times should also be adjusted to account for other amines collected on the sorbent.

Supporting Information:

This method improves performance and is recommended over NIOSH Method 2007. The NIOSH method uses silica gel tubes which must be stabilized by spiking with HCl after sampling, which is inconvenient in the field. Sample preparation involves derivatisation with benzaldehyde, and GC/FID analysis exhibits poor chromatography and carryover problems.

When necessary the identity or purity of an analyte peak may be confirmed by photodiode array scan of the peak (using DAD detector), by wavelength ratioing, or by LC/MS.

Comments and Recommendation

Derivatisation and HPLC/UV offers improved sampling and analytical performance over silica gel collection and GC/FID analysis.

Method supported by Levin *et al.* (1989).

OSHA also uses this methodology for determination of diamines and piperazine. The implications of this were discussed under Method 60 in previous section.

OSHA Methods PV 2111, PV 2018 and PV 2145 are recommended for the routine analysis of volatile alkanolamines.

NIOSH Method 2007, Issue 2: Aminoethanol Compounds I

Principle and Application: Volatile alkanolamines in ambient and workplace air by GC/FID

Method Status: Partial evaluation, 2007

Target analytes: 2-aminoethanol (MEA), 2-dibutylaminoethanol, 2-diethylaminoethanol.

Collection: Sampling tube containing silica gel (uncoated).

Air Sampling Volume and Rate: 24L (maximum) at 0.01 to 0.2 L/min.

Storage and Stability: Stable at 25ºC for 4 weeks.

Preparative: Tube treated with concentrated HCl in the field. Desorbed with 4:1 methanol/water (v/v). Addition of alkalinizing solution to pH >9 2. Derivatise with benzaldehyde (to form.

Analysis: GC/FID, packed column.

Instrument MDL (GC/FID): not stated.

Procedural MDL: 5 µg/sample (equivalent to 210 µg/m^3 (84 ppbv MEA) using 24 L gas collection volume).

Recovery: Not stated. Bias -2.9%

Interferences: Procedural only.

Supporting Information: No further information of relevance.

Comments and Recommendation

Poorly performing method as reported by OSHA. Refer OSHA methods PV2111 and associated information.

NIOSH Method 2007 is not recommended for the analysis of volatile alkanolamines.

NIOSH Method 2509, Issue 2: Aminoethanol Compounds II

Principle and Application: Volatile alkanolamines in ambient and workplace air by ion chromatography (IC)

Method Status: Partial evaluation, 1994

Target analytes: Monoethanolamine (MEA), Diethanolamine (DEA), Triethanolamine (TEA).

Collection: Impinger charged with hexanesulfonic acid solution.

Air Sampling Volume and Rate: 300L (maximum) at 1 L/min.

Storage and Stability: Stable at 20ºC for at least 3 weeks.

Preparative: None required.

Analysis: Ion chromatography.

Instrument MDL (IC): not stated.

Procedural MDL: 7 to 20 µg/sample (equivalent to 23 to 66 µg/m^3 (9.4 to 27 ppbv MEA) using 300L gas collection volume).

Recovery: Not stated. Bias: Not determined.

Interferences: Other low molecular weight amines.

Sodium and ammonium ions can interfere with MEA.

Supporting Information: No further information of relevance.

Comments and Recommendation

Rudimentary method with low level validation and basic analytical and instrumental guidance.

OSHA Methods PV 2111, PV 2018 and PV 2145 implement solid sorbent sampling which is generally preferable over impinger sampling, and higher level validation.

NIOSH Method 3509 is recommended for consideration as it offers useful guidance where impinger sampling is required and where ion chromatography is a preferred or available technique.

Liquid Phase Methods

No standard test methods for determination of alkanolamines regulation of drinking water or wastewaters have been established. Method would require development.

4.3.6 Standard Methods Summary Recommendations

The previous section reviewed the major environmental standard test methods considered as possessing attributes most appropriate to the determination of alkylamines, ammonia, d-amines and alkanolamines specified for assessment in this study. Environmental methods were selected due to their applicability in trace level analysis and to gaseous and liquid matrices. The principle, analytical and instrumental requirements and performance of the methods was outlined and comments have been made as to their attributes and limitations. On this basis a summary of this review and the recommended methods is now presented.

The standard methods target analytes which include the majority of those compounds specified for assessment by the CCM project, with the exception of *N*-methyldiethanolamine. However the methods are applicable to gas phase analysis and there exists limited standard environmental methods for alkylamines, diamines and alkanolamines in the liquid phase. Those that are specific to this phase are for industrial monitoring purposes and hence have high detection limits (200 mg/L), which are unsuitable for trace level analysis. Whilst this may be suitable for process liquids it is considered that the basic nature and the presence of other less volatile and polar species make direct injection of these liquids unviable, and hence this method is not recommended. The methods used for analysis of gas phase components would require adaption for analysis of the liquid phase, if standard methods were given preference, or other non-standard methods investigated as published in the literature, and as will be discussed in the next section.

As the standard methods are applicable to amines of environmental relevance their applicability to gaseous and liquid samples from the PCC process would require development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. Also these compounds will be present at significantly different and/or higher relative concentrations than would be encountered in an environmental sample and this also requires attention in the development process. The impact of water and bulk amine solvents on the capacity of the gaseous sampling device to collect trace levels of alkylamines and ammonia, and their impact on the determinative technique, will require assessment. This means the standard method, or aspects of it, may be applicable as a starting point for application to the PCC process, but by no means guarantees its performance in that role, and indeed that alternative non-standard methods may be preferable.

On the bases described above, the standard methods which are considered to provide highest analytical quality for speciated analysis of specified alkylamines, ammonia, and diamines and alkanolamines in gaseous and liquid matrices are summarised as follows. The reasoning behind these recommendations is detailed for each method in the previous section.

Alkylamines – Gas phase

- OSHA Method 40: Methylamine
- OSHA Method 36: Ethylamine,
- OSHA Method 34: Dimethylamine
- OSHA Method 41: Diethylamine

Principle and Application (all methods): Volatile alkylamines in ambient and workplace air using NBD-Chloride coated XAD-7 sampling tubes and analysis by HPLC-Fluorescence.

Target analytes: Methylamine, Ethylamine, Dimethylamine, Diethylamine.

Procedural MDL:	Methylamine	35 µg/m^3 (28 ppbv)
	Ethylamine	29 µg/m^3 (16 ppbv)
	Dimethylamine	43 µg/m^3 (24 ppbv)
	Diethylamine	160 µg/m^3 (53 ppbv)

These MDLs based on the specified 10L gas collection volume.

Using the nominal 100 L gas volume would generate 10-times lower MDLs. However sorbent capacity would require evaluation.

Alkylamines – Liquid phase

- US EPA Method 1666: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS
- US EPA Method 1671: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID

Principle and Application: Volatile organic compounds (including alkylamines) in clean water and analysis by direct aqueous injection GC/MS, or GC/FID (respectively).

Target analytes (amines): Methylamine, Dimethylamine, Diethylamine

Procedural MDL:	GC/MS 200 mg/L all target amines (direct injection)	
	GC/FID 50 mg/L all target amines (direct injection)	

Comments:

This method provides a guide to GC/MS or GC/FID analysis for these compounds and can be used as stated only where process liquid characteristics are compatible with GC systems and where concentrations are high enough to allow direct aqueous injection.

Ammonia – Gas phase

- JIS Method K 0099: Methods for the Determination of Ammonia in Flue Gas

Principle and Application: Ammonia in flue gas by impinger collection and either absorption spectrophotometry in accordance with JIS K 0115, or ion chromatography (IC) in accordance with JIS K 0127.

The working range of the spectrophotometric method is 1.3 to 1200 mg/m^3 (1.9 to 1729 ppmv) and 1.2 to 11.8 mg/m^3 (1.7 to 17 ppmv) ion chromatography method, using 20L gas collection volume. At nominal volume of 100L the equivalent range would be 5-fold lower.

Estimated procedural MDL at nominal 100L volume and based on lower WR of 10x MDL is approximately 26 µg/m^3 (38 ppbv) for both methods.

- OSHA Method ID-188: Ammonia in Workplace Atmospheres – Solid Sorbent

Principle and Application: Ammonia in ambient and workplace air using carbon bead/sulphuric acid impregnated sampling tubes and analysis by ion chromatography (IC).

Procedural MDL: 400 µg/m^3 (600 ppbv) for 24L gas collection volume, under parameters stated. Equivalent to 100 µg/m^3 (140 ppbv) for 100L nominal gas collection volume.

Ammonia – Liquid phase

No standard test methods for determination of ammonia under regulation of drinking water or wastewaters have been established. Method would require development, using principles based on JIS Method K 0099, above.

Diamines – Gas phase

- OSHA Method 60: Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetramine (TETA)

Principle and Application: Volatile diamines in ambient and workplace air using NITC coated XAD-2 solid sorbent tube and analysis by HPLC/UV.

Procedural MDL: Ethylenediamine 370 µg/m^3 (150 ppbv) for 10L gas collection volume, under parameters stated. Equivalent to 37 µg/m^3 (15 ppbv) for 100L nominal gas collection volume.

The detection limit for EDA is impacted by the fact that it elutes on the tail of DMF, as shown by the MDL for diethylenetriamine of 16 µg/m^3 (4 ppbv) (10L) as this elutes well after the DMF. Optimisation of chromatographic parameters is likely to achieve a 20-fold lower detection limit for EDA.

- OSHA In-house Method: Piperazine

This is a non-validated method that OSHA outlines to have similar principles as Method 60, above, and hence one would expect similar performance. This method would be developed in-house under the protocols of OSHA Method 60.

Diamines – Liquid phase

No standard test methods for determination of diamines under regulation of waters or wastewaters have been established. Method would require development.

Alkanolamines – Gas phase

- OSHA Method PV 2111: Ethanolamine
- OSHA Method PV 2018: Diethanolamine
- OSHA Method PV 2145: 2-Amino-2-Methyl-1-Propanol (AMP)

Principle and Application: Volatile alkanolamines in ambient and workplace air using NITC coated XAD-2 solid sorbent tube and analysis by HPLC/UV.

Procedural MDL:	Monoethanolamine	150 µg/m^3 (60 ppbv)
	Diethanolamine	172 µg/m^3 (40 ppbv)
	AMP	146 µg/m^3 (40 ppbv)

These MDLs are based on the specified 10L gas collection volume.

A nominal 100 L gas volume would generate 10-times lower MDLs. However for this type of collection system, sorbent capacity would require evaluation under these sampling conditions.

Comments

NITC derivatising agent used in this method for the alkanolamines is also used in the OSHA methods for diamines under the same sampling and instrumental procedures. OSHA also intends that piperazine be measured in the same way (as indicated by in-house OSHA method).

OSHA does not mention the possibility of mixed component atmospheres or the interference this may cause in the analysis. Careful optimisation of the liquid chromatography may allow separation of all analytes and the use of a characteristic absorbance wavelength to enhance sensitivity for each class would be beneficial. For this reason a diode array detector is considered essential to enable programmed wavelength selection and diode array scans of the analyte peaks in order to improve selectivity, determine peak purity and provide a level of analyte confirmation, where mixed di-amine and alkanolamine analytes are expected.

Alkanolamines – Liquid phase

No standard test methods for determination of alkanolamines under regulation of drinking water or wastewaters have been established. Method would require development.

4.3.7 Non-Standard Methodologies

A comprehensive review of amines in the environment has been recently published by Fekete *et.al* (2010). A significant number of publications are cited for the determination of ammonia and alkylamines in gaseous and liquid matrices for application to various instrumental techniques. Methods which determine alkylamines along with monoethanolamine and diethanolamine are also mentioned, as well as methods for diamines. This document provides a current and useful reference. As does the review by Pielesz (2006), which describes the determination of amines by HPLC and LC-MS, GC and GC-MS, ion chromatography (IC) and capillary electrophoresis (CE) and cites numerous publications in support of these techniques in various environmental and process assessment applications.

The analysis of alkylamines in the liquid phase can be performed directly by aqueous injection and gas chromatography, as exampled by US EPA Methods 1666 and 1671, but of course this requires the amines to be at high concentrations, well above 200 mg/L, to keep determinations above instrument MDLs. In the case of process liquids this concentration may be applicable but the highly basic nature of the liquid and the high concentration of the alkanolamines makes this an unattractive option for direct GC analysis. Free amines also chromatograph poorly on GC columns and interact with injector components which can produce non-linearity in response and reduction in selectivity and sensitivity. Supap *et al.* (2006) performed compositional analysis for monoethanolamine and its oxidative degradation products during CO_2 absorption from flue gases and compared GC-MS, HPLC-RID and CE-DAD analytical techniques, with the conclusion that all techniques are complementary. These techniques were applied for characterisation purposes and provided compositional determinations as relative concentration, and hence were not strictly quantitative. For liquid phase samples, it is expected that some form of solid-phase extraction as clean-up or enrichment is likely to be required especially for determination of degradation products if GC instrumentation is used. This is not straightforward due to the similarity in chemical characteristics between bulk alkanolamines and trace alkylamines components and another reason direct analysis using LC/MS techniques is attractive.

Derivatisation is a technique which is commonly used for the determination of amines. It may be used to improve sensitivity, particularly in application to HPLC where alkylamines have low absorptivity in the UV range. Derivatisation with fluorescence reagents provides high sensitivity for LC analysis. The basic character of amines makes them difficult to analyse by GC; ammonia and higher amines have strong adsorption characteristics. The amino group also introduces a large dipole in the molecule which results in strong interactions with silanol groups and siloxane bridges which results in non-linear adsorption effects. These effects produce losses to injector components and peak tailing in the chromatogram and which reduces selectivity and sensitivity. The analysis of free amines requires the use of amine deactivated injector components and the use of base-deactivated columns which are treated to reduce surface activity from acidic fused silica. Derivatisation not only reduces polarity but also improves volatility, selectivity, sensitivity and separation of amines. Using GC/MS with electron impact (EI-MS), most alkylamines do not provide characteristic molecular ions in EI spectra and result in a base peak at m/z 30 when the amine is analysed in the free form. Consequently EI spectra provide low level information for the confirmation of identity or for the quantification of alkylamines using selected ion monitoring. When derivatisation

is used selectivity is enhanced and, if the derivative is incorporated with the sorbent for gas phase collection, it can also ensure analyte stability during sampling and reduces the preparative complexities of post collection derivatisation. A disadvantage of the technique is that the reagent can interfere in the determination or effect column performance and for this reason steps to remove excess reagent can be required. In some cases, multiple derivatisations may also be necessary to effectively isolate and distinguish between similar classes of compounds.

As supported in its inception by Elskamp and Schultz (1986), OSHA takes advantage of the benefits of derivatisation in their standard methods for gas phase *in-situ* collection and derivatisation. Alkylamines are derivatised with NBD-Chloride (7-chloro-4-nitrobenzo-2-oxa-1,3-diazole) to form derivatives for HPLC/UV analysis. Using a different derivative; NITC (1-naphthylisothiocyanate), the method effectively selects for alkanolamines. Levin *et al.* (1989) used a similar approach for the determination of mono- and diethanolamine in air except he sampled the more volatile monoethanolamine using NITC coated onto XAD-2 resin and the diethanolamine using an NITC impregnated filter, as this compound is present as an aerosol under ambient conditions. Detection limits are low, around 30 $\mu g/m^3$ (3 ppbv). This reagent also derivatises ethylenediamine as reported by Andersson *et al.* (1985) and is used in OSHA Method 60 and NIOSH Method 2540 for this and other diamines. An understanding of the environment under test and optimisation of the determinative method is likely to allow the volatile alkanolamines and diamines to be measured simultaneously.

A novel approach to derivatisation, which overcomes the disadvantages associated with excess reagent, is to use polymeric reagents. When the derivatising agent is bound to a polymer the reaction is heterogeneous, rather than homogeneously when both derivative and analyte are in solution, and the reagent can easily be removed from solution after the derivatisation is complete. Jedrzejczak *et al* (1993) and Jedrzejczak and Gaind (1993) have reported extensively on this topic and its application to the determination of aliphatic amines for GC-MS and HPLC determination. Where derivatisation is seen as beneficial, this approach may provide significant advantage in the analysis of process liquids, especially for LC/MS application where the elimination of matrix interferences (as previously discussed) are especially important.

Derivatisation reactions which take place in the liquid phase (homogeneous reactions) have been reported in their various forms by many authors in ambient and aqueous applications and for both gas and liquid chromatographic determinations. Fekete *et.al* (2010), Pielesz (2006) and Kataoka (1996) provide comprehensive reviews on this technique. Other publications of interest include Kataoka *et al.* (1993) who used benzenesulphonyldimethylaminomethylene to derivatise ammonia in water for detection by GC/FPD, with a further derivatisation to allow chromatographic separation of small primary alkylamines. Gaind *et al.* (1992) used cyclohexanone coated XAD-4 resin for *in-situ* derivatisation for the sampling of airborne monoethanolamine with analysis using GC/TSD (GC/NPD). Langvardt and Melcher (1980) used alumina to collect mono-, di- and tri-ethanolamine from air with desorption into 1-octanesulfonic acid. The resulting salts were derivatised with heptafluorobutyryl imidazole for detection using GC/FID. These methods are complex and the detectors still only provide non-specific information.

With respect to derivatisation for liquid chromatography Huang *et al.* (2009) proposed a method for the determination of atmospheric ammonia and primary amines (methyl-,

ethyl-, propyl- and butylamine) for application to HPLC analysis. A novel sampling approach is used which differentiates gaseous and aerosol species, and where OPA (*o*-phthaldehyde) and NAC (thiol n-acetyl-L-cysteine) reagents are used in an in-line system to produce highly fluorescent derivatives for HPLC analysis. Detection at low ppt levels was achieved equating to MDLs of 0.5 ppbv (0.3 µg/m^3) for ammonia and around 0.1 ppbv (0.13 µg/m^3 MA) for the amines. The contribution of NH_3 and NH_4^+ to NH_x in ambient atmospheres and similarly for the alkylamines could be determined using this method. A sophisticated method of post column fluorescence derivatisation after HPLC separation was reported by Whiteside *et al.* (1988) for detection of primary, secondary and tertiary amines in non-aqueous systems. OPA/2-mercaptoethanol was used to obtain selectivity to primary amines and derivatisation with NBD-Cl was used for secondary amines, after on-line masking of primary amines. Moliner-Martínez *et al.* (2007) used dual precolumn OPA and NAC derivatisation for analysis of ammonia and small primary aliphatic amines in water. Using micro-scale sample volumes they achieved 8 – 50 µg/L detection limits by HPLC/UV. Liu *et al.* (2001) used precolumn fluorescence derivatisation with *N*-hydroxysuccinimidyl 4,3,2'-naphthapyrone-4-acetate for primary and secondary alkylamines including monoethanolamine and isopropanolamine in aqueous solution. Smith *et al.* (1991) used the commonly applied derivative known as dansyl chloride in a pre-column derivatisation method to determine ammonia, methylamine, piperadine and other larger amines in industrial wastewaters by HPLC/UV, as did Lloret *et al.* (2002) who combined preconcentration and derivatisation on a C_{18} solid phase packing to the screening analysis of ammonium and aliphatic amines (methyl-, dimethyl-, ethyl-, diethyl-, propyl- and butylamine) in water by HPLC/UV/Fluoresence at the low µg/L level. Lloret *et al.* (2004) aimed for highest sensitivity using the dansyl derivatisation technique with the incorporation of post column peroxyoxalate reaction for analysis using HPLC with a chemiluminescence detector. This resulted in 2 to 75-times increases in sensitivity compared with UV and fluorescence detection and a minimum 0.15 µg/L detection limit. Derivatisation for electrochemical detection (HPLC/EC) has been reported by Wintersteiger *et al* (1995) for small aliphatic amines in liquid matrices. The amines react readily with salicylic acid chloride to produce electroactive amide derivatives, which are also amenable to UV detection. Amperometric detection reportedly produced comparable detection limits to UV at low ng/mL in biological liquids.

Analysis of derivatised analytes can be performed by GC/MS and LC/MS for the relevant derivative, to take advantage of what these instruments offer in furthering the quality of the result. Akyüz and Ata (2006) determined both aliphatic and aromatic amines in water and sediment using ion-pair extraction instead of SPE followed by isobutyl chloroformate derivatisation for determination as their *iso*BOC (isobutyloxycarbonyl) derivatives by GC/EI-MS and GC/CI-MS. Akyüz (2008) used a similar method to determine aliphatic and aromatic amines in ambient air and on particulate matter after their collection into an acidified medium. The procedures are complex but produce unequivocal information for trace level determinations of more than 30 amines with pg/m^3 and 0.1 ng/L detection limits. Gaind and Chai (1990) developed a simple technique for in-injector derivatisation of primary amines (only) for use in GC/EI-MS analysis. Sacher *et al.* (1997) suggests benzenesulfonyl chloride as the preferred derivative to 2,4-dinitrofluorobenzene for GC/MS analysis of primary and secondary amines in waste and surface waters. Certainly the development of a derivative-based method suitable for analysis of PCC process samples would require a thorough

investigation of various alternative techniques and a knowledge of the chemical characteristics of the sample.

Whilst LC/MS can be used for certain of the derivatives commonly used for HPLC analysis they are not all amenable to API, where they must be capable of protonation. A suitable derivative is dansyl chloride used in a well described methodology by Fournier *et al.* (2008). Here alkylamines and alkanolamines were simultaneous measured by LC/ESI-MS analysis after their collection from air on acid impregnated glass fibre filters and subsequent derivatisation with dansyl chloride. Sun *et al.* (2009) used PIBA (4-(1H-phenanthro[9,10-d]imidazol-2-yl) benzoic acid as a pre-column labelling reagent for the determination of aliphatic primary amines in water by LC/Fluorescence and LC/APCI-MS. An improved reagent (DBCEC-Cl) for the sensitive determination of aliphatic amines in wastewater by LC/Fluorescence and post column online LC/APCI-MS was developed by You *et al.* (2010) which achieved 0.3 to 3.0 fmol (10^{-15} mole).

Capillary electrophoresis (CE) has emerged as a powerful alternative to HPLC and is gaining acceptance in many areas and it often used where other techniques fail. It is applicable to the analysis of amine species where UV or similar detection is appropriate, and has mainly been used for analysis aromatic and polyamines. Fekete *et al.* (2010) list a small number of publications for CE analysis where certain alkanolamines are also addressed. Supap *et al.* (2006) compared CE-DAD with GC-MS and HPLC-RID techniques for the analysis of monoethanolamine solvent and its degradation products during CO_2 absorption from flue gases, with the conclusion that all methods are complementary. Pereira and Tavares (2004) presented an effective CE method for the determination of alkanolamines (MEA, DEA, TEA, DEEA) and two cyclic amines present in corrosion inhibitors. The advantages of rapid chromatography were realised with good sensitivity (MDL 0.5 – 1.5 mg/L). Hui *et al.* (2010) reported a CE method for the determination of derivatised ammonia and 22 aliphatic amines at the ng to pg level in environmental waters. However, it is considered that the ruggedness and sensitivity of ion chromatography, CE's main rival, makes the CE technique suitable only where very specific characterisations might be required.

For the analysis of amines by HPLC instrumentation the most commonly employed detector is UV (especially DAD) and electrochemical (EC) detection. UV detection of alkylamines and alkanolamines usually incorporates a derivatisation method as these compounds have low absorptivity in the UV range, and higher sensitivity is achieved in the fluorescence detection mode. Heterocyclic amines have characteristic UV spectra and are also electrochemically oxidisable and these and aromatic amines can be determined directly by UV, fluorescence and EC detectors. EC detectors are more sensitive than UV however their performance is highly dependent on the type of samples analysed as they tend to be prone to contamination (Pielesz, 2006).

For application to LC techniques, collection from the gas phase commonly uses an acidic liquid or the impregnation of a sorbent, glass wool of filter, and requires little subsequent sample preparation. Rampfl *et al.* (2008) implements phosphoric acid coated glass wool to form a quaternary ammonium salt for analysis using LC/ESI-MS. Dye *et al.* (2008) used citric or oxalic acid impregnated glass fibre filters for analysis of certain amines and alkanolamines of relevance to PCC process assessment for analysis by LC/ESI-TOFMS.

A method commonly applied to the analysis of amines is ion exchange chromatography (IC), which is a process that allows the separation of ions and polar molecules based on their charge. The technique uses various forms of electrochemical detection (such as conductivity or amperometry). Amines and alkanolamines are detected as cations after their separation on a cation exchange column. The methodology has been in use for a long time and was developed for the determination of ammonia, methylamine, dimethylamine, and trimethylamine by Bouyoucos and Melcher (1983) in air collected on sulphuric acid treated tubes, or by impingers in aqueous solution (Bouyoucos, 1977). The method combines the principles of OSHA ID-188 (for determination of ammonia by ion chromatography) and extends it to the alkylamines. It is likely that optimisation of chromatographic conditions and detection would allow the analysis also of alkanolamines and possibly higher amines. For example, Page *et al.* (2005) successfully applied ion chromatography to the analysis of a number of alkanolamines and various cyclic and other amines in concrete derived liquids and the method is commonly used in process solutions. In the analysis of ground waters and for bioreactor monitoring, Mrklas *et al*. (2003) determined MEA along with ammonium and other cations using cation exchange chromatography. They also measured certain anions by anion exchange chromatography with suppressed conductivity, and ethanol and glycols by ion exclusion chromatography with amperometric detection. An alternative to acidic collection is a method by Bouyoucos and Melcher (1986) who used alumina to collect ethanolamines (MEA, DEA, TEA) with good recovery from air for analysis by ion chromatography. Peru *et al* (2004) determined alkanolamines in cattails by ion chromatography utilizing LC/ESI-MS with selected reaction monitoring. Analysis of aqueous samples is performed after solid phase extraction, for example Casella *et al.* (2008), who determined aliphatic amines by cation-exchange chromatography with suppressed conductivity detection after solid phase extraction

4.3.8 Analytical Strategy for Determination of Amines and Alkanolamines

LC instrumental techniques, including ion chromatography, are powerful tools for the routine analysis of amines and alkanolamines of interest in this study. Where derivatisation is selected, for the collection of volatile amines or to enhance selectivity or sensitivity for example, derivatives for LC determination are more commonplace as established in standard methods, and the methods hold higher maturity than derivatisation designed for GC analysis. When applied to liquids, derivatisation using polymeric reagents advances the science of this technique and offers significant advantages. As such, HPLC techniques incorporating UV/fluorescence and EC detection are the techniques of choice for routine analysis of amine compounds specified in the CCM project.

With the exception of *N*-methyldiethanolamine, standard methods are established for all of the alkylamines, di-amine solvents and alkanolamines specified for assessment in this study, and in all cases OSHA methods are recommended over NIOSH. The OSHA method for piperazine is not validated and is at in-house status only and would therefore require full evaluation and validation. It is considered that the inclusion of *N*-methyldiethanolamine in an ion chromatographic method would also be feasible. These methods are necessarily rugged in nature and will normally provide adequate results for routine analyses and are well suited to screening analysis. Their performance when applied to sampling and analysis under the conditions of the PCC process would require thorough investigation. The use of more specialist techniques for collection,

preparation and instrumental analysis is recommended to take full advantage of the quality information that these methods can provide.

Sorbent collection suitable for direct thermal desorption of volatile amines in gaseous samples is recommended for investigation, as discussed in section 4.1.1. Analysis using GC/MS, for amine compounds amenable to gas chromatography, would provide complementary information to that from the standard methods.

Another option for investigation is the use of chemiluminescence detection of volatile amine compounds. Current TEA systems are available with three modes of analysis enabling the determination of aliphatic amines and ammonia as well as nitrosamines. Thus the development of a suitable sorbent system, for gas phase collection, and suitable solvent extraction system for liquid phase samples would allow the use of GC/TEA or LC/TEA as an effective means of routine or screening analysis for these three classes of volatiles, possibly with confirmation using GC/MS and LC/MS methods.

One limitation of GC based techniques is their relatively poor performance in the analysis of amine compounds due to the basicity and polarity of the amine when presented in its free form. Base deactivation of components and columns has progressed their efficient analysis to some extent but this is dependent on the characteristics of the amine and its matrix and would require evaluation for any application where GC is considered, such as thermal desorption, TEA and MS. Alternative GC methods involving derivatisation of the analytes are complex and best avoided unless preferable instrumental options are unavailable or where this technique meets a specific requirement.

LC/MS combines the advantages of HPLC with the sensitivity and selectivity of mass spectrometry, as has been discussed at length in relation to nitrosamine analysis. Additionally chromatographic analysis of the process solution without pre-treatment is a more likely possibility by LC than by GC/MS analysis which would find difficulties with the basicity of the solution and the presence of high levels of alkanolamine solvent. LC/MS requires a high level of expertise in the method development and would be chosen for specialist speciated analyses of gas and liquids from the PCC process.

The maturity of LC methodologies ranks these as the major priority for routine analyses for the specified compounds. However a significant level of method development is still required, and more than one method is likely to be needed to cover volatile and non-volatile compounds in gaseous products and in process liquids. Target concentrations will obviously differ between gaseous and liquid samples, and within a sample, where there will be large differences in concentration between the amine solvent and the alkylamine degradation products. Dependent on the relative concentrations, and whether these fit to the linear range of the method, more than one analysis may be required to optimise sensitivity to minor components. It is considered that this is not beyond the scope of an advanced analytical contract laboratory.

4.4 Amides

4.4.1 Significance and Properties

Amides contain the acyl functional group (R-C=O) linked at the carbon to a nitrogen atom. The amides specified for assessment in the CCM Project are the simplest primary amides; formamide and acetamide.

Compared to amines, amides are very weak bases. Formamide and acetamide are soluble in water but less soluble than the comparable amine. Water solubility for as expressed by their octanol/water partition coefficient, log $K_{o/v}$ are around -1.5 compared to methylamine -0.57 and ethylamine -0.13, and their solubility is similar to piperazine and diethanolamine as examples. Small amides such as dimethylformamide exhibits low solubility in water. They have relatively high boiling points 210ºC/222ºC and formamide partially decomposes at 180ºC. Vapour pressures of formamide and acetamide are 0.008 kPa and 0.005 kPa at 25ºC, respectively, and they are much less volatile that the similar amines and akin to higher nitrosamines (NMor for example).

Environmentally the monitoring of formamide and acetamide are not of major priority, and ambient air and water quality regulation do not call for their monitoring. As such methods for workplace assessment are the only source of reference; these from OSHA and even then they are not fully validated. Also sourced is an industrial standard of use in discharge waters. A description of these methods follows. These methods are rudimentary and full method development of collection and analysis procedures would be required for application to PCC process liquids and gaseous emissions monitoring.

4.4.2 Standard Methodologies

Gas phase methods

OSHA In-house method: Formamide

OSHA Method 2084: Acetamide

Principle and Application: Amides in ambient and workplace air by GC/NPD

Method Status: Formamide not validated. Acetamide partially evaluated, 1987

Target analytes: Formamide, Acetamide (respective methods)

Collection: Sampling tube containing silica gel (uncoated)

Air Sampling Volume and Rate: 10L at 0.1 L/min

Storage and Stability: Stable at room temperature for at least 7 days

Preparative: Silica gel is desorbed with 1 mL methanol.

Analysis: GC/NPD (nitrogen phosphorous detector)

Instrument MDL (GC/NPD):	Formamide	Not validated
	Acetamide	10 ng

Procedural MDL: Acetamide 1.0 mg/m^3 (0.4 ppmv) (parameters as stated)

Recovery: 88.4% as recovery from retention efficiency based on liquid standard spikes to tube and 10L flow of humidified air.

Interferences: None reported

Supporting Information:

It may be possible to analyse other compounds at the same time using this method

Comments and Recommendation

Formamide degradation in hot injector may be an issue (partial degradation at 180ºC, injector temperature 200ºC is specified)

Method is rudimentary and detection limits are high

Method is not recommended for routine analysis of formamide and acetamide before further development and validation or alternative methods considered.

Liquid phase methods

US EPA Method 1666: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS

US EPA Method 1671: Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID

Principle and Application: Volatile organic compounds in clean water by purge and trap or direct aqueous injection GC/MS, or GC/FID

Method Status: Not stated, Revision A, 1998

Target analytes: VOCs including formamide

Collection: Amber bottle. Dechlorination with sodium thiosulphate where presence of chlorine is determined in the field by US EPA methods 330.4, 330.5.

Sampling Volume: 500 mL

Storage and Stability: Refrigerated at 0 - 4ºC for 14 days.

Preparative: Addition of isotopically labelled analogs of the compounds of interest.

Analysis: Formamide is not applicable to the purge and trap method and is analysed by direct injection. Gas chromatography with MS detection in the electron impact mode (GC/EI-MS). Identification based on agreement between retention time and mass spectrum of authentic standards. Quantitation by extracted ion current profile and isotope dilution technique or internal standard technique as applicable.

Gas chromatography with FID detection (GC/FID). Identification based on agreement between retention time of authentic standards and samples. Quantification by internal standard technique.

Instrument MDL: Not stated.

Procedural MDL: GC/MS 1000 mg/L formamide GC/MS 100 mg/L formamide

Recovery: Approximately 60 - 286% formamide

Interferences: Procedural only

Supporting Information: Method used for surveying and monitoring purposes specific to the pharmaceutical industry.

Comments and Recommendation

Rudimentary method as per requirements of industrial monitoring.

High detection limits due to low response of formamide by GC/FID. GC/MS not explainable apart from m/z in region of noise.

Under direct injection technique, method detection limits are high and inadequate for trace level analysis. Where lower concentrations are required the development of a solid phase extraction technique for the concentration of analytes would be required.

The target analyte list does not include acetamide however the method is likely to be suitable for its analysis.

Analysis of alkylamines was also applicable under this method, as previously discussed.

This method is not recommended for analysis of process liquids due to the basic nature of the liquid and the presence of other non-volatile or highly polar compounds.

4.4.3 Standard Methods Summary Recommendations

Methods from OSHA for analysis of formamide and acetamide are not fully validated and use rudimentary collection procedures. GC/NPD is a useable detector for underivatised amides and could be considered for this analysis after considerable method development and validation. A preferred detector would be GC/MS. Overall the standard method, as it stands, is not recommended.

US EPA methods for analysis of waters are for industrial monitoring purposes and as such have high detection limits. The method uses direct injection to GC/FID or GC/MS which is unlikely to be suitable for process liquids due to their high basicity and the likelihood of non-volatile or interfering compounds at high concentration. These methods are not recommended for routine analysis of gaseous or liquid samples from the PCC process. These or alternative methods require full development.

4.4.4 Non-Standard Methodologies

The literature addresses the analysis of amides largely from a biological and pharmaceutical focus. In these applications the amides are very large and techniques bear little relationship with the collection and analytical requirements for this study. Environmentally formamide and acetamide compounds are not traditional, nor are they emerging as contaminants of importance. Dimethylformamide (DMF) is represented more strongly in the literature as it is used as a solvent and is associated with the manufacture of resins and polymers, and in other areas of industry. Its properties are quite different to the primary amides however some analytical aspects may be applicable. Of the few papers, the following were of some relevance. Snorek *et.al* (1988) analysed low molecular weight amides, the smallest being DMF, in a pharmaceutical application. They used reverse phase HPLC/UV analysis from an aqueous matrix and achieved approx 10-fold higher sensitivity than analysis by GC/FID and GC/NPD. Rastogi (1993) reported the analysis of formamide in solvents by headspace analysis and used GC/FID as this was preferable for other hydrocarbon components in the mixture. Santoni *et al.* (1992) applied HPLC after SPE purification of urine samples using an ion exclusion column and sulphuric acid mobile phase with UV detection for determination of *N*-methylformamide and higher amides. SPME techniques have also been applied to the analysis of small amides. DMF and dimethylacetamide (DMA) have been determined by SPME techniques from air by GC/FID (Parreira *et al.*, 2006) and DMF and methyformamide in the headspace of saliva by GC/MS (Wang and Lu, 2009). Perhaps a more applicable application to process gaseous is the use of solid sorbent sampling. Pitts *et al.* (1978) used Tenax-GC™ to sample amides, nitrosamines and nitramines to determine products from photochemical oxidation of aliphatic amines. An assessment of artifact formation was not performed but this is considered unlikely to effect the integrity of amides and thermal desorption to some extent overcomes issues with decomposition of formamide. Sorbent collection and thermal desorption would be the method of choice for gas phase samples when GC based instrumentation was to be applied.

GC analysis is an option for small amides, although their chromatographic resolution is not ideal. The partial decomposition of formamide at temperatures below its boiling point also present issues for hot injection in GC analysis, although this could be accounted for and preferably overcome in various ways. Samples would also need to be clean of non-volatile or basic components, or the sample would require clean-up for their removal. GC/FID methods lack sensitivity due to the low carbon response and GC/NPD would be preferable offering sensitivity to nitrogen containing species. For these samples, where it is likely other amine and nitrogen containing species are present GC/MS would be a detector of choice, albeit at non-optimum sensitivity for these particular compounds. Their low molecular weight puts them in the region of high background signal and hence increases detection limits in GC/MS analysis. It is considered that GC/EI-MS would be sufficient if only amides were targeted but if the analysis is combined with that for other compounds of interest, then GC/CI-MS/MS could be considered for higher level of confirmation. For GC analysis, chemiluminesence detection is also recommended. It should be possible to analyse for amides using the nitrogen mode of a TEA analyser if it is possible to obtain a suitable clean solvent extract, and optimise columns and conditions to separate these compounds in the presence of amines, and possibly nitrosamines. Unfortunately literature as searched to

date has not been able to support this opinion but the authors feel that this is worth investigation.

Although little literature information is available, HPLC is an obvious choice for these compounds given their polarity. LC techniques would be especially suited to liquid phase samples, where the presence of other compounds may impact unfavourably on a GC technique. Direct injection is unlikely to provide sufficient sensitivity and some form of analyte enrichment would be required, as discussed in Section 4.1.2. LC analysis of gas phase samples is also an option if a compatible sorbent and solvent combination was found suitable for LC analysis without the requirement to swap solvents. LC/MS analysis could also be used with a significantly higher investment in method development.

4.4.5 Analytical Strategy for Determination of Amides

The CCM project calls for the assessment of formamide and acetamide. Under environmental regulation, these are not of major priority, and ambient air and water quality regulation do not call for their monitoring, nor are they emerging as contaminants of importance. As such few standard methods have been established. Methods from OSHA for analysis of formamide and acetamide are not fully validated and use rudimentary collection procedures. US EPA methods for analysis of waters are for industrial monitoring purposes and as such have high detection limits. Overall the standard methods, as they stand, are not recommended.

The literature addresses the analysis of amides largely from a biological and pharmaceutical focus. Smalls amides from solvents and manufacturing applications provide some analytical guidance and may be applicable. GC analysis is an option for small amides, although their chromatographic resolution is not ideal. Sorbent collection and thermal desorption would be the method of choice for gas phase samples. MS detection is preferable to other detectors for reasons of confirmation in mixed amine and amide matrices. Chemiluminescence detection is also a consideration. It should be possible to analyse for amides using the nitrogen mode of a TEA analyser if it is possible to optimise preparative and determinative methodologies. Unfortunately literature as searched to date has not been able to support this opinion but the authors feel that this is worth investigation.

HPLC is an obvious choice for these compounds given their polarity. LC techniques would be especially suited to liquid phase samples incorporating a form of analyte enrichment and may also be applicable to gas phase samples. LC/MS analysis could also be incorporated into the analytical strategy with a significantly higher investment in method development.

Overall, there are no absolute recommendations for procedures for analysis of formamide and acetamide, due to the lack of mature methods and their limited priority in the literature. Development of methods based on the liquid chromatographic technique is favoured, and a simultaneous method may be possible for analysis of amides along with amines if these compounds were to remain a priority.

4.5 Aldehydes

4.5.1 Significance and Background

Carbonyl compounds (aldehydes and ketones) have featured strongly as compounds of environmental and health concern for a long time. They occur as direct emissions from industrial processes and products and as products of incomplete combustion or oxidation of other organic compounds. They are also present as products of photochemical processes and they play a major role in the formation of photochemical smog. Formaldehyde is listed as a Group 1 carcinogen and acetaldehyde a Group 2A probable carcinogen by the IARC (IARC, 2006). As such these compounds are prioritised for regulation and monitoring by international agencies and as such analytical methodologies are well established

Short-chain aldehydes (such as the specified compounds; formaldehyde and acetaldehyde) and certain other carbonyl compounds (aldehydes and ketones) are classed as reactive and are likely to undergo reactions during the sampling and/or analytical processes. They are also highly water soluble, making their dissolution into an aqueous matrix likely and their separation from this matrix difficult. Concentration of the analytes is usually required to achieve the desired sensitivity in environmental analysis, as is expected to be required for samples from PCC processes. Certain aldehyde biosensors have also been used where direct determinations are possible, such as the determination of the enzyme NADH generated by enzymatic activity of immobilised aldehyde dehydrogenase (Schultheiss *et al.,* 2000), but these applications are not common. The most effective way to ensure analyte integrity is to render the aldehyde stable and the technique of derivatisation is universally used. This chemisorption technique uses a selected compound (the derivatising agent) which reacts with the analyte to form a new compound (the derivative). Using an agent which offers specificity to the target analyte class and high detectability to the chosen detection system, derivatisation also enhances method performance by providing greater selectivity and higher sensitivity. Numerous derivative compounds can be used, each of which can provide a favourable outcome for specific applications or analytes, or to comply with a specific instrumental or detection methodology.

4.5.2 Standard Methodologies

Methodologies incorporating some form of derivatisation are specified in all internationally recognised procedures for determination of carbonyl compounds in both gas and liquid phase applications. These methods specify a particular derivatising agent, and different methods use different agents, mainly dependent on the target analytes and the instrumental technique employed. The sample can be exposed to the derivative in liquid form (termed impinger sampling) or a solid sorbent coated with the derivative can used (termed cartridge sampling) The derivative most commonly specified is 2,4-dinitrophenylhydrazine (DNPH) and the characteristics of this derivative make HPLC the preferred determinative method using UV absorbance detection. The principles behind this and other methodologies are discussed later in this section.

Standard methods for the determination of aldehydes of relevance to this study and which specify the DNPH/HPLC technique include:

- US EPA Method 0011: for application to stationary source emissions using liquid collection and impinger sampling
- US EPA Method 8315A: for analysis of samples collected using Method 0011
- CARB Method 430: stationary source emissions using impinger sampling
- US EPA Method TO-5: ambient air assessment using impinger sampling
- US EPA Method TO-11A: ambient air assessment using cartridge sampling
- CARB Method 022: ambient air assessment using cartridge sampling
- ASTM Method D 5197 – 03: ambient air assessment using cartridge sampling
- NIOSH Method 2016, 2018: workplace assessment using cartridge sampling
- US EPA Method 0100: indoor air assessment using cartridge sampling
- US EPA Method 554: drinking and source water assessment using DNPH treatment and solid phase extraction.

Standard methodologies also provide gas chromatographic analysis as an alternative to liquid chromatography. In this case different derivatisation techniques are generally used. US EPA Method 556 applies to analysis of drinking and source water and uses pentafluorbenzylhydroxylamine (PFBHA) as the derivatising agent. This produces a halogenated derivative which provides high sensitivity using an ECD detector. In the workplace application, OSHA Method 52 and Method 68 for formaldehyde and acetaldehyde respectively, NIOSH Method 2541 and Method 2538 for formaldehyde and acetaldehyde, respectively and Method 2539 for aliphatic aldehydes specify derivatisation using 2-(hydroxymethyl)piperadine (2-HMP). This is coated onto XAD-2 sorbent and forms a stable oxazolidine derivative suitable for GC/NPD, GC/FID or GC/MS analysis. NIOSH Method 3500 uses impinger collection into sodium bisulphite solution for determination of formaldehyde by visible absorption spectrometry and Method 3507 uses a Girard T reagent for analysis of acetaldehyde and higher carbonyls by HPLC/UV.

4.5.3 Non-Standard Methodologies

The general literature overwhelmingly supports the derivative method for the determination of carbonyl compounds. In their review of derivatising agents for carbonyl compounds in environmental analysis, Vogel *et al.* (2000) found that the most popular, reliable and robust group of agents were the hydrazine reagents, in particular 2,4-dinitrophenylhydrazine (DNPH), for determinations in both air and water matrices. This opinion is reiterated by Pal and Kim (2007) in their review of experimental methods for determination of carbonyls in air. Many papers have been published on the use of this technique in various applications and it is therefore not considered necessary to

itemise or prioritised these here, and the reader is directed to the above publications for further reference if required.

On consideration of the standard methodologies and of the literature, the DNPH derivative method is recommended as the preferred option for stable collection and treatment of gas and liquid phase samples relevant to this study. This method is available as an accredited method at contract laboratories albeit that these laboratories often require the matrix to be that applicable to the standard method (drinking water, ambient air, combustion gases etc), as it is under these conditions that the method is validated and accredited. The DNPH methodology and the options for detection and quantitation of the specified carbonyl analytes will therefore be the focus of the following discussion.

Principle of DNPH Derivatisation and HPLC Method

Carbonyl compounds react with the derivatising agent 2,4-dinitrophenylhydrazine (DNPH) by nucleophilic addition on the carbonyl followed by 1,2-elimination of water and the formation of a 2,4-dinitrophenylhydrazone. Acid is required to promote protonation of the carbonyl because DNPH is a weak nucleophile. The hydrazones are extracted into a suitable solvent for subsequent chromatographic analysis, usually using HPLC. The DNPH technique is applied to the sampling of both liquids and gases. For liquids an aliquot is treated with the DNPH reagent. Often, solid phase extraction is implemented to concentrate the hydrazone derivatives prior to analysis. Gas phase collection is performed by flowing the gas sample through an impinger charged with liquid DNPH reagent or through a cartridge containing the DNPH derivatising agent coated onto a support, as described in Task 2 (Azzi *et al.,* 2010). The hydrazone derivative is formed *in-situ* and is eluted from the cartridge, or extracted from the liquid, using a suitable solvent; typically acetonitrile. Standard methodologies specify that samples so collected are stable for up to 1 month on a cartridge and 7 days in the liquid state, under refrigeration.

Instrumental liquid chromatography (HPLC) is the preferred separation technique and this is generally performed using reverse-phase separation on a C_{18} column and binary or ternary eluents comprising water and organic solvents such as acetonitrile, methanol and tetrahydrofuran, to provide the required selectivity. HPLC detection of carbonyl-hydrazones has routinely been performed using UV absorption at 360 nm, as the hydrazones are highly chromaphoric and are detected at high sensitivity. The use of a diode array detector (DAD) is of benefit in that a diode array scan of the peak can determine the level of peak purity, which may be helpful in assessing the presence of interferences, and may provide information which allows the identity of unknowns to be predicted.

Detector sensitivity to formaldehyde measured at 360 nm is typically around 55 pg/20µL injection; equivalent to 0.003 µg/mL (Waters Corporation, 1994, and our own work). On this basis, a method detection limit for gas phase samples of around 0.15 µg/m^3 (0.12 ppbv at 25°C of formaldehyde) would be achieved for cartridge collected samples and on a sampling basis of 100L nominal gas collection volume and 5mL cartridge extraction volume. Impinger collected and process liquid samples would return around 0.3 µg/L using 100mLs of DNPH treated sample for SPE concentration and a 10mL extraction volume.

GC separation and analysis of carbonyl DNPH derivatives has found limited application due mainly to the low volatility of the hydrazones and reduced chromatographic resolution, particularly for C_4 compounds and higher. Residual DNPH reagent in the sample extract is reported to effect column and detector performance and for this reason a cleanup step, using a cation exchange resin, is often implemented for FID or MS detectors, and is essential for ECD detectors and NDP detectors (Dalene *et al.,* 1992). NPD detectors offer high selectivity and sensitivity to the hydrazones but the acetonitrile eluant will overload the detector and causes interference, requiring the extract to be dried and re-solubilised in a suitable solvent. Alternative techniques for application to GC analysis, for example using more volatile derivatising agents, engendering higher sensitivity for specific detection systems, using adsorptive enrichment on solid sorbents (usually requiring thermal desorption and cryogenic focussing) or solid phase microextraction, have been put forward by many authors, some of which are reviewed by Vogel *et al.* (2000) and Pal and Kim (2007). For example, Andrzejewski *et al.* (2008) reports the use of *o*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine (PFBHA) for detection of certain aldehydes resulting from ozonation of dimethylamine containing water. The reaction takes place directly in water and can be extracted using hexane for analysis using GC/ECD at high sensitivity. Most review publications generally consider that the requirements for method rigour and efficiency make many of these techniques somewhat specific, unreliable or cumbersome for the sampling and analysis of simple carbonyl species in various matrices, compared to DNPH derivatisation and HPLC methods.

More recently LC analysis with MS detection has been applied as is accordant with the advantage of mass spectral analysis in expanding the selectivity of the technique particularly for higher isomeric carbonyls and oxygenated carbonyls. Its application to DNPH derivatisation of carbonyl compounds found as disinfection by-products in water is reported by Zweiner *et al.* (2002), for example. The method uses LC-ESI-MS-MS analysis and its validation is described for the quantitative determination of a wide range of carbonyl compounds. Detection limits in the µg/L range were achieved without sample preconcentration and with solid phase extraction a further 25 to 250-fold improvement in sensitivity was obtained. Other authors report a number of limitations in LC/MS of DNPH derivatives (as reviewed in Vogel, 2000), particularly with respect to the similarity in mass spectra for hydrazones of structurally related analytes, where only small differences are seen even in tandem MS experiments. In the case of the specified analytes in this study, this would not be relevant and method development may well produce a reliable method. However, the sensitivity and overall ease of implementation of HPLC/UV for this determination would hold sway against LC/MS under the requirements of this study. Where more complex characterisation is required, for oxygenated carbonyls for example, or where it is found that interferences were in some way extreme, LC/MS would become a viable analysis strategy.

DNPH derivatisation has also been applied to the analysis of a number of other compounds, particularly oxidant compounds such as nitrogen dioxide (NO_2), where the respective azide derivative is formed (Grömping *et al.*, 1993). Using this principle a method for measurement of HNO_2 in the atmosphere has been developed by Zhou *et al.* (1999). It is possibly on this basis that the NILU laboratories have applied DNPH derivatisation to the collection and LC analysis of nitramine compounds (Nielson *et al.*, 2010), however little detail is presented and substantiation of this approach has not be found from journal literature.

The main limitation to the DNPH/HPLC methodology is the co-collection of certain compounds which may impact on its efficiency and/or its chromatographic performance. In ambient gas phase sampling, ozone effects the collection of certain carbonyls due to *in-situ* interactions on the cartridge and the occurrence of artifacts in the LC chromatogram. This is overcome with the use of a potassium iodide, or other, ozone scrubbing cartridge placed upstream of the sampling cartridge (Pires and Carvalho, 1998). Nitrogen dioxide (NO_2), a component of combustion gases, is derivatised by DNPH to form an azide (Karst *et al.,* 1993). This reaction will deplete the DNPH and hence reduce the capacity of the cartridge for reaction with carbonyl compounds. When sampling in high NO_x atmospheres an assessment of the likely NO_2 levels must be undertaken to determine if cartridge carrying capacity will be exceeded. Where levels are acceptable, the NO_2 derived azide can interfere in chromatographic resolution of carbonyl analytes as it has an adsorption at the wavelength used for carbonyl-hydrazone analysis and it elutes in the region close to formaldehyde. This is overcome by careful optimisation of the solvent mixture and gradient elution used for the chromatography to allow selectivity to this compound. In fact NO_2 can be accurately quantified in this way (Grömping *et al.*, 1993). Acrolein has been found to degrade under the conditions of the acid catalysed derivatisation reaction, forming a by-product which will increase over time on-cartridge or in solution, and will present as an extra peak in the LC chromatogram. For this reason, the DNPH method is no longer recognised by some international agencies for acrolein analysis. This, and the limitations described above, is not considered to in any way effect the collection and analysis of specified carbonyl products from the PCC process.

Of particular relevance to this study with respect to gas phase sampling is the water content and temperature of the sample gas and the range over which the sampling cartridges are suitable. A sampling temperature of between 10°C and 100°C is specified by Waters (Waters Corporation, 1994) for their Sep-pak XpoSure™ cartridges. Supelco do not provide a temperature range for their cartridges but warn that elevated temperatures may result in an increased level of carbonyl impurities migrating from the cartridge body to the DNPH bed. They rate their cartridges as suitable above 20% relative humidity and at high humidity, provided water does not condense to any large extent in the cartridge body. Condensation of small amounts of water in the cartridge has been evaluated and does not unduly affect their performance. Under these conditions a potassium iodide ozone scrubbing cartridge cannot be used as this is affected by excess moisture which in turn effects the collection to the DNPH cartridge. This scrubber is not required for flue gas sampling.

4.5.4 Analytical Strategy for Determination of Aldehydes

The DNPH derivatisation method is recommended for the determination of specified compounds; formaldehyde and acetaldehyde in PCC process gaseous and liquid samples, using protocols based on stationary source and ambient methodologies. The recommended guidance is the US EPA or CARB standard test methods, as follows:

- US EPA Method 0011 or CARB 430 for collection of gas phase samples from stationary source emissions using an impinger charged with the DNPH liquid.

- US EPA Method TO-11A for collection onto a solid DNPH sorbent cartridge, as used in ambient air sampling, and analysis using HPLC analysis with UV detection.

- US EPA Method 8315A or Method 554 for analysis of impinger collected or liquid samples with DNPH treatment, SPE enrichment and analysis by HPLC/UV

  A superior detector is diode array (DAD) and this is the preferred determinative technique.

  The instrument MDL is 50 pg, equivalent to 0.003 ug/mL in extract

  The procedural MDL in the gas phase is 0.15 µg/m^3 (0.12 ppbv as formaldehdye) using nominal 100L gas volume, and in the liquid phase; 0.3 µg/L.

The gaseous and liquid phase methods would required development and evaluation to ensure that matrix components peculiar to the PCC process do not impact on the efficiency of the carbonyl-DNPH reaction and the SPE procedures and on the chromatographic resolution of the target species.

The analytical method is selective and sensitive and readily adaptable to both gaseous and liquid collections. It is mature and would be readily available at environmental contract laboratories. It is also straight-forward and cost effective.

4.6 Method Development Protocol

The methodologies implemented for analysis of PCC process samples will require significant adaptation or development from standard or non-standard procedures. Sampling and analytical methods will need to address:

a) the wide range of analytes specified for assessment

b) the complexity of the gas and liquid matrices

c) the similarity in characteristics between bulk and trace components

d) the relative concentrations between bulk and trace components

e) the level of aqueous dilution

It is likely that the standard methods designed for ambient or industrial workplace application or the analysis of drinking or waste water may not be directly implementable. Alternative non-standard methods may be more applicable or offer a higher level of performance. A number of methods will be required for the different classes and/or compounds within each class and the collection, work-up or instrumental techniques may need to be specific to a class, or compounds within the class. The method development protocol will therefore incorporate all aspects of sampling, the analytical preparative steps and the instrumental determinations; the outcome of which is the establishment of methodologies capable of sensitive and accurate quantitative results for application to environmental emissions assessment of the PCC process.

It is considered that the exact requirements of the methods development and subsequent validation will evolve as various techniques are tested and the results of necessary checks and modifications are evaluated. This practical work is the objective of Task 5 in the establishment of analytical procedures.

As a general overview, the method development protocol will need to evaluate the following aspects of sampling and analysis:

Sampling

The sampling protocol and its requirements and considerations has been described in Task 2 (Azzi et al., 2010). In general, the efficiency of the techniques used for sample collection would be evaluated by way of variations to this sampling protocol. In the gas phase the effect of such parameters as flow rate, sampling period, dewpoint, temperature etc, the type of liquid and/or solid collection system, the sorbent media, and the requirement for physical or chemical quenching agents would be addressed. Minimisation of low system backgrounds is also required. Where *in-situ* derivatisation is the method of choice, the impact of bulk amine constituents on the capacity of the sampling media and the efficiency of collection of trace components will require evaluation, as is also the case for other solid sorbent media. Where bulk amines themselves are the analyte, capacity of the sorbent is obviously an issue and in this case direct wet collection may be used. Evaluation of methods to ensure analyte integrity is then required, as is also required for non-derivative solid sorbent systems. In all cases the level of co-collected water would be ascertained for solid sorbents; and their tolerance for water. Where gases are sampled above their dewpoint the temperature constraints of the sampling media will be a consideration. The retention efficiency would

be determined by the use of multiple collection devices to determine possible carry over, the use of liquid surrogates added to the sampling media or preferably, in the case of gas phase sampling, by the inclusion of gaseous surrogate standard compounds into the actual sampling stream of the process itself.

Preparative Techniques

A development protocol for the preparative aspects of the methodology applies to all steps in the sample work-up and the various means of analyte extraction, enrichment or isolation which may be necessary to effectively isolate the compounds of interest from the bulk constituents. This aspect includes the maintenance of sample integrity through this process and the evaluation of non-analyte sample species as interferants or as reactants, and methods for their elimination or minimisation. It also includes the demonstration of low system backgrounds and minimisation of various procedural contaminants. It is possible that the efficiency of various pre-treatment techniques would be tested and compared, for example using a number of materials for SPE and a number of different solvent extraction regimes. The residence time of the sample in contact with the SPE media is also an important consideration in the optimisation of an SPE technique. For PCC process samples the similarity in chemical characteristics of trace and bulk analytes where these are both present in the liquid sample makes the development of SPE techniques particularly challenging. Where post sampling derivatisation is used, a number of reagents and the method of implementation would be tested, as described in the body of this report. The impact of these factors would be determined through recovery studies using surrogate standards applied to both innocuous and real liquid samples and the inoculation of sorbent media.

Instrumental Parameters

Optimisation of instrumental parameters is another component of the method development process. For certain instrumental techniques, such as spectrophotometry, this process is relatively straight forward, for others such as GC/MS and LC/MS this can be considerably more complex.

In the case of GC based techniques the mode of sample injection and the parameters associated with the injector require optimisation. Also important in the determination of amine and related compounds is the success of methods for base deactivation of silica sites and associated effects due to adsorption losses in the injector and column and loss in chromatographic resolution. The injector temperature and the mode of introduction in reducing exposure to temperature is an important consideration for thermally labile compounds of relevance to this project.

Sample introduction to HPLC systems is relatively straight forward. However for LC/MS assessment of flow and concentration dependence, particularly in ESI mode, and the effect of the solvent regime and the sample matrix is required. These and other parameters can affect the ionisation process and hence the analyte response, as has been reported in publications discussed in the body of the report.

The choice of GC or LC column and its effect on the chromatography, and the conditions used for component separation must be optimised to achieve efficient resolution of target compounds and of interfering components. Testing for coelution in

non-MS systems can also be carried out using two columns of differing polarity as a means of qualitative confirmation. The optimisation of detector response is relatively straight forward in non-MS detection but is more complex in MS applications, which can also incorporate chemical ionisation and tandem MS techniques. The response and stability of the mass analyser itself is also a quality assurance component of all MS based techniques using on-board standards and instrumental tuning protocols.

These techniques provide a powerful tool for qualitative and quantitative analysis but, like all other aspects, the evaluation of the quality of the result is required. These multitude of factors are assessed through various efficiency studies using standard compounds, and using surrogate and internal standard compounds which are present in innocuous and real samples, singularly and in combination and at extremes of relative concentration.

Validation of Method Performance

The method development also incorporates the validation process and the establishment of method performance criteria for initial demonstration of capability and on-going quality control (QC). These processes use statistical analysis of data generated from calibration and multiple injection and include instrumental detection limits, linearity, range, precision, accuracy (recovery), bias and repeatability. Some of these criteria are extended to the determination of procedural limits and minimum reporting levels (reliable quantification limits), uncertainty and perhaps also traceability of the data generated by the methodologies. Reproducibility can only be determined from inter-laboratory assessment. Selection and evaluation of the suitability of surrogate and internal standards covering the range and response of different analytes is also part of the method development and validation. For MS determinations isotopically labelled standards can be used to check and correct for procedural and instrument losses or variability. As is generally advised for LC/MS analysis, an analog of each and every analyte may be required, where this is possible, to account for response variability commonly encountered with this technique. Storage conditions and the stability of the analytes in the collection media and in the sample presented for analysis must also be ascertained. The implementation of protocols to assess on-going analytical performance using field, preparative and instrumental blanks, various QC standards and samples and duplicate testing are also the requirements of a fully validated methodology designed for quantitative determinations.

5. CONCLUSIONS

The literature review and evaluation of analytical procedures has enabled the following recommendations to be made regarding methodologies for the quantitative determination of compounds of relevance to the assessment of PCC process emissions:

N-Nitrosamines

The standard methods established by international environmental agencies are applicable to the specified suite of volatile nitrosamine compounds (NDMA, NDEA, NMor, NPip) in ambient air and water, and to one non-volatile nitrosamine (NDELA) in ambient air. The specified compounds *N*-nitrosopiperazine and 1,4-dinitrosopiperazine are not addressed by any of the standard methods, however it is considered that these would be applicable for determination under similar principles, after appropriate method development and validation. There are no standard methods available for NDELA in aqueous samples and the SPE technique used for volatile nitrosamines would require evaluation and validation. GC based methods may not provide the necessary efficiency or chromatographic resolution for the less volatile and more polar species and liquid chromatography would be evaluated as a more viable alternative for analysis of these compounds.

The standard methods carry maturity based on their on-going validation through agency protocol and also through their use and verification in various applications as attested by the literature. Hence they are likely to be available at contract laboratories specialising in environmental or food and drug applications. As these methods are applicable to nitrosamines of environmental relevance they apply to the assessment of ambient and workplace environments and to drinking and wastewaters. Hence their applicability to gaseous and liquid samples from the PCC process would require development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. This also means the standard method, or aspects of it, may be applicable as a starting point for application to the PCC process, but by no means guarantees its performance in that role, and indeed that alternative non-standard methods may be preferable.

On these bases, the following methods are recommended as candidates for investigation in the quantitative analysis of specified volatile nitrosamines and *N*-nitrosodiethanolamine in gaseous and liquid matrices:

- OSHA Method 27: Volatile Nitrosamines Mixture I

  Gas phase sampling using Thermosorb/N sampling cartridges and analysis by GC/TEA and HPLC/TEA.

  Procedural MDL: 0.13 µg/m^3 (0.04 ppbv) NDMA using 75L gas sample volume Equivalent to 0.10 µg/m^3 (0.03 ppbv) NDMA using nominal 100L gas volume.

  It is also recommended that INRS Method 031: N-Nitrosamines volatiles, be assessed for possible improvement in analytical efficiency.

- OSHA Method 31: N-Nitrosodiethanolamine (NDELA)

Gas phase sampling using glass fibre filters open faced cassettes and analysis by GC/TEA or HPLC/TEA.

Procedural MDL: 0.42 µg/m^3 (0.08 ppbv) NDELA using 480L gas volume. Equivalent to 2.0 µg/m^3 (0.37 ppbv) NDELA using 100L nominal gas volume.

GC based method for NDELA would require further evaluation as to its efficiency. HPLC is recommended for this and other non-volatile nitrosamines.

- US EPA Method 521: Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionisation Tandem Mass Spectrometry (MS/MS)

  Liquid sampling and solid phase extraction (SPE) and analysis by GC/CI-MS/MS.

  Procedural MDL: 0.28 ng/L NDMA using 500 mL nominal liquid sample volume.

  It is recommended that the efficiency of SPE be evaluated using alternate methods such as that based on AWWA Method 6450: Nitrosamines.

Non-standard methodologies for the determination of nitrosamines, as drawn from the literature, are also recommended for incorporation into the overall analytical strategy, and are summarised as follows:

Chemiluminescence techniques are utilised in the standard methodologies and offer superior selectivity and sensitivity compared with other non-MS GC and LC detection systems. The literature provides performance information in various applications including the recognition and address of interferences and artifacts. The maturity of the chemiluminescence approach, as exemplified by TEA or NCD, its sensitivity and selectivity and the associated reduction in preparative requirements, makes this technique a valuable tool for quantitative analysis of both liquid and gas phase samples from the PCC process. With incorporation of GC for volatiles and LC for non-volatile compounds, it has particular appeal in screening and group type analytical requirements and will provide adequate performance in speciated analysis where unequivocal confirmation is not a necessity. On this basis the chemiluminescence technique is highly recommended.

GC/MS techniques, using the more advanced systems of analysis such as GC/CI-MS/MS, achieve selectivity based on conformational mass spectral information and ultimate sensitivity. It is recommended that this MS mode, incorporating chemical ionisation and tandem MS functionality be incorporated as standard practice. The technique is limited to volatile nitrosamines, if derivatisation is to be avoided; however volatile analytes are a major portion of the contaminant suite. Its main applicability is to analysis of gas phase samples, due also to the nature of PCC process liquids. GC/CI-MS/MS instrumental procedures would be taken from US EPA Method 521 and it is considered likely that these methods could be developed to include *N*-nitrosopiperazine. As the principles of the technique are highly mature, its development for PCC process samples should be within the capacity of contract laboratories dealing in trace-level environmental analyses.

The LC/API-MS technique is recommended to form a significant part of the overall analytical strategy, possibly also incorporating tandem MS to further the level of confirmation attained. Its superior performance for the direct analysis of non-volatile, thermally labile and polar compounds in aqueous matrices or in matrices dominated by

the amine solvent makes it a valuable and necessary tool. LC/MS presents certain, but not insurmountable, challenges in attaining quantitative quality particularly for complex samples as would be encountered from the PCC process. As the technique is not mature in this application and no standard methodologies exist, a laboratory more aligned with the advancement of techniques and instrumental capability would be required to perform analyses of this type.

Amines and Alkanolamines

The standard methods target the majority of compounds specified for assessment by the CCM project, with the exception of *N*-methyldiethanolamine. It is considered that the inclusion of this compound into the target suite would also be feasible. These methods are all applicable to gas phase collection and limited standard methods exist for the liquid phase as there are no environmental drinking or wastewater methods for the determination of these compounds. If standard methods were given preference, the methods used for determination of gas phase components would require development for analysis from the liquid phase.

The standard methods are necessarily rugged in nature and will provide adequate results for routine analyses, and are well suited to screening analysis. As they are applicable to amines of environmental relevance their application to gaseous and liquid samples from the PCC process would require development, optimisation and validation to ensure that the efficiency of the standard method as designed is also achieved with these matrices. In particular the relative concentrations of the components will influence the efficiency of the method for a particular analyte and this also requires attention in the development process.

On these bases, the standard methods which are considered to provide highest analytical quality for speciated analysis of specified alkylamines, ammonia, diamines and alkanolamines in gaseous and liquid matrices are summarised as follows.

- OSHA Method 40: Methylamine

  OSHA Method 36: Ethylamine

  OSHA Method 34: Dimethylamine

  OSHA Method 41: Diethylamine

  Gas phase sampling using NBD-Chloride coated XAD-7 sampling tubes and analysis by HPLC-Fluorescence.

Procedural MDL:	Methylamine	35 µg/m^3 (28 ppbv)
	Ethylamine	29 µg/m^3 (16 ppbv)
	Dimethylamine	43 µg/m^3 (24 ppbv)
	Diethylamine	160 µg/m^3 (53 ppbv)

  These values based on a 10L gas collection volume.

  Equivalent to 3.5 to 16.0 µg/m^3 (2.8 to 5.3 ppbv) across the compounds using a nominal 100L gas volume. Note that higher volume would require evaluation of sorbent capacity.

- JIS Method K 0099: Methods for the Determination of Ammonia in Flue Gas

  Gas phase sampling using impinger collection into boric acid solution and analysis by either absorption spectrophotometry in accordance with JIS K 0115, or ion chromatography (IC) in accordance with JIS K 0127.

  Estimated procedural MDL at nominal 100L volume; 26 µg/m^3 (38 ppbv) for both methods.

- OSHA Method ID-188: Ammonia in Workplace Atmospheres – Solid Sorbent

  Collection using carbon bead/sulphuric acid impregnated sampling tubes and analysis by ion chromatography (IC).

  Procedural MDL: 400 µg/m^3 (600 ppbv) for 24L gas collection volume.

  Equivalent to 100 µg/m^3 (140 ppbv) for 100L nominal gas collection volume.

- OSHA Method 60: Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetraamine (TETA)

  Collection using NITC coated XAD-2 solid sorbent tubes and analysis by HPLC/UV.

  Procedural MDL: Ethylenediamine; 370 µg/m^3 (150 ppbv) for 10L gas volume.

  Equivalent to 37 µg/m^3 (15 ppbv) for 100L nominal gas collection volume.

  The detection limit for EDA is impacted by the chromatography as evidenced by a 20-fold lower detection limit for diethylenetriamine. Optimisation of chromatographic parameters is likely to achieve a lower detection limit for EDA.

- OSHA In-house Method: Piperazine

  This is a non-validated method that OSHA outlines to have similar principles as Method 60, above, and hence one would expect similar performance.

  This method would be developed in-house under the protocols of OSHA Method 60.

- OSHA Method PV 2111: Ethanolamine

  OSHA Method PV 2018: Diethanolamine

  OSHA Method PV 2145: 2-Amino-2-Methyl-1-Propanol (AMP)

  Collection using NITC coated XAD-2 solid sorbent tubes and analysis by HPLC/UV.

Procedural MDL:	Monoethanolamine	150 µg/m^3 (60 ppbv)
	Diethanolamine	172 µg/m^3 (40 ppbv)
	AMP	146 µg/m^3 (40 ppbv)

  These MDLs are based on the specified 10L gas collection volume.

  Equivalent to around 15 µg/m^3 (5.0 ppbv, dependent on compound) using a nominal 100L gas volume.

Note that the NITC derivatising agent used in this method for the alkanolamines is also used in the OSHA methods for diamines under the same sampling and instrumental procedures. OSHA also intends that piperazine be measured in the same way. Careful optimisation of the liquid chromatography may allow separation of all analytes and the use of a characteristic absorbance wavelength to enhance sensitivity for each class would be beneficial. For this reason a diode array detector is considered essential to enable programmed wavelength selection and diode array scans of the analyte peaks in order to improve selectivity, determine peak purity and provide a level of analyte confirmation, where mixed di-amine and alkanolamine analytes are expected.

Non-standard methodologies for determination of amines, as drawn from the literature, are also recommended for incorporation into the overall analytical strategy. The use of more specialist techniques for collection, preparation and instrumental analysis is recommended to take full advantage of the quality information that these methods can provide. Additionally the analysis of trace analytes such as the alkylamines in the presence of high levels of alkanolamines, in the case of process liquids, may not allow the use of standard methods without significant modification.

Sorbent collection suitable for direct thermal desorption to an instrument is recommended for investigation, for compounds amenable to gas chromatography. This negates the requirement for solvent extraction and provides associated advantages, and would be applied for analyte introduction to GC/MS. The method would be used for volatile amines in gaseous samples, where the gas has been treated in a manner acceptable for collection onto Tenax or other solid sorbents, and would provide complementary information to that from the standard methods.

Another option for investigation is the use of chemiluminescence for the detection volatile amine compounds. Current TEA systems are available with three modes of analysis enabling the determination of aliphatic amines and ammonia as well as nitrosamines. Thus the development of a suitable sorbent system, for gas phase collection, and suitable solvent extraction system for liquid phase samples would allow the use of GC/TEA for compounds amenable to gas chromatography or LC/TEA as an effective means of routine analysis or screening for these three classes of volatiles, possibly with confirmation using other GC/MS and LC/MS methods.

LC instrumental techniques, including ion chromatography, are powerful tools for the routine analysis of amines and alkanolamines of interest in this study. Where derivatisation is selected, for the collection of volatile amines or to enhance selectivity or sensitivity to these compounds, derivatives for LC determination are more commonplace, as established in standard methods, and the methods hold higher maturity than derivatisation designed for GC analysis. When applied to liquids, derivatisation using polymeric reagents advances the science further and offers significant advantages. As such, HPLC techniques incorporating UV/fluorescence and electrochemical detection are the techniques of choice for routine analysis of amine compounds specified in the CCM project.

LC/MS combines the advantages of HPLC with the sensitivity and selectivity of mass spectrometry, as has been discussed in relation to nitrosamine analysis. If the process solution can be chromatographed without significant pre-treatment, this provides significant advantage. This technique requires a high level of expertise in the method

development and would be chosen for specialist speciated analyses of gas and liquids from the PCC process.

The maturity of LC methodologies ranks these as the major priority for routine analyses for the specified amine compounds. However a significant level of method development is still required, and more than one method is likely to be needed to cover volatile and non-volatile compounds in gaseous products and in process liquids. Target concentrations will obviously differ between gaseous and liquid samples, and within a sample where there will be large differences in concentration between the amine solvent and the alkylamine degradation products. Dependent on the relative concentrations, and whether these fit to the linear range of the method, more than one analysis may be required to optimise sensitivity to minor components. It is considered that this is not beyond the scope of an advanced analytical contract laboratory.

Amides

The CCM project calls for the assessment of formamide and acetamide. Under ambient air and water quality regulation and monitoring these are not of major priority, nor are they emerging as contaminants of importance.

As such few analytical methods have been established. Methods from OSHA for gas phase analysis of formamide and acetamide are not fully validated and use rudimentary collection procedures. GC/NPD is specified, but for PCC process application it is considered that if GC based methods were used, GC/MS would be a preferable detector, although at some cost to sensitivity. The entire method would require development appropriate to the matrices. Overall the standard methods, as they stand, are not recommended.

US EPA methods for analysis of waters are for industrial monitoring purposes and as such have high detection limits. The method uses direct injection to GC/FID or GC/MS which is unlikely to be suitable for process liquids due to their high basicity and the likelihood of non-volatile or interfering compounds at high concentration. These methods are not recommended for routine analysis of gaseous or liquid samples from the PCC process. These or alternative methods require full development.

The literature addresses the analysis of amides largely from a biological and pharmaceutical focus. In these applications the amides are generally large and techniques bear little relationship with collection and analytical requirements for small amides in this study. Dimethylformamide (DMF) is represented more strongly in the literature; it being used extensively in industry. Its properties are quite different to the primary amides however some analytical aspects may be applicable.

GC analysis is an option for small amides, although their chromatographic resolution is not ideal. Sorbent collection and thermal desorption would be the method of choice for gas phase samples when GC based instrumentation was to be applied. MS detection is preferable to other detectors for reasons of confirmation in mixed amine and amide matrices, as discussed at length previously, albeit that small amines and amides would not be detected at non-optimum sensitivity. Chemiluminescence detection is also a consideration, particularly as a screening type determination. It may be possible to analyse for amides using the nitrogen mode of a TEA analyser if it is possible to

optimise preparative and instrumental parameters for their determination in the presence of amines. Unfortunately literature as searched to date has not been able to support this opinion but the authors feel that this is worth investigation.

HPLC is an obvious choice for these compounds given their polarity. LC techniques would be especially suited to liquid phase samples, where the presence of other compounds may impact unfavourably on a GC technique. Direct injection is unlikely to provide sufficient sensitivity and a form of analyte enrichment would be required. LC analysis of gas phase samples is also possible with appropriate selection of sorbent and solvent. LC/MS analysis could also be incorporated into the analytical strategy with a significantly higher investment in method development.

Overall, there are no absolute recommendations for procedures for analysis of formamide and acetamide, due to the lack of mature methods and their limited priority in the literature. Development of methods based on the liquid chromatographic technique is favoured, and a simultaneous method may be possible for analysis of amides along with amines if these compounds were to remain a priority.

Aldehydes

The DNPH derivatisation method is recommended for the determination of specified compounds; formaldehdye and acetaldehyde in PCC process gaseous and liquid samples. The recommended guidance is the US EPA or CARB standard methods.

- US EPA Method 0011 or CARB Method 430 for collection of gas phase samples from stationary source emissions using an impinger charged with the DNPH liquid.

- US EPA Method TO-11A for collection onto a solid DNPH sorbent cartridge as used in ambient air sampling and analysis using HPLC analysis with UV detection.

- US EPA Method 8315A or US EPA Method 554 for analysis of impinger collected and liquid phase samples using DNPH treatment, SPE enrichment and analysis by HPLC/UV.

  A superior detector is diode array (DAD) and this is the preferred determinative technique.

  The procedural MDL in the gas phase is 0.15 µg/m^3 (0.12 ppbv as formaldehdye) using a nominal 100L gas volume and in the liquid phase; 0.3 µg/L.

All aspects of the gaseous and liquid phase methods would required evaluation to ensure that matrix components peculiar to the PCC process do not impact on the efficiency of the carbonyl-DNPH reaction and SPE procedures and on the chromatographic resolution of the target species.

The method is selective and sensitive and readily adaptable to both gaseous and liquid collections. It is mature and would be readily available at environmental contract laboratories. It is also straight-forward and cost effective.

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APPENDIX 1. STANDARD METHODS REFERENCE

R1: Recommended as the most suitable method

R2: Recommended with exceptions or inclusions, or as further guidance to R1 method

R3: Not Recommended – alternative methods offer higher performance

Methods are listed in alphabetical order by agency, by component class and by method number in numerical order.

ASTM (American Standard Test Methods) International			
Method D 5197-03	Standard Test Method for the Determination of Formaldehyde and Other Carbonyl Compounds in Air (Active Sampler Methodology) (HPLC/UV)	DNPH cartridge	R2
AWWA (American Water Works Association), APHA (American Public Health Association) and AWEF (American Water Environment Federation)			
Method 6450	Nitrosamines (GC/CI-MS/MS)	Aqueous collection	R2
CARB (California Air Resources Board)			
Method 430	Determination of Formaldehyde and Acetaldehyde in Emissions from Stationary Sources (HPLC/UV)	DNPH impinger	R1
Method 022	Standard Operating Procedure for the Determination of Carbonyl Compounds in Ambient Air (HPLC/UV)	DNPH cartridge	R2
INRS (Institute National de Reserche et de Securite)			
Method 031	N-Nitrosamines Volatiles (GC/TEA)	Sulfamic acid, Florisil® cartridge	R2
Japanese Industrial Standard (Japanese Standards Association)			
JIS K 0099	Methods for the Determination of Ammonia in Flue Gas (Spectrophotometry and IC)	Impinger - Boric acid solution	R1

NIOSH (US National Institute for Occupational Safety and Health)			
Nitrosamines			
Method 2522, Issue 2	Nitrosamines (GC/TEA)	Thermosorb/N cartridge	R3
Amines			
Method 2010, Issue 2	Aliphatic Amines (GC/FID)	Silica gel (uncoated) tube	R3
Method 6015, Issue 2	Ammonia (Visible absorption spectrophotometry)	Sulphuric acid treated silica gel tube	R3
Method 6015, Issue 2	Ammonia by IC	Sulphuric acid treated silica gel tube	R3
Method 2540, Issue 2	Ethylenediamine (HPLC/UV)	NITC coated XAD-2 tube	R2
Method 2007, Issue 2	Aminoethanol Compounds I (GC/FID)	Silica gel (uncoated) tube	R3
Method 2509, Issue 2:	Aminoethanol Compounds II (IC)	Impinger – hexane sulphonic acid solution	R2
Aldehydes			
Method 2016, Issue 2	Formaldehyde (HPLC/UV)	DNPH cartridge	R3
Method 2018, Issue 1	Aliphatic Aldehydes (HPLC/UV)	DNPH cartridge	R3
Method 2538, Issue 1	Acetaldehyde by GC/FID	2-HMP coated XAD-2 tube	R3
Method 2539, Issue 2	Aldehydes, Screening (GC/FID, GC/MS)	2-HMP coated XAD-2 tube	R3
Method 2541, Issue 2	Formaldehyde by GC/FID	2-HMP coated XAD-2 tube	R3
Method 3500, Issue 2	Formaldehyde by Vis (Visible Absorption Spectrophotometry)	Impinger – sodium bisulphite solution	R3
Method 3507, Issue 2	Aldehydes by HPLC/UV	Impinger – Girard T reagent	R3

OSHA (US Occupational Safety and Health Executive)			
Nitrosamines			
Method 27	Volatile Nitrosamines Mixture I (GC/TEA)	Thermosorb/N cartridge	R1
Method 31	N-Nitrosodiethanolamine (NDELA) (GC/TEA, LC/TEA)	Glass fibre filter - open faced cassette	R1
Amines			
Method 34	Dimethylamine (HPLC/Flu)	NBD-Chloride coated XAD-7 tube	R1
Method 36	Ethylamine (HPLC/Flu)	NBD-Chloride coated XAD-7 tube	R1
Method 40	Methylamine (HPLC/Flu)	NBD-Chloride coated XAD-7 tube	R1
Method 41	Diethylamine (HPLC/Flu)	NBD-Chloride coated XAD-7 tube	R1
Method ID-164	Ammonia in Workplace Atmospheres (ISE)	Impinger – sulphuric acid solution	R3
Method ID-188	Ammonia in Workplace Atmospheres – Solid Sorbent (IC)	Sulphuric acid impregnated carbon beads	R1
Method 60	Ethylenediamine (EDA), Diethylenetriamine (DETA), Triethylenetetramine (TETA) (HPLC/UV)	NITC coated XAD-2 tube	R1
In-house method	Piperazine (HPLC/UV)	NITC coated XAD-2 tube	R2
Method PV 2018	Diethanolamine (HPLC/UV)	NITC coated XAD-2 tube	R1
Method PV 2111	Ethanolamine (HPLC/UV)	NITC coated XAD-2 tube	R1
Method PV 2145	2-Amino-2-Methyl-1-Propanol (AMP) (HPLC/UV)	NITC coated XAD-2 tube	R1

Amides			
In-house method	Formamide (GC/NPD)	Silica gel (uncoated) tube	R2
Method 2084	Acetamide (GC/NPD)	Silica gel (uncoated) tube	R2
Aldehydes			
Method 52	Acrolein and Formaldehyde (GC/NPD)	2-HMP coated XAD-2 tube	R3
Method 68	Acetaldehyde (GC/NPD)	2-HMP coated XAD-2 tube	R3
US EPA (United States Environmental Protection Agency)			
Nitrosamines			
Method TO-7	Method for the Determination of N-Nitrosodimethylamine in Ambient Air using Gas Chromatography (GC/EI-MS)	Thermosorb/N cartridge	R3
Method 521	Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionisation Tandem Mass Spectrometry (GC/CI-MS/MS)	Aqueous collection	R1
Method 607	Nitrosamines (GC/NPD) Appendix A, Part 136: Methods for Organic Chemical Analysis of Municipal and Industrial Wastewater	Aqueous collection	R3
Method 1625C	Semivolatile Organic Compounds by Isotope Dilution GC/EI-MS	Aqueous collection	R2
Method 8070A	Nitrosamines by Gas Chromatography (GC/NPD)	Aqueous collection	R3
Method 8270D	Semivolatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/EI-MS)	Aqueous collection	R3

Amines, Amides			
Method 1666	Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/EI-MS	Aqueous collection	R3
Method 1671	Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID	Aqueous collection	R3
Aldehydes			
Method TO-5	Method for the Determination of Aldehydes and Ketones in Ambient Air using High Performance Liquid Chromatography (HPLC/UV)	DNPH impinger	R2
Method TO-11A	Determination of Formaldehyde in Ambient Air using Adsorbent Cartridge followed by High Performance Liquid Chromatography (HPLC/UV). Active Sampling Methodology	DNPH cartridge	R1
Method 554	Determination of carbonyl compounds in drinking water dinitrophenylhydrazine derivatization and high performance liquid chromatography (HPLC/UV)	Aqueous collection	R1
Method 556	Determination of carbonyl compounds in drinking water by pentafluorobenzylhydroxyamine derivatization and capillary gas chromatography with electron capture detection (GC/ECD)	Aqueous collection	R3
Method 0011	Sampling for Selected Aldehyde and Ketone Emissions from Stationary Sources	DNPH impinger	R1
Method 0100	Sampling for Formaldehyde and Other Carbonyl Compounds in Indoor Air	DNPH cartridge	R2
Method 8315A	Determination of Carbonyl Compounds by High Performance Liquid Chromatography (HPLC/UV)	DNPH treatment	R1

GLOSSARY

AMP	2-amino-2-methyl-1-propanol
APCI	Atmospheric pressure chemical ionisation
APHA	American Public Health Association
AWEF	American Water Environment Federation
AWWA	American Water Works Association
CARB	California Air Resources Board
CCM	CO_2 Capture Mongstad
CI-MS	Chemical ionisation mass spectrometry
CISA	Carbon beads impregnated with sulphuric acid
DAD	Diode array detector
DEA	Diethanolamine
DETA	Diethylenetriamine
DMA	Dimethylamine
DMF	Dimethylformamide
DNPH	2,4-dinitrophenylhydrazine
EDA	Ethylenediamine,
FDA	Food and Drug Administration (US)
EA	Ethylamine
EC	Electrochemical (detection)
ECD	Electron capture detector
EDA	Ethylenediamine (1,2-diaminoethane)
EI-MS	Electron impact mass spectrometry
ESI	Electrospray ionisation
ESI-MS	Electrospray ionisation mass spectrometry
FPD	Flame photometric detector
GC	Gas chromatograph or gas chromatography
GC/CI-MS	GC utilising chemical ionisation mass spectrometry
GC/CI-MS/MS	GC utilising chemical ionisation with tandem mass spectrometers
GC/ECD	GC utilising an electron capture detector
GC/EI-MS	GC utilising electron impact mass spectrometry
GC/FID	GC utilising a flame ionisation detector
GC/FPD	GC utilising a flame photometric detector
GC/MS	GC utilising a mass spectrometer analyser
GC/MS/MS	GC utilising tandem mass spectrometers
GC/NCD	GC utilising a nitrogen chemiluminescence detector

GC/NPD	GC utilising a nitrogen phosphorous specific detector
GC/TEA	GC utilising a thermal energy analyser
GC/TSD	GC utilising a thermionic sensitive detector
2-HMP	2-(hydroxymethyl)piperadine
HPLC	High performance (or pressure) liquid chromatograph(y)
HPLC/UV	HPLC utilising a ultraviolet absorbance detector (UV/Visible detector)
HPLC/DAD	HPLC utilising a diode array detector
HPLC/TEA	HPLC utilising a thermal energy analyser
HS	Headspace
HSE	Health and Safety Executive (UK)
IARC	International Agency for Research on Cancer (WHO)
IC	Ion chromatography
INRS	Institute National de Reserche et de Securite (France)
ISE	Ion selective electrode
JIS	Japanese Industrial Standard
LC	Liquid chromatograph or liquid chromatography
LC/EC	Liquid chromatography utilising electrochemical detection
LC/ESI	LC utilising an electrospray ionisation source
LC/ESI-MS	LC utilising electrospray ionisation mass spectrometry
LC/APCI	LC utilising an atmospheric pressure chemical ionisation source
LC/API	LC utilising an atmospheric pressure ionisation source (both ESI and APCI are forms of an API source)
LC/API-MS	LC utilising atmospheric pressure ionisation mass spectrometry
LC/MS	LC utilising a mass spectrometer
LC/MS/MS	LC utilising tandem mass spectrometers
LC/TEA	LC utilising a thermal energy analyser
LLLME	Liquid-liquid-liquid microextraction
LPME	Liquid-phase microextraction
MDHS	Methods for the Determination of Hazardous Substances (UK)
MDEA	*N*-Methyldiethanolamine
MDL	Minimum detection limit
MEA	Monoethanolamine
MMA	Monomethylamine
MS	mass spectrometer or mass spectrometry
MS/MS	tandem mass spectrometer(y)
NBD-Cl	7-chloro-4-nitrobenzo-2-oxa-1,3-diazole
NCD	Nitrogen chemiluminescence detector
NDMA	*N*-nitrosodimethyamine

NDEA	*N*-nitrosodiethylamine
NDBA	*N*-nitrosodi-n-butylamine
NDELA	*N*-nitrosodiethanolamine
NDPA	*N*-nitrosodi-n-propylamine
NDPhA	*N*-nitrosodiphenylamine
NIOSH	National Institute for Occupational Safety and Health (US)
NITC	1-naphthylisothiocyanate
NMEA	*N*-nitrosomethylethylamine
NMor	*N*-nitrosomorpholine
NMPhA	*N*-methylphenylamine
NMR	Nuclear magnetic resonance
NPD	Nitrogen phosphorous detector, also NSD (nitrogen selective detector)
NPyr	*N*-nitrosopyrrolidine
NPip	*N*-nitrosopiperidine
NPz	*N*-Nitrosopiperazine
OPA	*o*-phthaldehyde
OSHA	Occupational Safety and Health Administration (US Dept. of Labour)
PAH	Polyaromatic hydrocarbons
PCC	Post combustion capture
PFBHA	*o*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine
PIP or PIPA	Piperazine (1,4-diethylenediamine). Also PZ Note PIP is also Piperidine (pentamethyleneamine)
PTFE	Polytetrafluoroethylene (Teflon)
PTV	Programmed Temperature Vaporising (inlet system)
PZ	Piperazine (1,4-diethylenediamine)
Q-TOF	Quadrupole time-of-flight mass spectrometer
SIM	Selected ion monitoring, in mass spectrometry
SPE	Solid phase extraction
SPME	Solid phase micro extraction
TEA	Thermal energy analyser
TETA	Triethylenetetramine
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TOF	Time-of-flight mass spectrometer
UCMR 2	Unregulated Contaminant Monitoring Rule (US EPA 2010)
US EPA	United States Environmental Protection Agency
WHO	World Health Organisation
XAD-2, XAD-7	Crosslinked polystyrene copolymer resin

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