UNIVERSITY OF TARTU

Faculty of Science and Technology

Institute of Chemistry

Sander Sannik

VALIDATION OF THE GAS CHROMATOGRAPHIC METHOD FOR DETERMINATION OF VOLATILE ORGANIC COMPOUNDS (VOCs) IN INDUSTRIAL WORKPLACE AIR

Master's Thesis

Supervisor: Ivo Leito, PhD

Tartu 2013

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Abbreviations

VOC	Volatile organic compound
VVOC	Very volatile organic compound
SVOC	Semi-volatile organic compound
POM	Particulate organic matter
OHSA	Occupational Health and Safety Act
EU	European Union
EC	European Council
EEC	European Economic Community
REACH	Registration, Evaluation and Authorisation of Chemicals
CAS	Chemical Abstract Service
ISO	International Organization for Standardization
GUM	Guide to the expression of uncertainty in measurement
QC	Quality control
QA	Quality assurance
PT	Proficiency testing
GC	Gas chromatography
FID	Flame ionisation detection/detector
MSD	Mass spectrometric detection
ECD	Electron capture detection
HPLC	High-performance liquid chromatography

LoD	Limit of Detection
LoQ	Limit of Quantitation
CRM	Certified reference material
LRM	Laboratory reference material
CS_2	Carbon disulfide
RMS	Root mean squared
S/N	Signal-to-noise ratio
D	Desorption efficiency
A	Adsorption efficiency
R	Recovery
IARC	International Agency for Research on Cancer
NIOSH	National Institute of Occupational Safety and Health

1. Introduction

Organic pollutants, especially volatile organic pollutants (VOCs), are an important group of chemical pollutants that are one of the main causes of indoor and outdoor air pollution problems. Some of them may cause short- and long-term adverse health effects. Like other air pollutants, one of the most significant characteristics of VOC exposure is the great variability of the concentration levels in both occupational and non-occupational (environmental) settings. The highest VOCs levels have been observed in industrial settings.

The Occupational Health and Safety Act (OHSA) of Estonia, states that the physical, chemical, biological, physiological and psychological agents must not endanger the life or health of the employee or any other person present in the workplace. The parameters of the chemical exposure in the workplace must not exceed the national occupational exposure limit values set by the regulation established by government. The OHSA also states that employer must conduct occupational risk assessment, which will identify occupational hazards, if necessary, measure the values of these parameters and assess the risks to health and safety of workers.

When a customer commissions analytical work from a laboratory, it is assumed that the laboratory has a degree of expert knowledge that the customer does not have themselves. The customer expects to be able to trust results reported and usually only challenges them when a dispute arises. Thus the laboratory and its staff have a clear responsibility to justify the customer's trust by providing the right answer to the analytical part of the problem, in other words results that have demonstrable ''fitness for purpose''. International Standard ISO/IEC 17025 states that: „Laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use.''

The aim of this work was to set up and validate the analytical method for determination of volatile organic compounds (toluene, styrene, orto-, para- and meta-xylene) in industrial workplace air. The method is based on International Standard – ISO 16200-1:2001 and during the method validation, different experimental tests with calibration and reference standard

solutions were conducted to characterise the important method performance parameters – confirmation of identity, selectivity, linear and working ranges, limit of detection and quantitation, recovery, trueness, precision and measurement uncertainty.

For the purpose of recovery experiments and assessment of method LOD and LOQ, trueness, precision and measurement uncertainty, an experimental in-house setup was constructed for the preparation of laboratory reference materials. The reference materials were prepared by spiking a specially designed T-piece with reference solutions while pumping air through the T-piece followed by a sorbent tube used for sampling. As a quality control implementation, a control R-chart was designed and will be used during the routine use of this validated method.

2. Literature overview

2.1 Volatile organic compounds (VOCs)

Organic pollutants, especially volatile organic compounds (VOCs), are an important group of chemical pollutants that are one of the main causes of indoor and outdoor air pollution problems. They evaporate easily at room temperature, emitted as gases from certain solids or liquids (e.g. organic solvents). VOC means any compound of carbon, excluding carbon monoxide, carbon dioxide, carbonic acid, metallic carbides or carbonates, and ammonium carbonate, which participates in atmospheric photochemical reactions. In the European Union (EU), a common definition is that VOCs are organic compounds with a vapour pressure greater than 10 Pa at 20 °C. This means that their composition makes it possible for them to evaporate under normal indoor atmospheric conditions of temperature and pressure. The higher the volatility (lower the boiling point), the more likely the compound will be emitted from a product or surface into the air. VOCs typically detected in indoor air belong mostly to 9 groups of compounds, which most of them are used as solvents: alkanes, cycloalkanes and alkenes, aromatic hydrocarbons, halogenated hydrocarbons, terpenes, aldehydes, ketones, alcohols and esters. World Health Organization (WHO) has classified VOCs based on their boiling points as following [1-8]:

- very volatile organic compounds (VVOCs), bp = < 0°C ... 100°C
- volatile organic compounds (VOCs), bp = 50°C ... 260°C
- semi-volatile organic compounds (SVOCs), bp = 240°C ... 400°C
- particulate organic matter (POM), bp = > 380°C

This classification, based on the boiling point, takes into account aspects of the analysis, especially gas chromatography. VOCs give rise to concern on both local and global scales because of their important roles in photochemical reactions and their toxic or mutagenic impact on human and other organisms. Some of them may cause short- and long-term adverse health effects. Key signs or symptoms associated with exposure to VOCs at low or moderate concentrations in air include eye irritation, nose and throat discomfort, allergic skin reaction, headache, nausea, fatigue, dizziness (vertigo) or euphoria, while higher levels may lead to anaesthesia, cardiovascular and respiratory diseases and even death. Damage caused by long-

term exposure to the Central Nervous System may include cognitive and emotional deficits as well as overall chronic brain dysfunction. Toxic effects of VOCs were reported to harm the liver, kidney and skin. In addition, according to International Agency for Research on Cancer (IARC), there is sufficient evidence from both human and animal studies to believe that some VOCs have carcinogenic and mutagenic effects on living organisms and human health [1-4, 6, 9].

Like other air pollutants, one of the most significant characteristics of VOC exposure is the great variability of the concentration levels in both occupational and non-occupational (environmental) settings. The problem of health risk resulting from exposure to VOCs present in the workplace is very important for physicians, employers, the local government and workers. The highest VOCs levels have been observed in industrial settings. The relationship between adverse healt effects and exposure to VOCs was first recognised in the chemical industry, where there were high concentrations of a great number of compounds. For instance, in the USA, the National Institute of Occupational Safety and Health (NIOSH) estimated that in the late 1980s about 100 000 workers were likely to have some degree of toluene exposure. About 140 000 individuals have potential exposure to xylenes during their work. So it is a very important problem, considering the number of people exposed to VOCs. Common exposures to VOCs involve workers at many different industry areas, e.g spray painting, wood based, metals or other. Oils, gasoline, industrial solvents, paints and dyes are the major sources of VOCs in the workplace. High temperature and improper manufacturing or operational practice causes rapid evaporation of liquid organics into air. Lack of efficient administrative or engineering pollution control brings high levels of VOCs in the workplace within a short time. Workers are exposed to VOCs by inhaling the contaminated air, which is the dominant route of VOC exposure. The health effects depend on the specific composition of the VOCs, the concentration, and the frequency and length of exposure. The concentration of a VOCs in the space of a workplace varies with time over both short and long periods. Moreover, workers move in varying patterns through an environment where the VOC concentration varies within location, and the actions of the workers themselves may cause the concentration to vary [5, 7, 9, 10].

2.2 Regulations for VOC contents in workplace air in the EU and in the Republic of Estonia

The concern about the uncontrolled production, emission and use of many chemical substances and the lacking information on their environmental and health effects has increased in the EU during the last decade. In this way, the aim of Registration, Evaluation and Authorisation of Chemicals (REACH) system that came into force in June 2007 is to protect human health and the environment from the impact of more than 34 millions of chemical substances registered to the Chemical Abstract Service (CAS). REACH places a great responsibility on industry to manage the risks that chemicals may pose to the human health and surrounding environment. An employer following REACH regulation must also meet the requirements of European Union Council Directive 98/24/EC of 7 April 1998. The objective of this directive is to lay down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents. According to this directive, every EU Member state must establish a national occupational exposure limit value for any chemical agent for which an indicative or binding limit value is established at EU Community level, taking into account the Community limit value, determining its nature in accordance with national legislation and practice [2, 11,12].

The paragraph 5 of the Chemicals Act (law of Estonian Parliament of 6 May of 1998) states: dangerous chemicals are chemicals that can be harmful to human health, surrounding environment or property. The handling of dangerous chemicals and materials containing such chemicals is regulated by the Chemicals Act and the Occupational Health and Safety Act. The requirements for the use of dangerous chemicals and materials containing such chemicals has been established by the regulation of Government of Estonia: Regulation No. 105 ,,The Occupational Health and Safety Requirements for the Use of Hazardous Chemicals and the Materials Containing These Chemicals'' of 20 March of 2001, which is again based on the European Union Council Directive 98/24/EC of 7 April 1998. The Occupational Health and Safety Act of Estonia, paragraph 3, states that the physical, chemical, biological, physiological and psychological agents must not endanger the life or health of the employee or any other person present in the workplace. The parameters of the chemical exposure in the workplace must

not exceed the national occupational exposure limit values. The occupational exposure limit value is the average value of the measured exposure parameter in a unit of time, which does not endanger employee's health in an 8-hour workday (of a 40-hour workweek). Limit values are mostly set for reference periods of 8-hour, but can also be set for shorter periods (15-minute). The national chemical occupational exposure limits are established by the regulation of government of Estonia: Regulation No. 293 ,,Chemical Occupational Exposure Limits'' of 18 September of 2001, which have established binding or indicative exposure limits from the European Union Directives 91/322/EEC, 2000/39/EC, 2006/15/EC and 2009/161/EU to implement the Directives 80/1107/EEC and 98/24/EC [11,13-15, 31].

The Occupational Health and Safety Act of Estonia, paragraph 13, states that the employer must conduct occupational risk assessment, which will identify occupational hazards, if necessary, measure the values of these parameters and assess the risks to health and safety of workers. A new risk assessment must be organized everytime when the conditions of a workplace change, tools or technology is replaced or upgraded, if there is new data available about the effects of the exposed chemicals on human health, if the risk level compared to the initial level has changed after an accident or dangerous situation or if the occupational physician has discovered a new work-related illness during a medical health check [13].

2.3 Measurement of occupational chemical exposures

Occupational chemical exposure is the condition of being subjected through employment to a chemical agent. Exposure to a chemical agent is typically the contact of that agent with the outer boundary of a subject, such as the respiratory system, skin or digestive system. In occupational hygiene, the most concerned exposure is through the respiratory system. Exposure assessments are used to investigate complaints of symptoms in workplaces, and, for this purpose, the investigator may make measurements of symptomatic and control populations. Another use for exposure assessment includes determining the need for, and effectiveness of engineering controls, in which case measurements are made before and after implementation or changes in the control technology. Perhaps the most common motivation for assessments is the need to support allegations of non-compliance with regulations and standards covering exposure limits.

Typically, measurements are targeted using professional judgement to those considered to have the highest exposures. Since workplace contamination can vary significantly both in time and space, close attention must be paid to monitoring the route of exposure as close to the worker as possible. For airborne contamination measurements, these should be made as close as possible to the breathing zone. Breathing zone is defined as space around the nose and mouth from which breath is taken. Technically the breathing zone corresponds to a hemisphere (generally accepted to be 30 cm in radius) extending in front of the human face, centered on the mid point of a line joining the ears. The base of the hemisphere is a plane through this line, the top of the head and the larynx. Nevertheless, dramatic differences between exposures measured at different points over the head and upper torso may be observed if the atmosphere is at all heterogeneous, as is frequently the case for vapour exposures from point sources [14, 16].

2.4 Analytical methods for VOC measurements in indoor air

There are three basic approaches for analysis and determination of VOCs in indoor air. These differ with regard to the amount of work involved and the degree of information they provide. The simplest way is to use a chemical detection system which does not separate the mixture into its individual components. This principle is used in direct-reading instruments. Direct-reading instruments are easy to use. They are portable and provide a real-time signal which makes it possible to detect rapid concentration changes. As the instruments are calibrated with only one compound, the signal represents all compounds of the mixture as an equivalent of this compound. The output signal gives no information about the qualitative composition of the mixture. In a more elaborate procedure the components of a chemical mixture are separated, and the approach is then to sum the instrumental responses for the individual compounds, although no identification is accomplished. Following the third approach, the constituents of the mixture are separated to permit an identification of individual compounds [17].

In many cases the information obtained from direct-reading instruments is insufficient because details are needed on individual organic compounds. To fulfill this need, the chemical mixture has to be separated into its constituents. Most VOC analyses of indoor air are carried out using sampling on a sorbent and subsequent separation by gas chromatography (GC). However, if

special attention is paid to specific classes of VOCs, analytical techniques other than GC may be used. As an example, aldehydes are frequently determined using high-performance liquid chromatography (HPLC). Still, GC is by far the most common technique applied to determine VOCs in air. VOCs analysis, whether in a gaseous, liquid or solid matrix, usually starts with pre-concentration of VOCs. Sampling and pre-treatment end up with target VOCs in different physical states. Being gaseous, dissolved in a liquid, trapped cryogenically or adsorbed on a solid material, VOCs have to be introduced into the GC for separation. Injection of liquid or gaseous samples is typically carried out by syringes and sample loops, employing on-column, split and splitless injection. The proper selection of the column as well as the temperature program are crucial as they influence the number of VOCs that can be identified by retention times or subsequent mass spectrometric analysis. VOCs are typically separated on capillary columns, which are commercialised under different names, e.g. AT-1, EC-1, DB-1, BP-1, HP-1, OV-1, SPB-1 and MXT, for 100% polydimethylsiloxane. In most applications, separation of VOCs is based mainly on the interaction with the stationary phase, since interactions with mobile phases, such as He, N_2 or H_2, are negligible. Capillary GC analysis of VOCs typically employs FID (flame-ionisation detection), MSD(mass-spectrometry detection) or ECD (electron-capture detection). FID is the most common detector used for VOCs because it detects a very large number of VOCs and is very stable and robust. In the FID, an organic compound is burned in a hydrogen flame giving rise to ions which are attracted to a collector electrode. The resulting electric current is amplified and recorded. The intensity of the signal depends primarily on the number of carbon atoms of the molecule, but to some extent it is also influenced by the character or structure of the chemical. Therefore, the same amount of molecules of two different VOCs with the same number of carbon atoms can give rise to two different signals [2, 8, 17-18].

2.5 Sampling and sample preparation of VOC air samples

Air is a complicated analysis object. It is a heterogeneous system composed of gases, liquid droplets and solid particles and its composition can be affected by meteorological conditions, diffusion, and reactivity. Therefore, sampling is crucial in air analysis. Sampling procedure must allow representative samples to be taken, avoiding any variation in their composition. The most common techniques used to sample and to preconcentrate VOCs in air are sampling of whole air in special recipients or collection onto solid adsorbents. Selecting the right method or combination of methods may depend on the compounds of interest, expected concentration range, required sensitivity, accuracy and precision, selectivity, presence of interferences, portability and cost [19].

Adsorptive enrichment on solid adsorbents is a technique often used to combine sampling with preconcentration and is a well-established sample preparation technique for VOCs in air. Sampling can be done either passively or actively. Depending on which alternative is chosen, the sampling time will differ: whereas active sampling generally extends over periods of minutes to hours, passive sampling is mostly covering hours or days. Active sampling consists of pumping a measured volume of air containing gas and vapour molecules through few centimeters long and a few millimeters wide sorbent tube that contains sorbent bed. The type of sorbent used for sampling depends on the nature of the VOC mixture studied. Primarily, porous polymers or charcoal-type sorbents are used. In the case of charcoal, the sorbent section contains approximately 100 mg of charcoal and the back-up section approximately 50 mg. The sections are separated and their contents are held in place with an inert material; for example glass wool plugs (preferably silanised). Small battery-powered air pumps are attached to the belts of workers and the inlets of the pumps are connected by flexible tubing to the sorbent tube, which is attached to the lapel of the worker's shirt, or some equivalent point near to the mouth or nose (breathing zone). The pumps pull air at a fixed, calibrated flowrate through the sorbent tube. At the end of the designated sampling period the pump is switched off and the start and stop time and flow-rate are recorded. Typically the flow-rate has been calibrated at least at the beginning and end of the sampling period, if not more often, and so the total volume of air sampled can be recorded. Once the VOCs are collected on the sorbent, the sample is transported to the laboratory for analysis. The procedure for transferring the pollutants from the sorbent to the separation and

identification instruments has a strong influence on the sensitivity of the overall analytical method [16-17, 19-20].

Collecting gases and vapours is only the first step in analysis. The second step is to recover the collected species in a form that is presentable to an analyzer. There are essentially two methods for the sample transfer: solvent extraction of the trapped VOCs from the sorbent and injection of an aliquot of the extract into a gas chromatograph or thermal desorption of the adsorbed VOCs from the sorbent into the flow of a pure carrier gas. Solvent extraction allows longer sorbent beds, higher flow rates and larger total-sample volumes than thermal desorption. Furthermore, samples can be analyzed repeatedly, and no expensive equipment is required. However, the sample is diluted, and can be contaminated by the solvent. Still, usually most of the sorbents are desorbed using solvent displacement. The choice of solvent is very important, as it must be compatible with further steps of the process, especially considering the solvent molecules will outnumber the collected molecules by about 1000:1. In the case of charcoal, CS_2 has a unique combination of good penetration into pores, high heat of adsorption on charcoal, and relatively good solvation ability, at least for non-polar vapours. Additionally, it has a fast gas-chromatographic elution and low background on the flame ionization detector. These properties have made it a very popular desorbing solvent. However, it poses a serious risk to human health and the environment. Also, low boiling compounds can evaporate due to the adsorption heat released during desorption. Commonly, VOCs trapped in activated carbon are extracted by adding 1 ml of CS_2 and using ultrasonication or mechanical shaking to achieve better desorption efficiency [15-17, 19-20].

2.6 Method validation

It is internationally recognised that validation is necessary in analytical laboratories. The use of validated methods is important for an analytical laboratory to show its qualification and competency. ISO 17025 states that: „Laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use.'' When a customer commissions analytical work from a laboratory, it is assumed

that the laboratory has a degree of expert knowledge that the customer does not have themselves. The customer expects to be able to trust results reported and usually only challenges them when a dispute arises. Thus the laboratory and its staff have a clear responsibility to justify the customer's trust by providing the right answer to the analytical part of the problem, in other words results that have demonstrable ''fitness-for-purpose'' [21-23].

Method validation is a process of defining an analytical requirement, and confirming that the method under consideration has performance capabilities consistent with what the application requires. The basis of a good analysis rests on a clear specification of the analytical requirement. The latter reflects the minimum fitness-for-purpose criteria or the different performance criteria that the method must meet in order to solve the particular problem. On the one hand, the extent of validation and the choice of performance parameters to be evaluated depend on the status and experience of the analytical method. The laboratory has to decide which method performance parameters need to be characterised in order to validate the method. Characterisation of method performance is an expensive process and inevitably it may be constrained by time and cost considerations. The laboratory should do the best it can within the constraints imposed, taking into account customer requirements, existing experience of the method, and the need for compatibility with other similar methods. Often a particular set of experiments will yield information on several parameters, so with careful planning the effort required to get the necessary information can be minimised. In the end, it is implicit in the method validation process that the studies to determine method performance parameters are carried out using equipment that is within specification, working correctly, and adequately calibrated. Likewise the operator carrying out the studies must be competent in the field of work under study and have sufficient knowledge related to the work to be able to make appropriate decisions from the observations made as the study progresses. And most of all, regardless of how good a method is and how skillfully it is used, an analytical problem can be solved by the analysis of samples only if those samples are appropriate to the problem. Therefore, taking appropriate samples is a skilled job, requiring an understanding of the problem and its related chemistry [21, 23].

2.6.1 Validation parameters

2.6.1.1 Confirmation of identity and selectivity, interferences

It is necessary to establish that the signal produced at the instrumental analysis stage is only due to the analyte and not from the presence of something chemically or physically similar or arising as a coincidence. Whether or not other compounds interfere with the measurement of the analyte will depend on the effectiveness of the isolation stage and the selectivity of the measurement stage. Selectivity is a measure which assess the reliability of measurements in the presence of interferences. The selectivity of a method is usually investigated by studying its ability to measure the analyte of interest in test portions to which specific interferences have been deliberately introduced (those thought likely to be present in samples). Where it is unclear whether or not interferences are already present, the selectivity of the method can be investigated by studying its ability to measure the analyte compared to other independent methods or techniques. For analytical methods using gas GC-FID, gas chromatography with mass spectrometric detection should be used to confirm the identity of the analyte. Organic compounds which have the same or nearly the same retention time as the analyte of interest during the gas chromatographic analysis will interfere. Interferences can be minimized by proper selection of gas chromatographic colums and conditions [20-21, 23].

2.6.1.2 Scope of application, working and linear ranges

For any quantitative method, it is necessary to determine the range of analyte concentrations over which the method may be applied. At the lower end of the concentration range the limiting factors are the values of the limits of detection and/or quantitation. At the upper end of the concentration range limitations will be imposed by various effects depending on the instrument response system. Within the working range there may exist a linear response range, where the signal response will have a linear relationship to the analyte concentration. The extent of this range is established during the evaluation of the working range. Usually, multi-point (preferably 6+) calibration will be necessary. Regression calculations on their own are insufficient to

establish linearity. In addition, residual values should be calculated by performing residual analysis. Residuals represent the differences between the actual y value and the y value predicted from the regression curve, for each x value. For linearity check, a visual inspection of the line and residuals may be sufficient. If residuals, calculated by simple linear regression, are randomly distributed about the regression line, linearity is confirmed, while systematic trends indicate non-linearity. If such a trend or pattern is observed, this suggests that the data are best treated by weighted linear regression. The relationship of the instrument response to concentration does not have to be perfectly linear for a method to be effective but the curve should be repeatable from day to day [21].

2.6.1.3 Limit of detection (LoD) and limit of quantitation (LoQ)

Where measurements are made at low analyte levels, it is important to know what is the lowest concentration of the analyte that can be confidently detected and identified by the method. The importance in determining this, and the problems associated with it, arise from the fact that the probability of detection does not suddenly change from zero to unity as some threshold is crossed. For validation purpose, it is normally sufficient to provide and indication of the level at which detection becomes problematic. For this purpose the ''blank + 3s'' approach will usually be sufficient. The limit of quantitation is the lowest concentration of analyte that can be determined with an acceptable level of repeatability precision and trueness. It corresponds to the analyte concentration of sample blank value plus 5,6 or 10 standard deviations of the blank mean. Limit of detection and limit of quantitation can be distinguished at two levels, instrumental and method. The instrumental limit of detection indicates the concentration that the used instrument is capable of detecting with certain reliability. The method limit of detection indicates the concentration that can be detected with certain reliability using the analysis method under consideration. The instrumental limit of quantitation is the concentration that can be quantitatively expressed with certain reliability for the instrument used. The method limit of quantitation indicates the concentration that can be quantitatively expressed with certain reliability using the method in concern [21, 25].

2.6.1.4 Accuracy (trueness and precision)

Trueness and precision studies, which form a part of the measurement uncertainty estimate, are the most important validation criteria. Accuracy expresses the closeness of a result to a true value. Method validation seeks to quantify the likely accuracy of results by assessing both the systematic and random effects on results. Accuracy is, therefore, normally studied as two components: trueness and precision. In addition, common expression of accuracy is measurement uncertainty, which provides a single figure expression of accuracy. The trueness of a method is an expression of how close the mean of a set of results is to the true value, and also an indicator of utility and applicability of that method with real samples. Trueness is normally expressed in terms of bias. Practical assessment of trueness relies on comparison of mean results from a method with known values, that is, trueness is assessed against a reference value (conventional true value). Two basic techniques are available: checking against reference values for a characterised material or from another characterised method. To check trueness using a reference material, determine the mean and standard deviation of a series of replicate tests, and compare with the characterised value of the reference material. The ideal reference material is a certified, natural matrix reference material, closely similar to samples of interest. Clearly, the availability of such materials is limited, therefore reference materials can be prepared in-house by spiking typical materials with pure certified reference materials or other materials of suitable purity and stability. Recovery is then calculated as the percentage of the measured spike of the matrix relative to the amount of spike added to sample. The smaller the recovery, the larger the bias that is affecting the method and thus the lower the trueness. Precision is a measure of how close results are to one another, and is usually expressed by measures such as standard deviation, which describe the spread of results. The two most common precision measures are repeatability and reproducibility. They represent the two extreme measures of precision which can be obtained. Repeatability (the smallest expected precision) will give an idea of the sort of variability to be expected when a method is performed by a single analyst on one piece of equipment over a short timescale, for example when a sample is analysed in duplicate. If a sample is to be analysed by a number of laboratories for comparative purposes then a more meaningful precision measure to use is reproducibility (the largest expected precision). It may be that some in-between measure is the most useful in particular cases, for example precision

measured between different analysts, over extended timescales, within a single laboratory. This is sometimes known as intermediate precision, but the exact conditions should be stated. Both, repeatability and reproducibility are generally dependent on analyte concentration, and so should be determined at a number of concentrations and if relevant, the relationship between precision and analyte concentration should be established. Relative standard deviation may be more useful in this case because concentration has been factored out and so it is largely constant over the range of interest provided this is not too great [21, 23].

2.6.1.5 Measurement uncertainty

Customers need measurement uncertainty together with the result to make a correct decision. The uncertainty of the result is important, for example when looking at allowable (legal) concentration limits. Laboratories need it to know the quality of their measurement results and to improve the required quality. Also, evaluation of measurement uncertainty is required by Standard ISO/IEC 17025. Measurement uncertainty is a single parameter (usually expressed as a standard deviation or confidence interval) defining the range of values possible on the basis of the particular measurement result. The basis for the evaluation is a measurement and statistical approach, where the different uncertainty sources are estimated and combined into a single uncertainty estimate. A measurement uncertainty estimate takes account of all recognised effects operating on the result; the uncertainties associated with each effect are combined according to well-established procedures. An uncertainty estimate for analytical chemistry should take into account [21, 24]:

- the overall, long-term precision of the method
- possible bias and its uncertainty, including the statistical uncertainty involved in the bias measurements, and the reference material or method uncertainty.
- calibration uncertainties. As most equipment calibration uncertainties will be negligibly small by comparison with overall precision and uncertainty in the bias; this needs only to be verified.
- any significant effects operating in addition to the above.

A common way of presenting the different contributions to the total measurement uncertainty is to use a so-called fish-bone (or cause-and-effect) diagram, especially in the ISO Guide to the expression of uncertainty in measurement (GUM). ISO GUM approach may prove useful when studying or quantifying individual uncertainty components separately. But, it has been shown that in some cases this methodology underestimates the measurement uncertainty, partly because it is hard to include all possible uncertainty contributions in such an approach. A more pragmatic method is the Nordtest method. By using existing and experimentally determined quality control (QC) and method validation data, the probability of including all uncertainty contributions will be maximised. The most common ways of estimating the reproducibility within laboratory component, u(Rw), is to periodically analyse stable control samples covering the whole analytical process (one sample at low concentration level and one at high), but also unstable control samples can be used. It is very important that the estimation must cover all steps in the analytical chain starting from sample preparation and ending with the actual analysis. If the laboratory does not have access to stable control samples, the reproducibility can be estimated using analysis of natural duplicate samples. The results from the duplicate sample analysis can either be treated in an R-chart, where the difference between the first and second analysis is plotted directly, or as an R%-chart, where the absolute difference between the sample pair is calculated in % of the average value of the sample pair. The latter approach is particularly useful when the concentration varies a lot from time to time [24].

The most common ways of estimating the bias components are the use of CRM, participation in interlaboratory comparisons (PTs) and recovery tests. Sources of bias should always be eliminated if possible. According to ISO GUM approach, a measurement result should always be corrected if the bias is significant and based on reliable data such as a CRM. However, even if the bias is zero, the possible bias has to be estimated and treated as an uncertainty component. For every estimation of the uncertainty from the method and laboratory bias, two components have to be estimated to obtain u(bias) [24]:

1) the root mean square (RMS) of the bias values (as % difference from the nominal or certified value for each CRM)
2) the uncertainty of the nominal/certified value, u(Cref) or u(Crecovery)

Recovery test, for example the recovery of a standard addition to a sample in the validation process, can be used to estimate the systematic error. In this way, validation data can provide a valuable input to the estimation of the uncertainty [24].

The Nordtest uncertainty model is a simplification of the model presented in the ISO guide [24]:

$$\boldsymbol{y = m + (\delta + B) + e} \quad (1)$$

y – measurement result of a sample

m – expected value for y

δ – method bias

B – laboratory bias

e – random error at within-laboratory reproducibility conditions, Rw

$$\boldsymbol{u(y)^2 = s_{Rw}{}^2 + u(bias)^2} \quad (2)$$

$s_{Rw}{}^2$ - the estimated variance of e under within-laboratory reproducibility conditions – intermediate precision.

$u(bias)^2$ – the estimated variance of method bias and laboratory bias.

The uncertainty of the bias, u(bias) can be estimated by:

$$\boldsymbol{u(bias) = \sqrt{RMS_{bias}{}^2 + u(Cref)^2}} \quad (3)$$

$$\boldsymbol{RMS_{bias} = \sqrt{\frac{\Sigma(bias_i)^2}{n_{CRM}}}} \quad (4)$$

Measurement uncertainty should normally be expressed as U, the combined expanded measurement uncertainty, using a coverage factor k = 2, providing a level of confidence of approximately 95% [24].

2.6.1.6 Recovery, adsorption efficiency, desorption efficiency

Recovery is defined as proportion of the amount of analyte, present in or added to the analytical portion of the test material, which is extracted and eventually presented for measurement and can be expressed as follows [25]:

$$\boldsymbol{Recovery} = \frac{\boldsymbol{amount\ of\ analyte\ determined\ from\ the\ sample}}{\boldsymbol{true\ amount\ of\ analyte\ in\ the\ sample}} \times \mathbf{100}\% \qquad (5)$$

Analytical methods do not always measure all of the analyte of interest present in the sample leading to recovery values below 100%. Because the true amount of a particular analyte present in a test portion is usually unknown the above definition cannot be directly applied and instead of the true concentration some reference concentration is generally used. An appropriate range of analyte concentrations should be investigated where that is technically and financially possible, because the recovery of the analyte may be concentration-dependent. One way to determine the efficiency of extraction is to spike test portions with the analyte at various concentrations, then extract the fortified test portions and measure the analyte concentration. The inherent problem with this is that analyte introduced in such a way will probably not be held as strongly as that which is naturally present in the test portion matrix and so the technique will give an unrealistically high impression of the extraction efficiency. Alternatively it may be possible to carry out recovery studies on certified reference materials (CRMs), if suitable materials are available. Spiking recovery testing is however the most common ways of determining recovery efficiency, and it is recognised as an acceptable way of doing so, and it is less costly than using certified reference materials [10, 21].

Although complete recovery (100%) of the analyte from the sampler is most desirable, at a minimum the estimated recovery of the analyte should be greater than or equal to 75%. If recovery varies with analyte loading, results should be graphed as recovery versus loading during the validation of the method, so that appropriate correction can be made to sample results, as long as recovery is greater than 75%. Recovery values should always be established as part of method validation, whether or not recoveries are reported or results are corrected, so that measured values can be converted to corrected values as needed and vice versa [10, 25].

In the context of VOC determination in air using sorbent tubes, recovery and desorption efficiency are defined as follows [20]:

$$\boldsymbol{D} = \frac{\boldsymbol{x}_{\boldsymbol{analyte\ measured}}}{\boldsymbol{x}_{\boldsymbol{analyte\ spiked\ onto\ sorbent}}} \times \mathbf{100}\% \quad (6)$$

$$\boldsymbol{R} = \frac{\boldsymbol{x}_{\boldsymbol{analyte\ measured}}}{\boldsymbol{x}_{\boldsymbol{analyte\ spiked\ into\ LRM}}} \times \mathbf{100}\% \quad (7)$$

Desorption efficiency (*D*) is an indicator for how well the VOC analytes are desorbed from the charcoal sorbent using a desorption solvent at the sample preparation stage. Recovery (*R*), in this case, is an indicator of how well the VOC analytes are adsorbed by charcoal sorbent in the sampling stage and how well they are desorbed in the sample preparation stage, therefore containing both adsorption and desorption efficiencies. When *R* and *D* have been determined then it is possible to also assess the adsorption efficiency (*A*), by using equation [20, 33]:

$$\boldsymbol{A} = \frac{\boldsymbol{R}}{\boldsymbol{D}} \times \mathbf{100}\% \quad (8)$$

2.6.2 Quality control (QC) and quality assurance (QA)

The International Standard ISO/IEC 17025 states that: ’’The laboratory shall have quality control procedures for monitoring the validity of tests and calibrations undertaken. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results. Quality control (QC) data shall be analysed and, where they are found to be outside pre-defined criteria, planned action shall be taken to correct the problem and to prevent incorrect results from being reported ’’ [22].

In practical terms quality control describes the individual measures which relate to the monitoring and control of particular analytical operations, whereas quality assurance (QA) relates to the overall measures taken by the laboratory to ensure and regulate quality. Method validation gives an idea of a method’s performance capabilities and limitations which may be experienced in routine use while the method is in control. During the validation stage the method

was largely applied to samples of known content. Once the method is in routine use, it is used for samples of unknown content. Suitable control can be applied by continuing to measure samples of known analyte content, thus allowing the analyst to decide whether the variety of answers obtained truly reflects the diversity of samples analysed or whether unexpected and unwanted changes are occurring in the method performance [21].

Internal QC includes the use of blanks, chemical calibrants, spiked samples, replicate analyses and QC samples. The use of control charts is recommended, particularly for monitoring results from QC control samples. Control charting is a powerful and a simple tool for the daily quality control of routine analytical work. Its essence is that the laboratory runs control samples together with the routine samples in analytical run. Material of control samples can be standard solutions, real test samples, blank samples, in-house control materials and certified reference materials. Preferably the control samples go through the entire analytical procedure, including sample preparation. Different sorts of quality control may be used to monitor different types of variation within the process. QC samples, analysed at intervals in the analytical batch will indicate drift in the system; use of various types of blank will indicate what are the contributions to the instrument signal besides those from analyte; duplicate analyses give a check of repeatability. A range chart (R, r%) serves above all the purpose of repeatability control. A range chart has a central line, an upper warning limit and an upper action limit. The range is defined as the difference between the largest and smallest single result for two or more separate samples. For practical applications in analytical laboratories the R-chart mostly appears only in its simplest form, only duplicate determination (of samples to be analysed) in each analysis series. Using a routine test sample as a control sample is valuable when it is not possible to have a stable control sample. Duplicate measurements give a realistic picture of the within-run random variations for natural samples [21, 26].

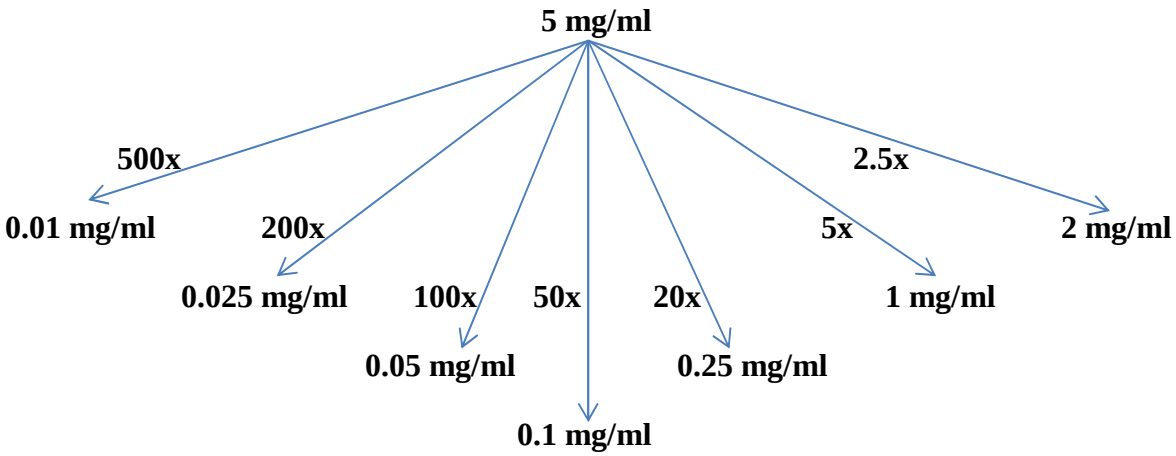
3. Experimental

3.1 Chemicals, solutions and materials

3.1.1 Calibration and reference solutions

Primary standards of orto-xylene (99.0% certified, Ehrenstorfer), para-xylene (99.0% certified, Ehrenstorfer), meta-xylene (99.5% certified, Ehrenstorfer), styrene (99.0% certified, Ehrenstorfer) and toluene (99.7% Chromasolv®, Rathburn) were used for the preparation of calibration and reference standard solutions, and for the identification of analyte peaks and determination of their retention times on chromatograms. Mixed calibration solutions containing each VOC at different concentration levels were prepared gravimetrically and the same desorption solvent solution (CS_2 with internal standard) that was used to desorb the samples was used as solvent to fill up the volumetric flasks. The primary standard solution(5 mg/ml) was prepared gravimetrically by weighing 0.125 g of each VOC's primary standard into 25 ml volumetric flask which was partially filled with desorption solvent solution. Six standard working solutions were prepared into 10 ml volumetric flasks by diluting primary standard solution to the following approximate concentration levels: 0.01, 0.025, 0.05, 0.10, 0.25, 1.00 and 2.00 mg/ml (Figure 1).

Figure 1. Preparation of calibration standard solutions from primary standard solution.



In need to prepare an in-house laboratory reference material, reference standard solutions were prepared, using cyclohexane (99.9%, HPLC grade, Sigma-Aldrich) as solvent. Primary reference standard solution (5 mg/ml) was prepared gravimetrically by weighing 0.125 g of each VOC's primary standard into 25 ml volumetric flask which was partially filled with cyclohexane solvent. The solvent used for the preparation of the reference solution had to be different than the solvent used for desorption (CS_2) to achieve a proper adsorption of the VOC analytes onto charcoal. Solvent used for spiking cannot be competitive with the analytes while spiking or with CS_2 while desorbing the analytes, meaning it needs to have worse ability to desorb the analytes. Three different solvents (heptane, methanol and cyclohexane) were tested for suitability using recovery and desorption efficiency experiments. The best results, with desorption efficiencies and recoveries near 100%, were obtained with cyclohexane. From the primary standard reference solution, a 10 times dilution was made for the preparation of the second reference standard solution (0.5 mg/ml).

For the gas chromatographic analysis, a suitable internal standard had to be found and 27 different chemical compounds available in the laboratory were tested. The criteria for the internal standard is given by Standard ISO 16200-1. Internal standard [20]:

- is not interfering with the compounds of interest (no chromatographic peak overlap)
- is not removed from the elution solvent by the sorbent
- is with average volatility compared to analytes
- is a stable compound
- is detected by FID
- is not usually found in industrial workplace air

The tested compounds were the following: acetonitrile; methyl tert-butyl ether; tetrahydrofuran; hexane; heptane; ethylbenzene; decane; acrolein; 4-hydroxy-4-methyl-2-pentanone; 2,2,4-trimethylpentane; 4-methyl-2-pentanol; methylacetate; methylisobutylketone; isobutylacetate; 2-ethyl-1-hexanol; 1,2,3 – trimethylbenzene; tetradecane; hexadecane; acetylacetone; methylmetacrylate; 3-methylstyrene; 2,3-butanediol; amylacetate; nonane; acetofenone; acrylonitrile; hexanal.

3.1.2 Laboratory reference materials (LRMs)

Since no certified reference materials (CRMs) of air contaminated with accurately known quantities of VOCs were available for purchase, laboratory reference materials (LRMs) had to be prepared using an in-house method. Six experimental setups were constructed for this purpose.

Method 1 - a 10 liter bottle was used as a container where to inject reference solutions into while letting a stream of N_2 pass through at a known flowrate (Figure 2). Reference solutions were weighed with syringe and injected into the glass container through a septum, located at the top of the container. Container was shaken for 10 times and introduced to nitrogen gas stream flow and a charcoal tube was connected to the side of the container bottle for the collection of the spiked analytes in the container.

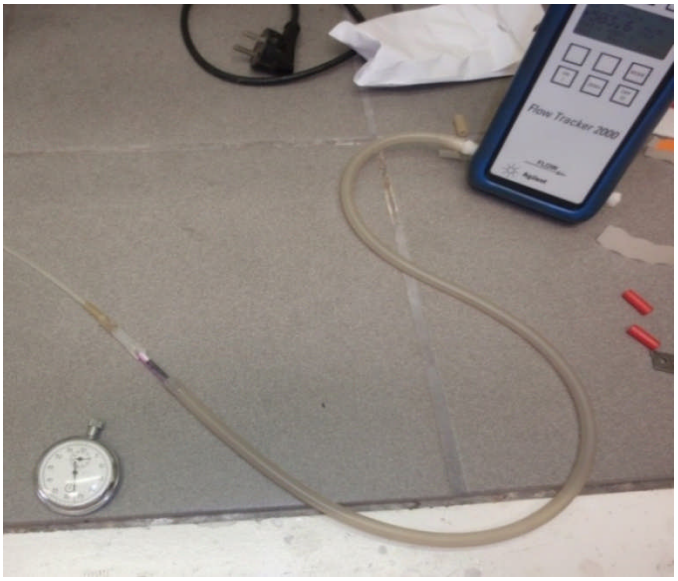
Figure 2. LRM experiment design for method 1.

Method 2 - the same design as for latter was used, but instead of letting a gas stream flow through, the air sampling pump was used to pump the spiked air out of the container at a known air flowrate (Figure 3).

Figure 3. LRM experiment design for method 2.

Method 3 – spiking of the weighed reference solution was done directly onto the charcoal sorbent tube and a gas stream of nitrogen was introduced through at a known flowrate (Figure 4).

Figure 4. LRM experiment design for method 3.

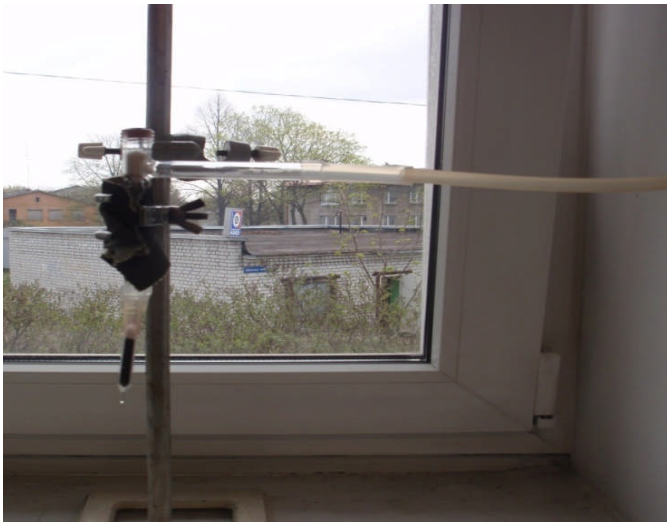


Method 4 - the same design as for latter was used, but with sampling laboratory air through the tube at a known flowrate using sampling pump (Figure 5).

Figure 5. LRM experiment design for method 4.

Method 5 – laboratory reference material was constructed using a glass T-piece (Figure 6). A plug of cotton wool was placed into the middle part of T-piece, where reference solution could be injected onto through a septum, which was placed at the one end of the T-piece. A sorbent tube was connected to the other end using plastic hosing and the third T-piece part was connected to a nitrogen gas stream with a known flowrate.

Figure 6. LRM experiment design for method 5.



Method 6 – the design was similar to latter, but instead of using a stream of nitrogen gas to flow through, the T-piece was connected vertically to sampling pump via the sorbent tube and laboratory air was pumped through the tube after injecting a weighed amount of reference solution through the septum onto the cotton wool plug (Figure 7).

Figure 7. LRM experiment design for method 6.

3.2 Sampling

Sampling of analytes (VOCs) was performed using charcoal sorbent tubes (Orbo™ 32 Small Activated Coconut Charcoal, 20/40 mesh, 100/50 mg) and air sampling pumps (SKC Aircheck Sampler, 50 – 5000 ml/min) to draw the air through the sampling tube during a 15-minute time period and at known air flowrate of about 500 ml/min to collect the analytes onto the surface of the sorbent. The accurate flowrate was measured in the beginning and in the end of every sampling period using a separate electronic rotameter (AGILENT FLOWTRACKER, 0 ml/min –

500 ml/min). The difference between the two flowrates cannot exceed 10%, or the sample can be considered as not representative and the sampling needs to be repeated [20]. Both ends of the sorbent tube were broken and connected to the sampling pump via tubing so that the back section would be nearer to pump and the arrow on the tube would be pointing downwards. Every sample was taken in two replicates. This was done for two purposes. Firstly, this was for back-up for avoiding the failure of the analysis when one of the samples is accidentally destroyed. Secondly, the difference between the results of the two replicate samples can be used to construct an R-control chart. Together with every sample, a field-blank sample was taken to account for possible contamination and impurities introduced during sampling, transportation and/or sample preparation, since it is treated similarly to real samples.

3.3 Sample preparation

Sample preparation was performed using desorption solvent solution to desorb the analytes from the sorbent tube. Desorption solvent solution was prepared gravimetrically using carbon disulfide (CS_2 – 99.9%, ReagentPlus®, Sigma-Aldrich) as a primary solvent and 2,2,4-trimethylpentane, also known as isooctane, (99.0%, Rathburn) as an internal standard. The concentration of the internal standard in the desorption solvent solution was approximately 0.1 mg/ml, staying in the middle part of the calibration range (Figure 1). The toxicity of carbon disulfide required that all preparation stages would be conducted under fume hood while wearing protection gloves.

1 ml of desorption solvent solution was placed into 2 ml GC-vial using micropipettes. Since CS_2 is a very volatile compound, pipetting had to be done in the following way: the solution pipetted was drawn in and let out of the pipette two times before performing the actual transfer of the solution at the third pipetting. The charcoal sorbent in the front and back section were placed into separate vials and analysed individually. The vials containing sorbent and desorption solvent were agitated for 30 minutes to ensure efficient desorption of the analytes. For the final measurement result, the analyte contents in both sections were summed. Vials were placed into mechanical shaker (ELMI SKYLINE Shaker DOS-10L) for 30 minutes to assure more efficient desorption. The desorbed solutions were removed from the initial vials using glass syringes (Optima 2 ml) and transferred into separate vials through microfilters (Whatman 0.45 μm PTFE)

to avoid possible clogging of GC injector by charcoal pieces or other impurities. These vials were taken to gas chromatography for subsequent instrumental analysis. When the collected samples were not analysed within 8 hours after the sampling, they were stored in a refrigerator.

3.4 Instrumental analysis

For instrumental analysis, gas chromatograph HP 6890 equipped with flame ionisation detector and HP 7683 series autosampler was used to determine the concentration of VOCs in the desorbed samples. The chromatographic conditions were the following:

Injection parameters:	1 µl, splitless, 200 °C
Oven parameters:	temperature-programmed, (50 – 280) °C, 31 minutes
Column parameters:	SPB-1, bonded poly(dimethyl siloxane), 30m×320µm×0.25µm
Carrier-gas:	N_2 with flowrate 1.8 ml/min, constant pressure at 8 psi
Detector parameters:	FID, 350 °C, hydrogen (30 ml/min) and air (300 ml/min)

Before the analysis of real samples, desorption solvent solution and field blank samples were analysed, to account for possible impurities introduced during the sampling and sample preparation stages. Field-blank sample was acceptable if the found chromatographic peak areas of VOCs of interest were smaller than 10% of the real sample peak areas [20]. Within every analysis run, two standard working solutions with different concentration levels (0.025 mg/ml and 1 mg/ml) were analysed to check if calibration curve stays within the required limits. The measured values of the standard solutions must not deviate from the initial calibration values by more than 5% [25]. Within every analysis run, one should always start with the analysis of sorbent tubes' back-section and follow with the front-section, since the back-section contains normally less or none of the VOC target analytes. This will prevent possible carry-over impurities between front- and back-section of the samples. If the back-section of sorbent tube contains more than 10% of the sample, or of any VOC component, sample needs to be discarded as unreliable, and the sampling needs to be repeated [20].

3.5 Calculation of results

All the measurement results were calculated according to following equation:

$$C = \frac{m_1 + m_2 - m_b}{R \times V} \quad (9)$$

C – concentration of analyte in the air sampled, corrected with recovery (mg/m^3 = μg/l)

m_1 – mass of analyte present in the front section of the sample (μg)

m_2 – mass of analyte present in the back section of the sample (μg)

m_b – mass of analyte present in the field-blank tube (μg)

R – recovery correction (unitless)

V – volume of sample taken (l)

The traceability of the result unit to SI has been achieved by the calibration process, as the calibration solutions used to construct a calibration curve had been prepared gravimetrically. The equipment used for validation and measurement, including analytical balances, glassware and the sampling pumps, were all appropriately calibrated.

3.6 Estimation of measurement uncertainty

For the estimation of measurement uncertainties, the Nordtest approach was used, where the systematic and random uncertainty effects obtained from the LRM recovery experiment results were combined. Since the LRM recovery experiments contained both - the sampling and analysis stage - there was no need to conduct separate experiments for the determination of sampling uncertainty. Although no uncertainty effect of the sample inhomogeneity was included into uncertainty estimation since the fluctuations of VOC concentrations in the location of space or in time were not estimated.

From the replicate measurements of LRM analysis, the standard deviation between the LRMs prepared on different days was accounted for random effects as an intermediate precision, and was defined according to the following:

$$\boldsymbol{u(R_w) = s} \quad (10)$$

R_w – reproducibility of the experiments performed on different days (intermediate precision)

s – standard deviation of the single experiments performed on different days

The results of the same replicated experiments were used to assess the systematic component, the uncertainty of bias. The systematic uncertainty components were the uncertainty of 100% recovery, uncertainty of recovery correction and uncertainty of air volume sampled. The u(bias) was calculated according to the following equation:

$$\boldsymbol{u(bias) = \sqrt{u(C_{100\%\,recovery})^2 + u(recovery\ correction)^2 + u(air\ volume\ sampled)^2}} \quad (11)$$

Since the value of 100% for recovery is not certified, but it is a spike value with own uncertainty added to LRM, the uncertainty of 100% recovery had to be estimated. Components within the uncertainty of 100% recovery include the uncertainty originating from the preparation of the reference solution u(ref.solut.prep.), which was used for spiking, and the uncertainty of the volume of this solution injected - u(volume of syringe). The calculation was performed according to the following equation:

$$\boldsymbol{u\left(C_{100\%\,recovery}\right) = \sqrt{u(ref.solut.prep.)^2 + u(volume\ of\ syringe)^2}} \quad (12)$$

The uncertainty of the reference solution contains the uncertainty of the calibration of the volumetric flask into where the solution was prepared u(calibration of vol.flask) and the uncertainty of the purity of the primary standards u(pure standard). The calculation was performed according to the following equation:

$$\boldsymbol{u(ref.solut.prep.) = \sqrt{u(calibration\ of\ vol.flask)^2 + u(pure\ standard)^2}} \quad (13)$$

The uncertainty of the syringe volume consists of the uncertainties of the precision and bias of the syringe and is calculated according to the following equation:

$$\boldsymbol{u(volume\ of\ syringe) = \sqrt{u(syringe\ precision)^2 + u(syringe\ bias)^2}} \quad (14)$$

The uncertainty of the air volume sampled was obtained from the sampling pump calibration certificate. Since, recovery correction was used in the calculation of results, the uncertainty of recovery correction estimation – u(recovery correction) – was accounted in the uncertainty budget instead of RMS_{bias}. The uncertainty of the recovery correction estimation is defined as standard deviation of the recovery experiments:

$$\boldsymbol{u(recovery\ correction) = s} \quad (15)$$

s – standard deviation of the single experiments performed on different days

The standard combined measurement uncertainty was calculated according to the following equation [24]:

$$\boldsymbol{u_c = \sqrt{u(R_w)^2 + u(bias)^2}} \quad (16)$$

And the expanded measurement uncertainty with coverage factor k = 2 was calculated according to [24]:

$$\boldsymbol{U(k = 2) = 2 \times u_c} \quad (17)$$

4. Results and discussion

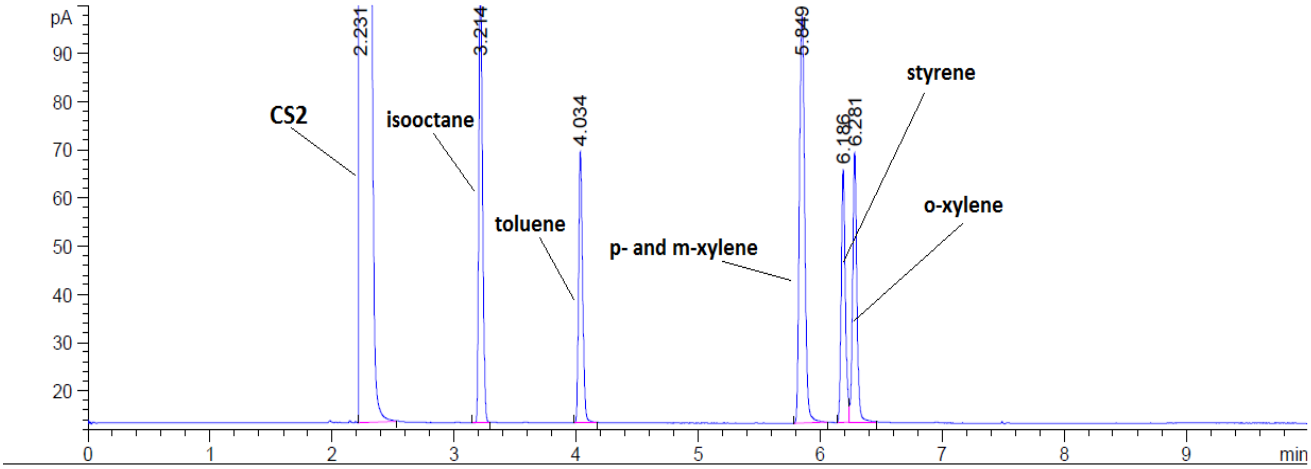
4.1 Confirmation of identity and selectivity, internal standard

A typical chromatogram of the VOCs is presented in Figure 8. Primary standards of VOCs were used for the identification of analyte peaks and determination of the retention times on chromatograms. Since the chromatographic peaks of p- and m-xylene overlap totally, their signal peak area was taken as a sum for the calculation of measurement results. This overlap was not a problem, because the national exposure limit for xylenes is given as a sum of all its three isomers (p-xylene, m-xylene and o-xylene) [15]. No other interfering compounds have been found during the validation and prior use of this method. During the method validation, a suitable internal standard had to be found and 27 chemical compounds available in the laboratory were tested for the suitability [20]. For the experiments, a drop of chemical standard was added to a GC-vial containing the calibration mixed standard solution and was analysed by gas chromatography. Many compounds were not suitable because they were either interfering with the analyte compounds by peak overlapping, had too low or too high volatility compared to analytes of interest or were found to be too probable to be found in workplace air and therefore not suitable as internal standards. 2,2,4-trimethylpentane (isooctane) complied with the criteria set by ISO 16200-1 method and was chosen as the internal standard, with retention time: t_r = 3.214. Isooctane does not interfere with the analytes, is not removed from the elution solvent by the sorbent, has an average volatility compared to analytes, is a stable compound, can be detected by FID and is usually not found in workplace air, according to the data from our laboratory [20].

The average retention times of analytes and desorption solvent were the following:

1) CS_2 – desorption solvent, t_r = 2.23
2) toluene – t_r = 4.03
3) p- and m-xylene – t_r = 5.85
4) styrene – t_r = 6.19
5) o-xylene – t_r = 6.28

Figure 8. Chromatogram for the identification of peaks and determination of retention times of VOCs.



4.2 Scope of application, linear and working ranges

The method was validated for determining 5 VOCs in industrial workplace air in the concentration range of (10 – 200) mg/m^3, except for p-and m-xylene, as their calibration curve is constructed as their sum and therefore their calibration concentrations are two times higher ranging from 20 mg/m^3 to 400 mg/m^3. For the analysis of non-industrial workplace air, method should be re-validated by extending the scope of application for lower concentrations (below 10 mg/m^3). The lower limit of the calibration range was chosen according to the concentration expected usually in industrial air, concentration found in laboratory's former testing results and according to the successful recovery results obtained with the laboratory reference material (LRM) experiments at low concentrations (see 4.4). The upper limit of the calibration range was chosen according to the national exposure limits set for the analyte VOCs in industrial workplace air and according to the usual maximum analyte concentrations tested on the same gas chromatograph which was also used for this method [15].

Each standard working solution (0.01 – 2.00) mg/ml was analysed in three replicates and using linear regression, an internal standard calibration curves were constructed for each individual VOC, except for m- and p-xylene whose calibration curve is constructed as their sum. Besides the visual linearity check, the obtained R-squared values (o-xylene: 0.9998; p- and m-xylene:

0.9998; styrene: 0.9996; toluene: 0.9997) and the performed residual analysis indicated that good linearity can be assumed for all the calibration curves within the working area (10 – 200) mg/m^3 (Figures 9 – 16).

Figure 9. Calibration curve for orto-xylene.

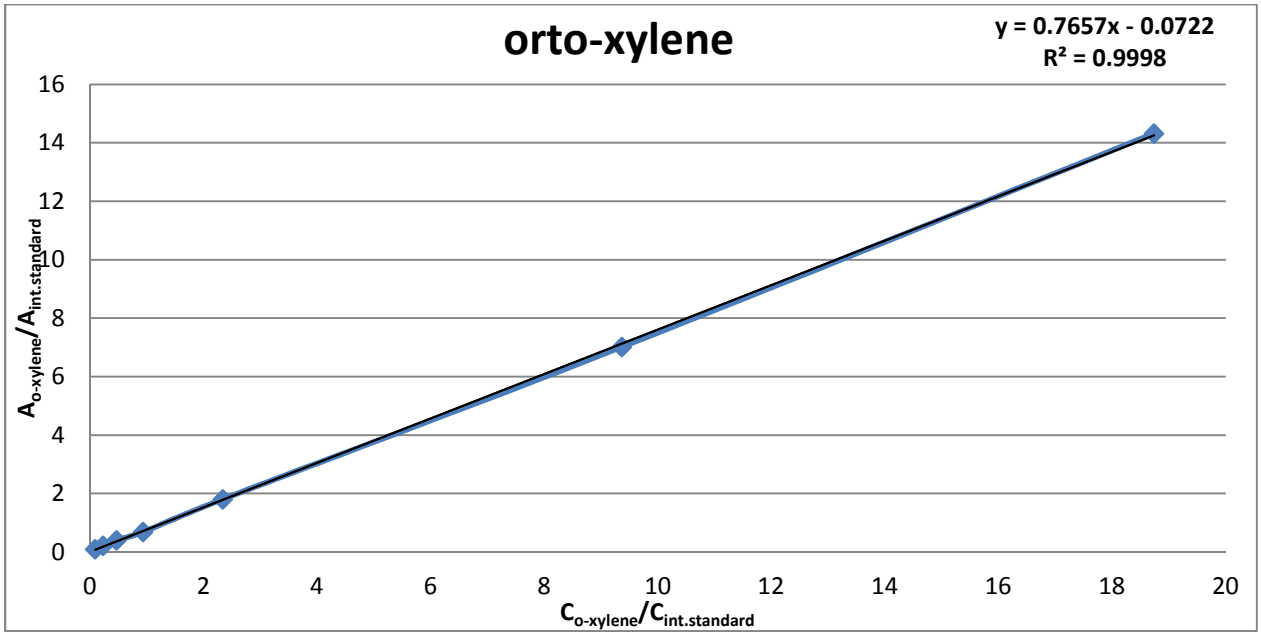


Figure 10. Residual analysis for orto-xylene.

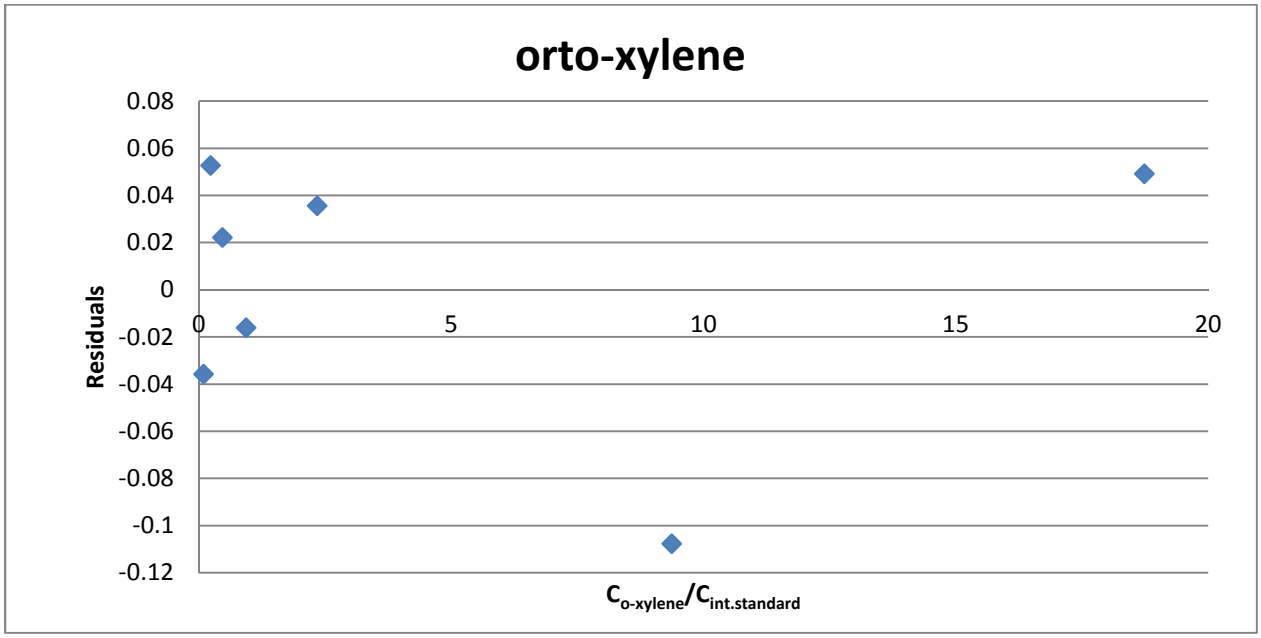


Figure 11. Calibration curve for para- and meta-xylene.

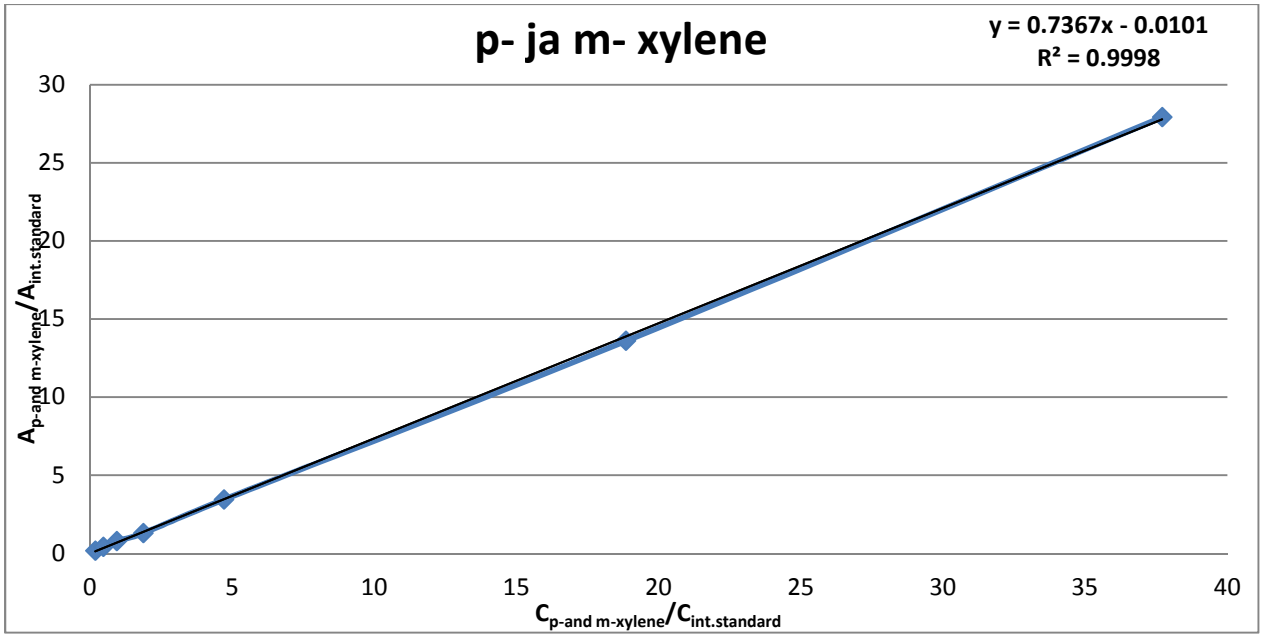


Figure 12. Residual analysis for para- and meta-xylene.

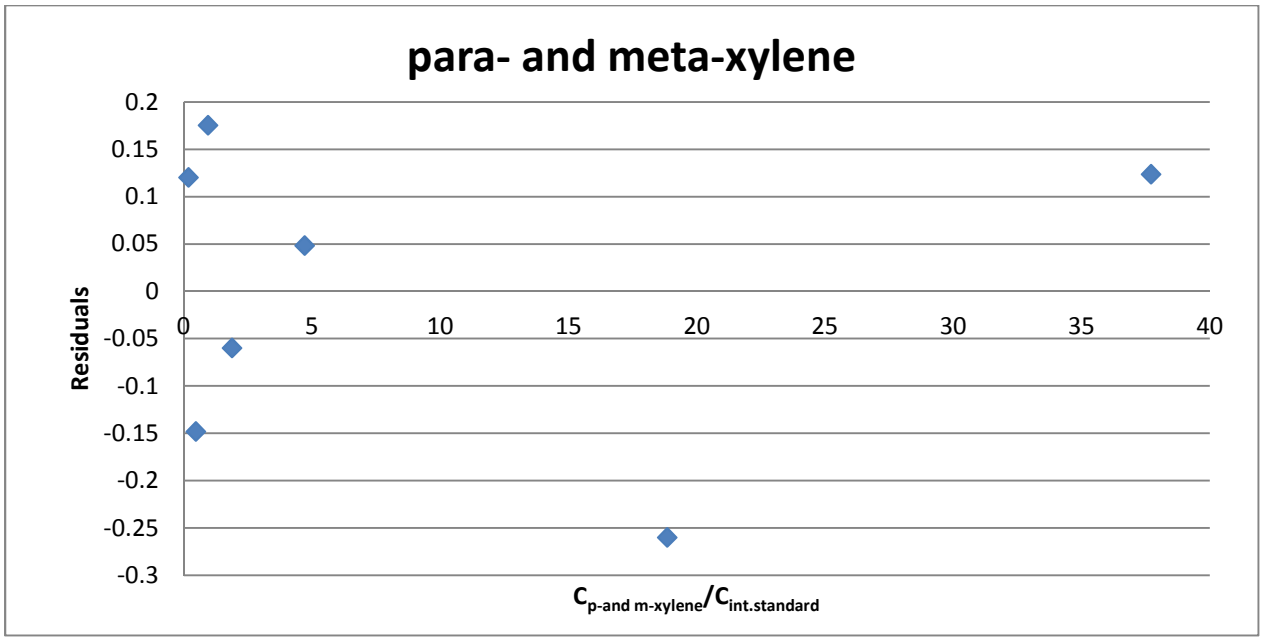


Figure 13. Calibration curve for styrene.

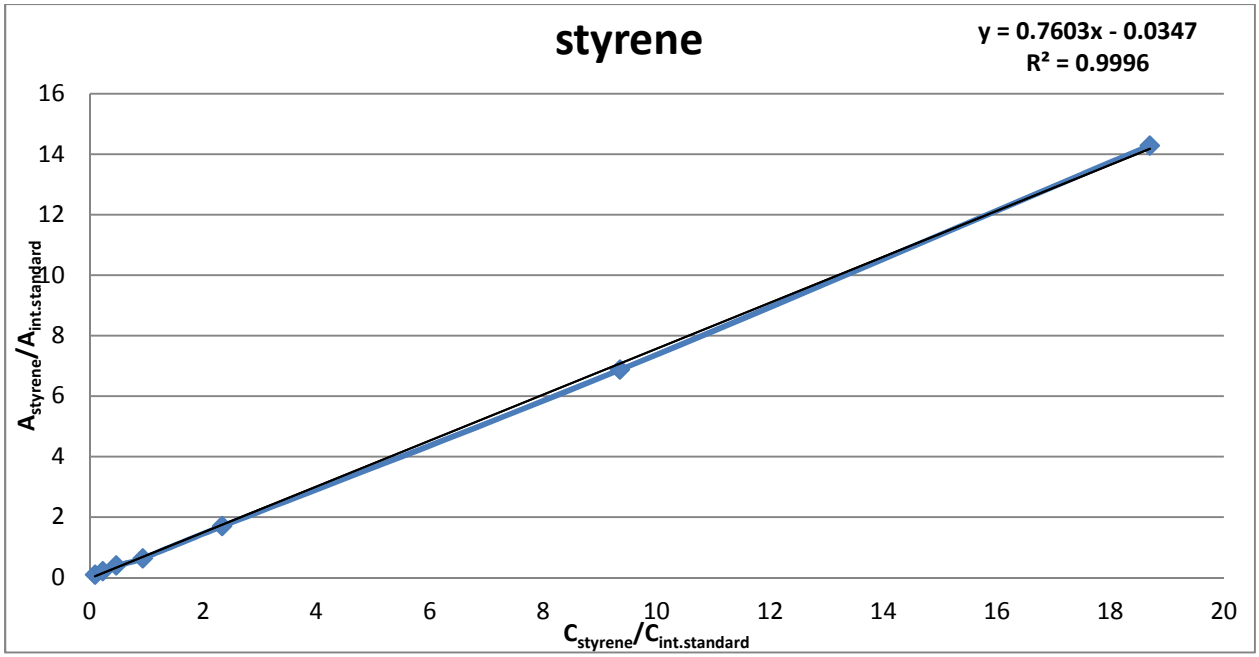


Figure 14. Residual analysis for styrene.

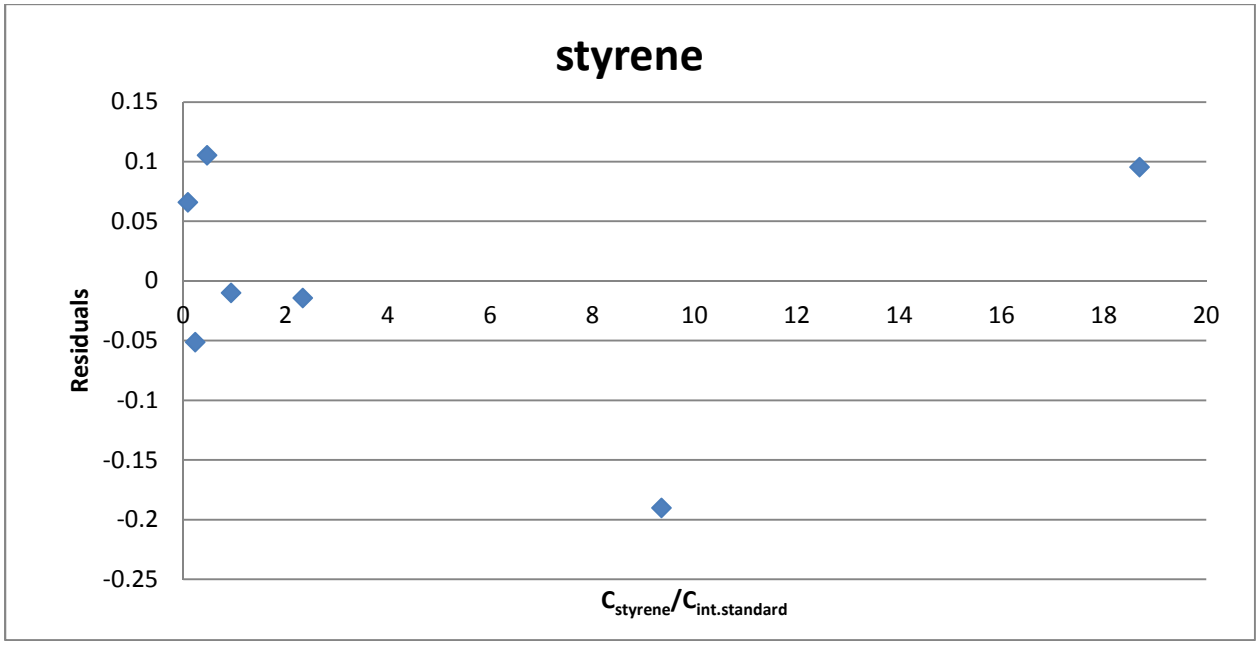


Figure 15. Calibration curve for toluene.

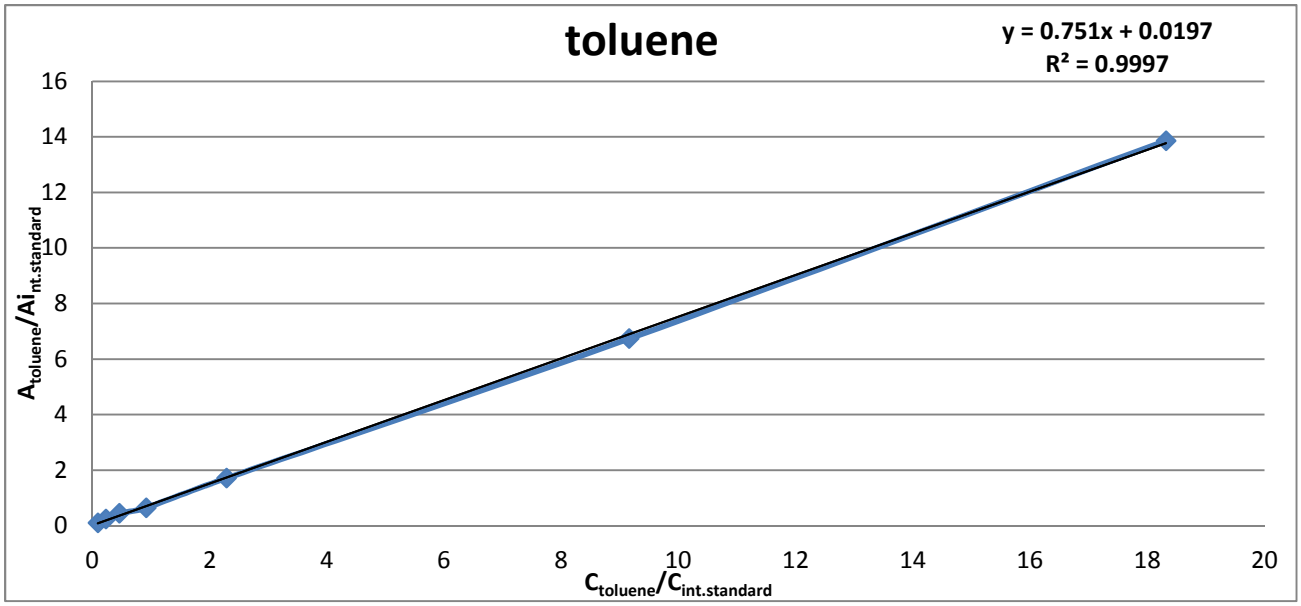
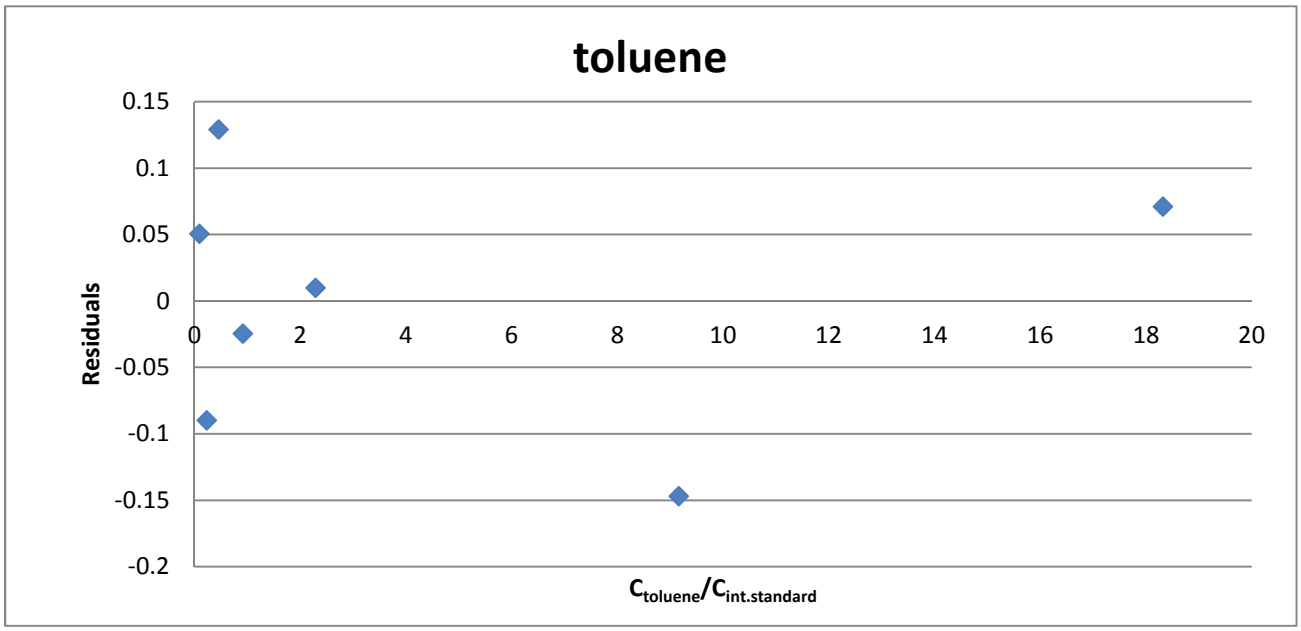


Figure 16. Residual analysis for toluene.

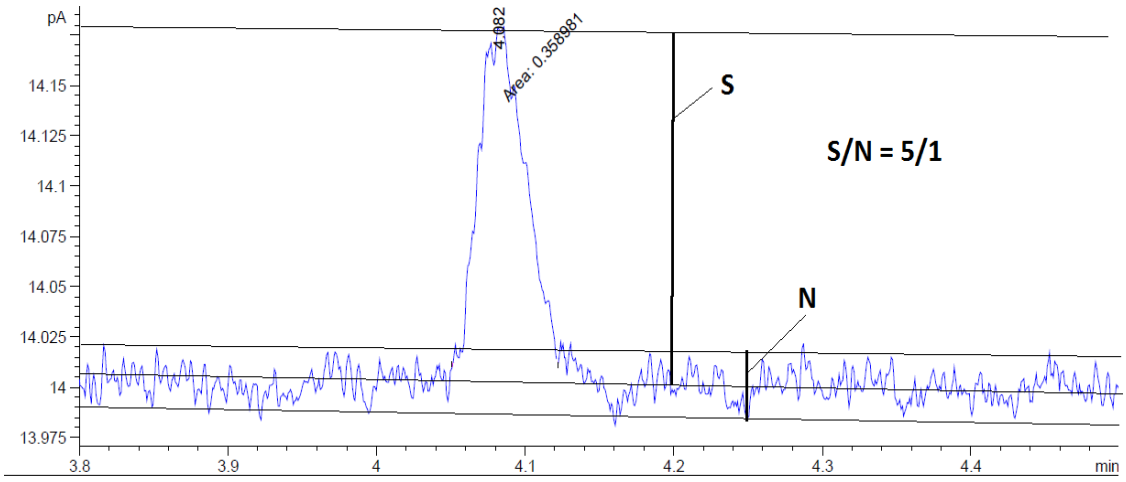


4.3 Signal-to-noise ratio (S/N), limit of detection (LoD) and limit of quantitation (LoQ)

4.3.1 Instrumental LoD and LoQ, S/N ratio

For the determination of signal-to-noise ratio (S/N) and instrumental LoD and LoQ, 20 times dilution was made from the lowest working standard solution (10 µg/ml) to get a standard solution with concentration 0.5 µg/ml and it was analysed in three replicates. Standard ISO 16200-1 requires that for this method a flame-ionisation detector, capable of detecting an injection of 0.5 ng toluene with a signal-to-noise ratio of at least 5 to 1, should be used. Injecting 1 µl of the above solution will introduce exactly 0.5 ng of the analyte. The chromatographic peak of toluene standard was used for the determination of S/N ratio and the obtained result is compatible with the ISO requirement (Figure 17) [20, 30]:

Figure 17. Chromatogram for the determination of S/N ratio of the instrument using toluene as analyte [30].



4.3.2 Method limit of detection (LoD) and limit of quantitation (LoQ)

For the determination of method LoD and LoQ, replicated experiments were conducted on different days using the LRM design method 6 (Figure 7), where 200 µl of reference solution with concentration 0.5 mg/ml was injected onto the cotton wool plug in the glass T-piece. The air flowrate and sampling time period was the same as with the real samples – 0.5 l/min during 15 minutes. Within an individual day when an experiment was conducted, a laboratory air blank was collected to account for impurities in the laboratory room.

For the determination of concentration which to use for LoD experiments, recovery experiments were conducted at several low concentrations and the concentration value of 10 mg/m^3 was found to be suitable, since all the experiments with lower concentrations gave recovery values lower than 75%, therefore being incompatible with the recovery criterion limit of 75% [25]. When comparing the obtained LoD and LoQ values (Table 1) to average VOC concentrations generally found in industrial environment according to the experience in our laboratory, they can be said to be fit for purpose, because the average concentrations of VOCs in most industries tend to be low, most lying in the range of 10 – 50 mg/m^3. In addition, it is a widespread convention for method validation criterion, that the LoD of the analyte should be approximately 10 times lower than the respective maximum permissible limit [25, 27]. This criterion is approximately fulfilled for all the VOC analytes in this work, since the corresponding national exposure limits are [15]:

1) Xylenes: 450 mg/m^3 (STEL, 15-min), 200 mg/m^3 (TWA, 8-h)
2) Toluene: 384 mg/m^3 (STEL, 15-min), 192 mg/m^3 (TWA, 8-h)
3) Styrene: 200 mg/m^3 (STEL, 15-min), 90 mg/m^3 (TWA, 8-h)

Table 1. Instrumental and method LoDs and LoQs of VOCs.

VOC	Instrumental LoD mg/m^3 X_{mean} + 3s	Instrumental LoQ mg/m^3 X_{mean} + 10s	Method LoD mg/m^3 X_{mean} + 3s	Method LoQ mg/m^3 X_{mean} + 10s
orto-xylene	0.34	0.37	11	13
meta- and para-xylene	0.58	0.63	25	31
styrene	0.86	0.90	10	13
toluene	0.30	0.32	12	15

4.4 Desorption efficiency (D), adsorption efficiency (A) and recovery (R)

For the determination of desorption efficiencies, spiking experiments were conducted on different days, where the charcoal sorbent of the first section of the sorbent tube was poured into GC-vial and sorbents were spiked with three different concentrations of the reference solutions and analysed similarly to real samples using GC. Initially, ultrasonic bath was used to agitate desorbing samples in the vials. But after comparing the desorption efficiency results obtained using a mechanical shaker and the ones obtained with ultrasonic bath, the results obtained with the mechanical shaker were closer to 100%. A possible reason was that, the water temperature in the ultrasonic bath increased during the work of the bath, thereby favoring evaporation of the VOC analytes and possibly causing analyte losses. The estimated desorption efficiencies stayed in the range of (88 – 106)% (Table 2). Possible reason for desorption efficiencies above 100% are low-level contaminants that interfere with the analyte peaks. Because of their very low level they do not cause problems at high analyte concentrations but they become significant at low analyte concentrations.

For the determination of method recoveries, replicated LRM analysis experiments using the LRM design method 6 (Figure 7) were conducted on different days at three different concentration levels. The concentrations and amounts of reference solution added in case of both, desorption and recovery experiments, were the following:

1) 10 mg/m^3: 100 µl of reference solution (0.5 mg/ml)
2) 100 mg/m^3: 200 µl of reference solution (5 mg/ml)
3) 200 mg/m^3: 400 µl of reference solution (5 mg/ml)

The obtained recovery results stayed in the range of (78 – 93)% (Table 2) and are compatible with the widespread convention that recovery should be equal to or greater than 75% [25]. Recovery correction should be used for the calculation of the measurement results if it is considered as a significant systematic effect, if the causal factor for the observed effect can be identified, if the estimate for the biases are sufficiently accurate and if the correction applied causes an useful reduction in uncertainty [29]. According to obtained recovery results, the initial relative RMS_{bias} values calculated ranged from 10% to 20%, which indicates that recovery is a systematic effect that can be considered significant compared to maximum overall measurement uncertainty requirement set by EVS-EN 482, which is $U \leq 50\%$ [28]. The obvious reason for less than 100% recoveries in the case of this work is the incomplete adsorption of the VOCs on the sorbent during sampling and their incomplete desorption during sample preparation. The obtained recovery results do not scatter significantly around their average, with the standard deviation approximately around 2% (Table 3). This leads to a sufficient accuracy of recovery. And finally, because of the use of recovery correction in the measurement results and the estimate of uncertainty correction in the overall uncertainty estimation, a very useful uncertainty reduction has been achieved. As a consequence, after the reduction, the calculated uncertainty remains safely below the maximum allowed value of $U \leq 50\%$ (4.6 and Table 3). Therefore recovery correction is justified [28, 29]. According to the obtained recovery results (Table 3), recovery correction will be used for all the calculated measurement results at all concentration levels, since the before mentioned criteria has been fulfilled for all the cases.

Table 2. Desorption efficiencies, adsorption efficiencies and recoveries of VOCs.

	10 mg/m^3			100 mg/m^3			200 mg/m^3		
	D %	A %	R %	D %	A %	R %	D %	A %	R %
orto-xylene	102	86	88	97	88	85	92	93	86
meta- and para-xylene	106	88	93	91	98	89	96	94	90
styrene	91	86	78	90	89	80	88	93	82
toluene	102	88	90	99	90	89	96	85	82

4.5 Accuracy (trueness and precision)

The results of the recovery experiments of LRMs were used to estimate the accuracy of the method. For the determination of trueness and precision, 6 different experimental setups for the preparation of in-house made LRMs were tested. The recovery values for method 1 (Figure 2) were very low, staying just below 20%. Method 2 (Figure 3) gave no better results as recovery was only increased to 30%. As the methods using a glass container gave no satisfactory results, different other approaches were tried. Method 3 and 4 (Figures 4 and 5), where reference solutions were injected directly onto the charcoal tube, gave recovery values at the other end of the extreme, with recovery values of (120-130)%. In response to this, a third kind of design was prepared using a glass T-piece, where the reference solution was injected onto a cotton wool plug inside the T-piece. Method 5 (Figure 6), where nitrogen gas was flown through the T-piece, did not still give satisfied results as recoveries stayed around 70%. Finally, the latter design was upgraded to method 6 (Figure 7), where sampling pump was used to sample air through the tube instead of the use of gas stream and satisfactory recovery results were obtained, staying in the range of (80-100)%. This last method design was used to determine the mean and standard deviation of the five replicated measurements conducted on different days and compared with the spiked values of VOC standards. The trueness of the method, expressed by obtained bias values (Table 3), is compatible with the requirements set by Standards EVS EN 482 and ISO

16200-1, staying below allowed maximum bias value of 5% [20, 28]. The precision of the method is expressed by obtained reproducibility R_w values (Table 3).

4.6 Measurement uncertainty

From the replicate measurements of LRM analysis, the standard deviation between the LRMs prepared on different days was accounted for random effect as an intermediate precision and the values of $u(R_w)$ were obtained (see Table 3), which stay near 2% for all the VOC analytes at all concentrations. The results of the same replicated experiments were used to estimate the systematic component, the uncertainty of bias. The systematic uncertainty components were the uncertainty of 100% recovery, uncertainty of recovery correction and uncertainty of air volume sampled. Since the uncertainty of recovery correction was estimated by the same standard deviations as the reproducibility component, the estimates are equal and values stay near 2%. The uncertainties of 100% recovery and air volume sampled are the same for all the cases with values 0.8% and 0.9%, respectively. Initially calculated RMS_{bias} values from the recovery experiments gave large bias values of (10 - 20)% raising bias values to 20%, but after a justified use of recovery correction, the overall uncertainty of bias component stay slightly above 2%, leading to a combined uncertainty values ranging between 2.5% and 3%. After using a coverage factor k=2 to expand the overall uncertainty, the calculated relative expanded measurement uncertainty values stay in the range of (5 - 6) %, which are compatible with the requirements set by EVS EN 482, staying below allowed maximum value of 50% [28]. It is important to stress that the obtained uncertainty takes into account the uncertainty of sampling the air (the uncertainty of air volume) but does not take into account the possible inhomogeneity of air at a sampling site (which is considered to be a property of the analysis object).

Figure 19. Fish-bone diagram of the uncertainty components, with recovery correction.

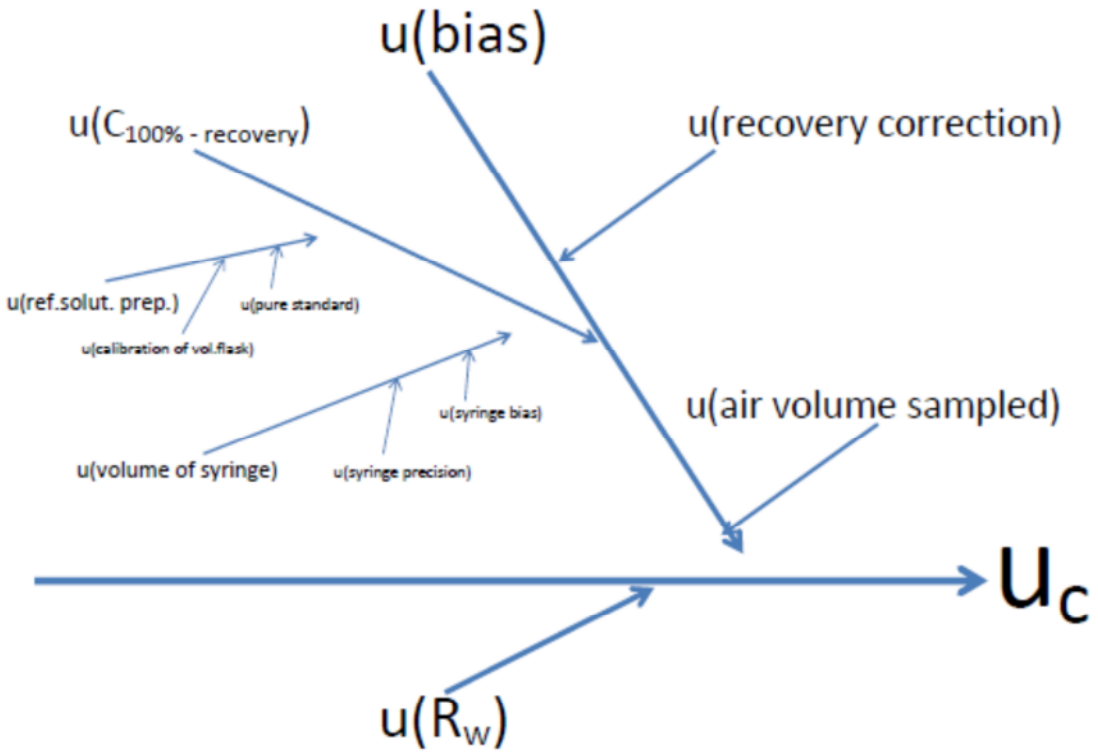


Table 3. Uncertainty components and expanded measurement uncertainties of determination of VOCs.

VOC	o-xylene			p- and m-xylene			styrene			toluene		
Concentration (mg/m3)	10	100	200	10	100	200	10	100	200	10	100	200
u(rec.correct), %	1.5	1.6	1.6	1.8	1.8	1.6	1.8	1.5	1.7	1.6	1.9	1.7
$u(C_{recovery})$, %	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
u(air volume), %	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
u(bias), %	**1.9**	**2.0**	**2.0**	**2.2**	**2.2**	**2.0**	**2.2**	**1.9**	**2.1**	**2.0**	**2.3**	**2.1**
u(Rw), %	**1.5**	**1.6**	**1.6**	**1.8**	**1.8**	**1.6**	**1.8**	**1.5**	**1.7**	**1.6**	**1.9**	**1.7**
u_c, %	2.5	2.6	2.6	2.8	2.8	2.5	2.8	2.5	2.7	2.5	3.0	2.7
U (k=2), %	**4.9**	**5.2**	**5.2**	**5.7**	**5.6**	**5.1**	**5.7**	**4.9**	**5.3**	**5.1**	**6.0**	**5.3**

4.7 R-control charts

For the preparation of the R-control charts, the difference between the parallel real samples taken within everyday analysis are plotted on a chart. By the time of the publication of this work, the laboratory had only analysed few real samples, therefore the control chart is in setup phase and the mean range and the limits of the control chart are changing continuously together with the new collected data. After collecting at least 10 control data values, the limits can be let remain stable and re-evaluated once a year. According to the initial QC data on R-charts, no interpretations can be done on the continuous working status of the method, since it requires stable control limits for a longer time to identify any change in the use of this method.

Figure 20. R-control chart of orto-xylene.

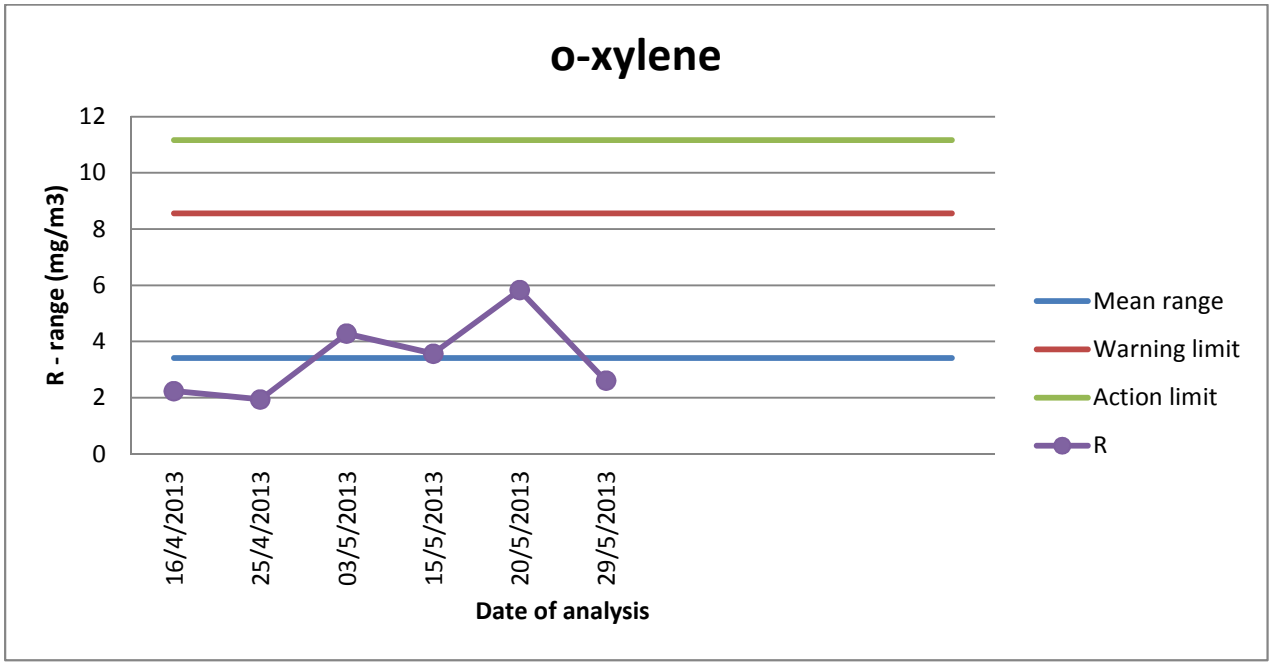


Figure 21. R-control chart of para- and meta-xylene.

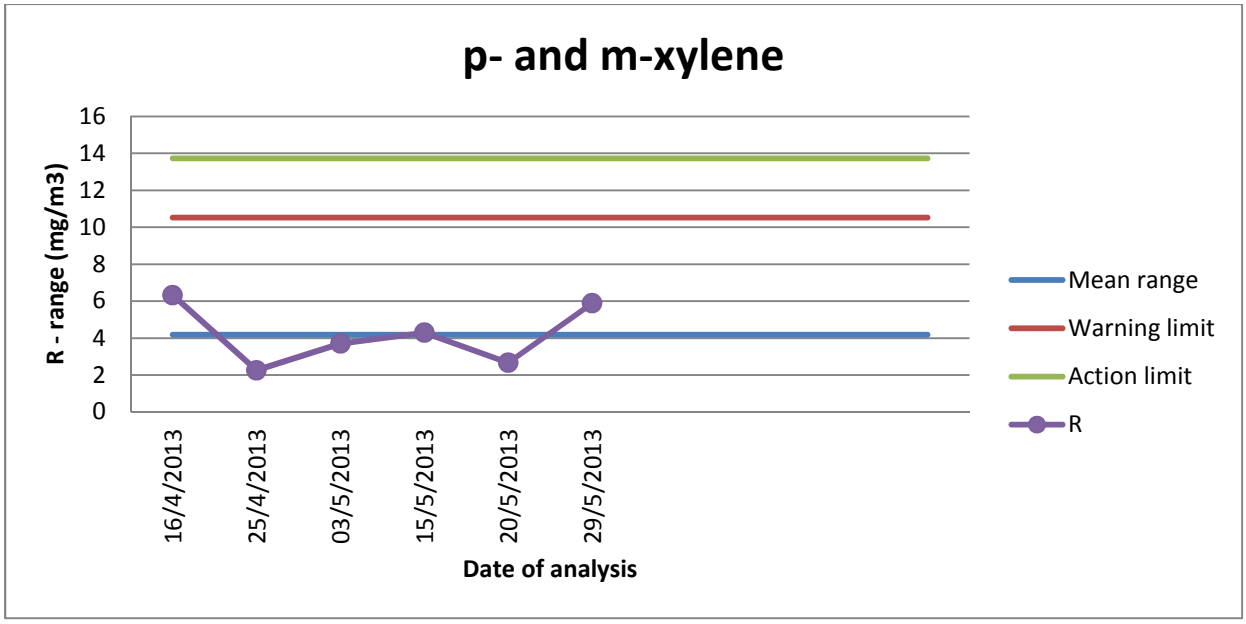


Figure 22. R-control chart of styrene.

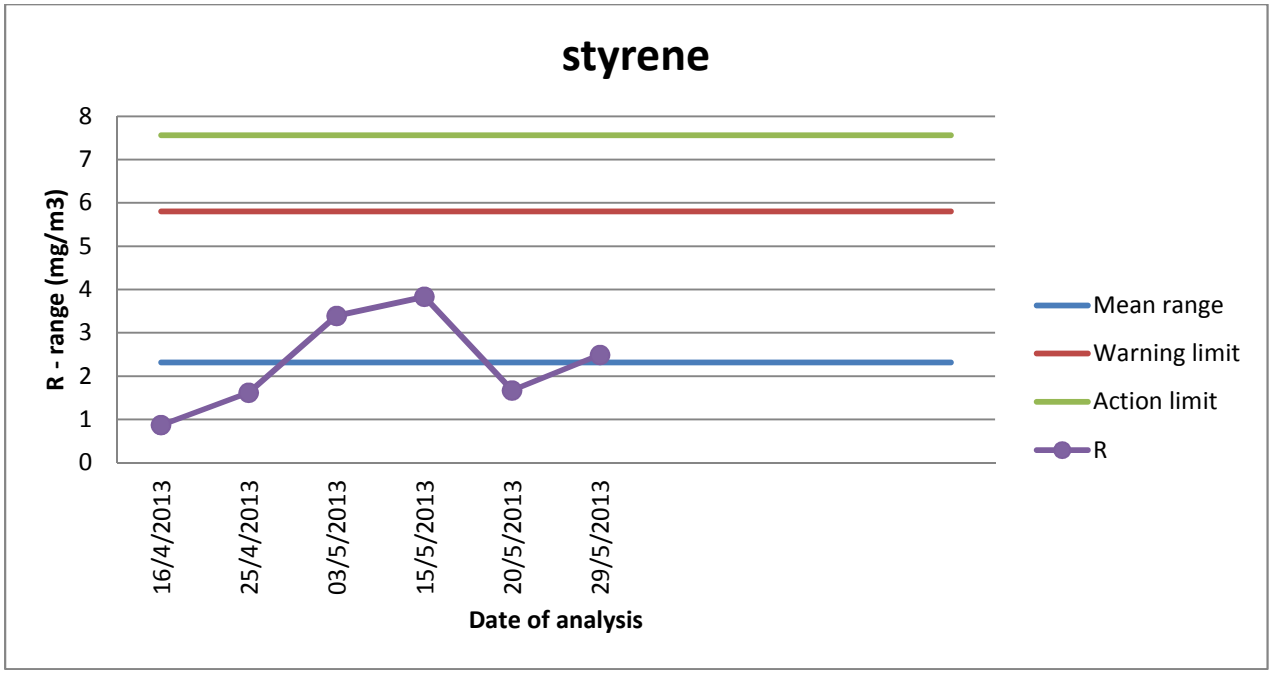
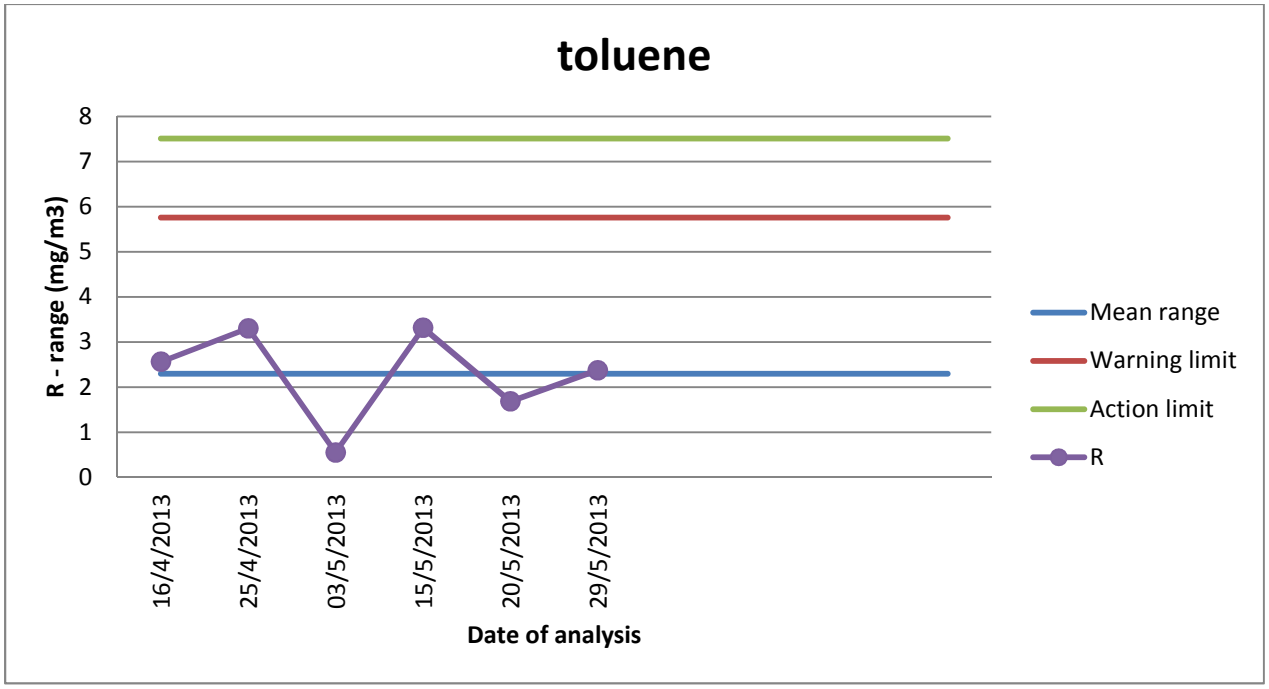


Figure 23. R-control chart of toluene.



5. Summary

The aim of this work was to set up and validate the analytical method for determination of 5 volatile organic compounds (toluene, styrene, orto-, para- and meta-xylene) in industrial workplace air. The method is based on International Standard – ISO 16200-1:2001 - *Workplace air quality - Sampling and analysis of volatile organic compounds by solvent desorption/gas chromatography – Part 1: Pumped sampling method*.

During the method validation, different experimental tests with calibration and reference standard solutions were conducted to characterise the important method performance parameters – confirmation of identity, selectivity, linear and working ranges, limit of detection and quantitation, recovery, trueness, precision and measurement uncertainty. For the purpose of recovery experiments and assessment of method LoD and LoQ, trueness, precision and measurement uncertainty, in-house made laboratory reference materials (LRMs) were prepared (sampling pump connected to a glass T-piece by a sorbent tube) by spiking them with reference solutions containing VOCs while pumping air through a sorbent tube. A specially designed experimental setup was created for the latter purpose.

Primary standards of VOCs were used for the identification of peak retention times on chromatograms and determination of retention times. No other interfering compounds have been found during the validation and prior to the use of this method. The method was validated for the use of concentration range of (10 – 200) mg/m^3, except for p-and m-xylene, as their calibration curve is constructed as their sum and therefore their calibration concentrations are two times higher ranging from 20 mg/m^3 to 400 mg/m^3. Besides the visual linearity check, the obtained R-squared values (o-xylene: 0.9998; p- and m-xylene: 0.9998; styrene: 0.9996; toluene: 0.9997) and the performed residual analysis indicated that good linearity can be assumed for all the calibration curves within the working area. For the determination of concentrations which to use for LoD and LoQ experiments, recovery experiments were conducted at several low concentrations and the concentration value of 10 mg/m^3 was found to be suitable. The estimated method LoD values were: o-xylene: 11 mg/m^3 , p- and m-xylene: 25 mg/m^3, styrene: 10 mg/m^3, and toluene: 12 mg/m^3; and method LoQ values were: o-xylene: 13 mg/m^3, p- and m-xylene: 31 mg/m^3, styrene: 13 mg/m^3, and toluene: 15 mg/m^3.

For the determination of desorption efficiencies, spiking experiments at three different concentration levels were conducted on the charcoal sorbent. The estimated desorption efficiencies stayed in the range of (88 – 106)%. For the determination of method recoveries, replicated LRM analysis experiments were conducted on different days at three different concentration levels. The obtained recovery results stayed in the range of (78 – 93)%. The recovery results are compatible with the widespread convention that recovery should be equal to or greater than 75%. From the estimates of desorption efficiencies and recoveries, adsorption efficiencies could be calculated, staying in the range of (85 – 98)%. According to the recovery results, recovery correction will be used for all the calculated measurement results at all concentration levels, since the criteria have been fulfilled for all the cases. Measurement uncertainties were estimated according to Nordtest approach. From the replicate measurements of LRM analysis on different days, intermediate precision as random components and uncertainty of bias as systematic, were estimated and combined. The expanded overall measurement uncertainties, using a coverage factor of k=2, stayed in the range of (5 – 6)%. As a quality control implementation, control R-charts were designed and will be used during the routine use of this method. The method has been already in routine use at the time of the publication of this work by Air and Materials Testing Group of Health Board Central Chemistry Laboratory. The method was assessed by the Estonian Accreditation Centre on 26th of March, 2013 and received flexible accreditation with no findings on non-conformities as it was validated with a sufficient degree to be fit for purpose.

6. Kokkuvõte

Gaasikromatograafilise metoodika valideerimine lenduvate orgaaniliste ühendite määramiseks tööstusettevõtete õhus.

Sander Sannik

Selle töö eesmärgiks oli valideerida analüütiline meetod 5 lenduva orgaanilise ühendi (tolueen, stüreen, orto-, para-, ja meta-ksüleen) määramiseks tööstusettevõtete õhus. Meetod põhineb rahvusvahelisel standardil - ISO 16200-1:2001 - *Workplace air quality - Sampling and analysis of volatile organic compounds by solvent desorption/gas chromatography – Part 1: Pumped sampling method*.

Meetodi valideerimise käigus viidi läbi erinevad eksperimentaalsed katsed kalibreerimis- ja referentslahustega, et iseloomustada tähtsamaid meetodi suutlikkuse parameetreid – analüütide identifitseerimine, selektiivsus, lineaarne ja töö-ala, avastamis- ja määramispiir, saagis, tõesus, kordustäpsus ja mõõtemääramatus. Saagise katsete läbiviimiseks, meetodi avastamis- ja määramispiiri, täpsuse ja määramatuse hindamiseks valmistati laborisiseselt referentsmaterjalid (proovipump ühendatud sorbenttoru kaudu klaasist T-tüki külge), kuhu süstiti kindlad kogused referentslahuseid, samal ajal tõmmates ruumiõhku läbi sorbenttoru. Selle jaoks loodi spetsiaalselt disainitud katseseade.

Lenduvate orgaaniliste ühendite põhistandardeid kasutati kromatogrammidel piikide retentsiooniaegade kindlaks tegemiseks. Ühtegi segavat ainet (interferentsi) ei ole leitud meetodi valideerimise ega varasemate labori analüüside käigus. Meetod valideeriti töötamiseks kontsentratsioonivahemikus (10 – 200) mg/m^3, välja arvatud p- ja m-ksüleenide korral, sest neile valmistati ühine kalibreerimisgraafik, muutes nende kalibreerimisvahemiku kaks korda kõrgemaks, jäädes vahemikku (20 – 400) mg/m^3. Peale visuaalse kalibreerimisgraafikute lineaarsuse kontrollimise, võib eeldada rahuldavat lineaarsust terve tööala ulatuses saadud R^2-väärtuste (o-ksüleen: 0.9998; p- and m-ksüleen: 0.9998; stüreen: 0.9996; tolueen: 0.9997) ja läbiviidud jääkliikmete analüüside põhjal. Selleks, et saada teada kontsentratsioon, millega viia läbi katsed avastamispiiri hindamiseks, viidi läbi saagise katsed laborireferentsmaterjaliga mitmetel madalatel kontsentratsioonidel ja väärtuse 10 mg/m^3 juures saadi kõige paremad

tulemused. Meetodi avastamispiiride väärtusteks saadi: o-ksüleen: 11 mg/m^3 , p- and m-ksüleen: 25 mg/m^3, stüreen: 10 mg/m^3, ja tolueen: 12 mg/m^3; ning meetodi määramispiirideks saadi: o-ksüleen: 13 mg/m^3, p- and m-ksüleen: 31 mg/m^3, stüreen: 13 mg/m^3, ja tolueen: 15 mg/m^3.

Desorptsiooniefektiivsuse hindamiseks viidi läbi lisamiskatsed proovivõtu toru sorbendile kolmel erineval kontsentratsioonil. Desorptsiooniefektiivsused jäid vahemikku (88 – 106)%. Meetodi saagise hindamiseks viidi läbi saagise katsed laborireferentsmaterjaliga erineval päeval ja kolmel erineval kontsentratsioonil. Saagiste väärtused jäid vahemikku (78 – 93)%. Saadud saagise katsete tulemused vastasid laialtlevinud saagise kriteeriumile, et saagis peaks olema võrdne või suurem kui 75%. Desorptsiooniefektiivsuse ja saagiste hinnangutest oli võimalik arvutada ka adsorptsiooniefektiivsused, mis jäid vahemikku (85 – 98)%. Vastavalt saadud tulemustele kasutatakse saagiseparandit kõikide tulemuste arvutamiseks kõikide analüütide ja kontsentratsioonide korral. Mõõtemääramatused hinnati kasutades Nordtest meetodit ning saadud laiendmõõtemääramatused, arvutatud katteteguriga k=2, jäid vahemikku (5 – 6)%. Kvaliteedikontrolliks valmistati R-kontrollkaardid, mida täidetakse ja jälgitakse käesoleva meetodi edasisel rutiinkasutusel. Meetod on käesoleva töö avaldamise ajaks juba rutiinkasutuses Terviseameti Kesklabori Keemialabori õhu- ja materjalide uuringute rühma töös. Meetodile viidi 2013-nda aasta 26. märtsil läbi väline audit Eesti Akrediteerimiskeskuse poolt ja meetod lisati Terviseameti Keemialabori paindlikku akrediteerimisulatusse, sest hindamiste käigus ei leitud ühtegi mittevastavust ISO 17025 standardi alusel, mis tähendab, et meetod oli piisava ulatuslikkusega valideeritud ja kohane kasutamiseks talle mõeldud eesmärgil.

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