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Application

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Application Note 132

Monitoring VOC emissions from respiratory medical devices in accordance with the new ISO 18562 international standard

Summary

This Application Note describes the monitoring of potentially harmful volatile and semi-volatile organic compounds (VOCs and SVOCs) emitted from respiratory medical devices, in accordance with the recently-released ISO 18562 standard. The sampling protocol involves passing the air stream through the medical device and onto a sorbent-packed tube, followed by automated analysis by well-established and reliable TD–GC–MS protocols. Emissions from two sets of face-mask supply tubing and three nasal cannulas were compared, and all were found to emit VOCs, with emission levels being relatively high in the first 24 hours of use.

Introduction

Exposure to harmful compounds from respiratory medical devices

Respiratory medical devices (RMDs) are widely used to deliver air, oxygen or anaesthetics to patients with a variety of short-term and long-term medical conditions. Until recently, the potential presence of contaminants in the air/gas stream was not questioned, but there is now growing awareness of the potential for polymeric components in the gas pathways to release harmful volatile organic compounds (VOCs), which are subsequently inhaled by the user. As a result, there is concern amongst clinicians that medium- to long-term use of RMDs could ultimately be detrimental to a patient's health.

The regulatory framework

Concern over patient health is the driving force behind ISO 18562 ("Biocompatibility evaluation of breathing gas pathways in healthcare applications"),[1] which was released in March 2017. The new standard is split into four parts, with parts 2–4 dealing with the measurement of three types of potentially harmful releases from RMDs, including VOCs. The predecessor to ISO 18562 (ISO 10993) did not cover VOC emissions directly, and was partly based on animal implant tests of uncertain scientific value.[2] In contrast, the new method is based on tests performed directly on the device, and does not involve animal experimentation. Consequently there are strong scientific and ethical reasons to start using the new ISO standard.

The ultimate outcome of testing in accordance with ISO 18562 is to assess the patient's exposure to chemicals from the RMD during their treatment (expressed in units of µg/day), which is then related to thresholds of toxicological concern (TTCs) specified in ISO 18562. The release of the method also has an impact on US FDA 510(k) submissions, which must include information regarding biocompatibility of any materials in contact with a patient (directly or indirectly) associated with medical devices.

Similarly, in May 2017 the European Commission published Regulation 2017/745,[3] which supersedes the existing EU Directive 2001/83/EC.[4] Like ISO 18562, 2017/745 requires the substances emitted by RMDs to be determined, and also requires an assessment of whether 'systemic absorption' of these occurs *in vivo*. It is probable that in due course ISO 18562 will be used to support Regulation 2017/745.

Devices covered by ISO 18562

ISO 18562 contains a comprehensive (but not exhaustive) list of medical devices, parts and accessories that contain gas pathways, and which need to be tested. These include ventilators, anaesthesia workstations, oxygen-conserving equipment, nebulisers, gas monitors, masks, mouthpieces, breathing tubes, and any breathing accessories intended to be used with such medical devices.

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Methodology

Overview

ISO 18562 is based on tests performed either on the final RMD assembly, on its components, or on representative samples of the materials involved, and part 3 deals with testing for emissions of VOCs. ISO 18562-3 describes in broad terms how evaluation of RMDs should be conducted, but references other standards for the analytical methods that should be used. Specifically, it states that emissions should be sampled either using sorbent tubes (in accordance with ISO 16000-6[5]) or canisters (in accordance with ASTM D5466[6]).

Both these approaches are well-established and popular for air monitoring and related applications, but generally speaking, tube-based methods such as ISO 16000-6 are preferred for investigating emissions from products and materials. This is partly for reasons of practicality, but is mainly because tubes can accommodate a wider analyte range than canisters. In particular, the semi-volatile compounds that are often associated with emissions from polymeric materials are more reliably monitored using tubes. In contrast, canister methods such as ASTM D5466 are predominantly intended for screening urban and industrial air for relatively short lists of volatile and very volatile toxic compounds (known as 'air toxics'), and are unsuitable for many SVOCs.[7] Analysis in accordance with the tube-based standard ISO 16000-6 is therefore the focus of this document.

ISO 16000-6 specifies determination of VOCs in air or gas streams by pumped sampling onto thermal desorption tubes (3½″ long, ¼″ outer diameter) packed with Tenax® TA sorbent. This is followed by analysis of the tubes using thermal desorption (TD) pre-concentration of the vapours, followed by gas chromatography (GC) with mass spectrometry (MS), with or without additional flame ionisation detection (FID).

Sampling

To carry out the ISO 16000-6-compliant sampling needed for ISO 18562-3, a sorbent tube is connected to the air/gas flow path of the component, and purge gas (*e.g.* high-purity air) is supplied at a defined flow rate for a specific time. This causes any organic vapours released from the device to be transferred into the sorbent tube, where they are selectively retained.

Sampled sorbent tubes are simply placed into the TD–GC–(MS or FID) system for analysis. The analytical sampling time used experimentally and the calculated rate of vapour emissions can then be correlated to the required exposure categories for each compound detected.

Thermal desorption

Thermal desorption (TD) is a versatile GC pre-concentration technology that is used to analyse VOCs and SVOCs in a wide range of sample types. By using a two-stage process to concentrate organic vapours from a sample into a very small volume of carrier gas (Figure 1), TD maximises sensitivity for trace-level target compounds, helps to minimise interferences, and routinely allows analyte detection at the ppb level or below. It also greatly improves sample throughput, by allowing full automation of sample preparation, desorption/extraction, pre-concentration and GC injection.

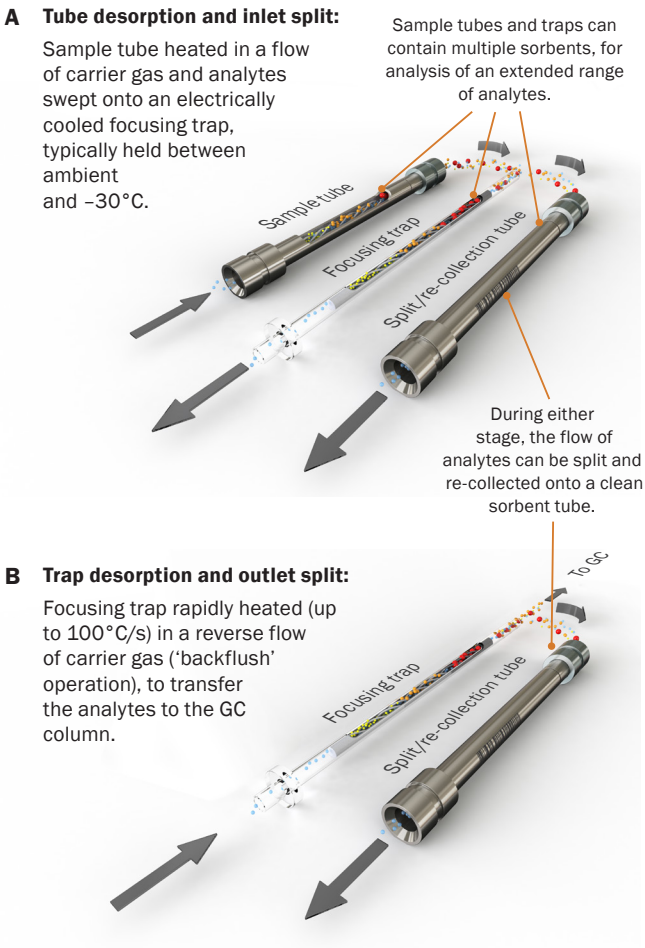


Figure 1: Schematic showing the operation of two-stage cryogen-free thermal desorption as used in Markes' instruments.

Markes International is the world's leading provider of analytical thermal desorption equipment, with every system offering state-of-the-art analytical performance and operating cryogen-free to minimise running costs. All Markes' TD instruments comply fully with the requirements of ISO 18562-3 and ISO 16000-6. ASTM D5466-compliant systems are also available for automated canister analysis if required. Some of the most relevant advantages of Markes' thermal desorption systems for this application include:

- Guaranteed data quality (automated tube leak-testing and robust seals prevent leaks and contamination).
- Compatibility with a wide range of vapour concentrations (sub-ppt to percent).
- Quantitative re-collection of any split flow for repeat analysis and method/data validation (as described in ISO 16000-6).

Extending the analyte range

ISO 18562-3 mentions that certain authorities may stipulate the monitoring of very volatile (VVOC) and semi-volatile (SVOC) compounds in addition to the usual n-C_6 to n-C_{16} range of VOCs, and it is likely that monitoring this extended analyte range will be made a requirement in future revisions. As outlined in Annex D of ISO 16000-6, this can be readily

achieved by packing the tubes with additional sorbents,[8] in order to quantitatively trap and release a wider range of compounds. The 'Material emissions' sorbent tube offered by Markes is an ideal ready-made sampler for this extended analyte range, and is employed in this study.

Experimental

RMD samples:
To assess the release of VOCs from RMDs, a number of products were purchased (Table 1 and Figure 2).

Sample	Type	Manufacturer
A	Face mask supply tubing	1
B	Face mask supply tubing	2
C	Nasal cannula	3
D	Nasal cannula	4
E	Nasal cannula	2
F	Nasal cannula	5

Table 1: Identity of the samples analysed.

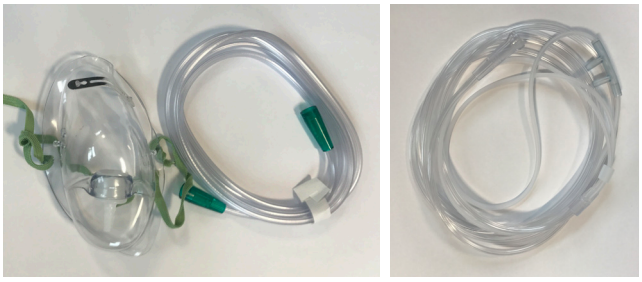


Figure 2: Examples of two of the samples analysed. Left: Face mask supply tubing (the face mask itself was not part of the sampling setup). Right: Nasal cannula.

Sampling:
VOC profiling of RMD samples (Figure 3): To acquire the VOC emission profile from each of the samples, a 'Material emissions' sorbent tube (Markes International part number C3-CXXX-5304) was directly inserted into the end of the tubing (which in each case was ~2 m long, as received). A regulated clean air supply, provided by a dual regulator pneumatics accessory (Markes International part number U-GAS01) through a supply line, was then passed through the setup at 100 mL/min for 1 h at room temperature (~21°C), to transfer released VOCs onto the sorbent tube.

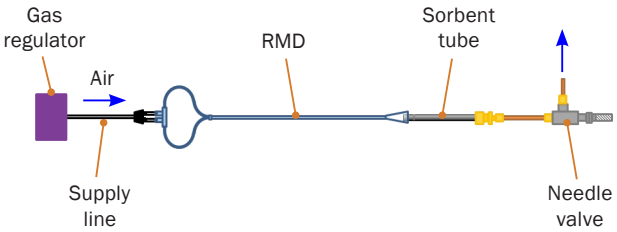


Figure 3: Setup for VOC profiling.

Checking of supply-line cleanliness: To confirm the cleanliness of the air supply line, the setup described above was used without the sample tubing itself in position.

Time-course study: Sample F was chosen for a study of the change in VOC profile with time, using a constant flow of 100 mL/min clean air for 7 days. At each time-point, emissions were sampled for 1 h as described above, and the procedure repeated on subsequent days using a clean sorbent tube.

Standard:
For the purposes of calculating analyte concentrations in terms of toluene equivalents,[9] a 10 ng/µL toluene-d_8 standard was loaded onto a clean sorbent tube using a Calibration Solution Loading Rig™ (Markes International), and the tube then analysed under the same conditions as for the sampled sorbent tubes.

TD:

Instrument:	TD100-xr™ (Markes International)
Trap:	'Material emissions' (Markes International part number U-T12ME-2S)
Tube pre-purge time:	1 min at 50 mL/min
Tube desorption:	300°C (10 min)
Pre-trap-fire purge:	1 min at 50 mL/min
Trap low:	30°C
Trap high:	310°C (3 min)
Heating rate:	Max (100°C/s)
Outlet split flow:	50 mL/min
Split ratio:	34:1
TD flow path:	180°C

GC:

Carrier gas:	Helium
GC column:	Rxi®-5HT, 30 m × 0.25 mm × 0.25 µm
Mode:	Constant-flow, 1.5 mL/min
Oven ramp:	40°C (3 min), then 8°C/min to 300°C (10 min)

Quadrupole MS:

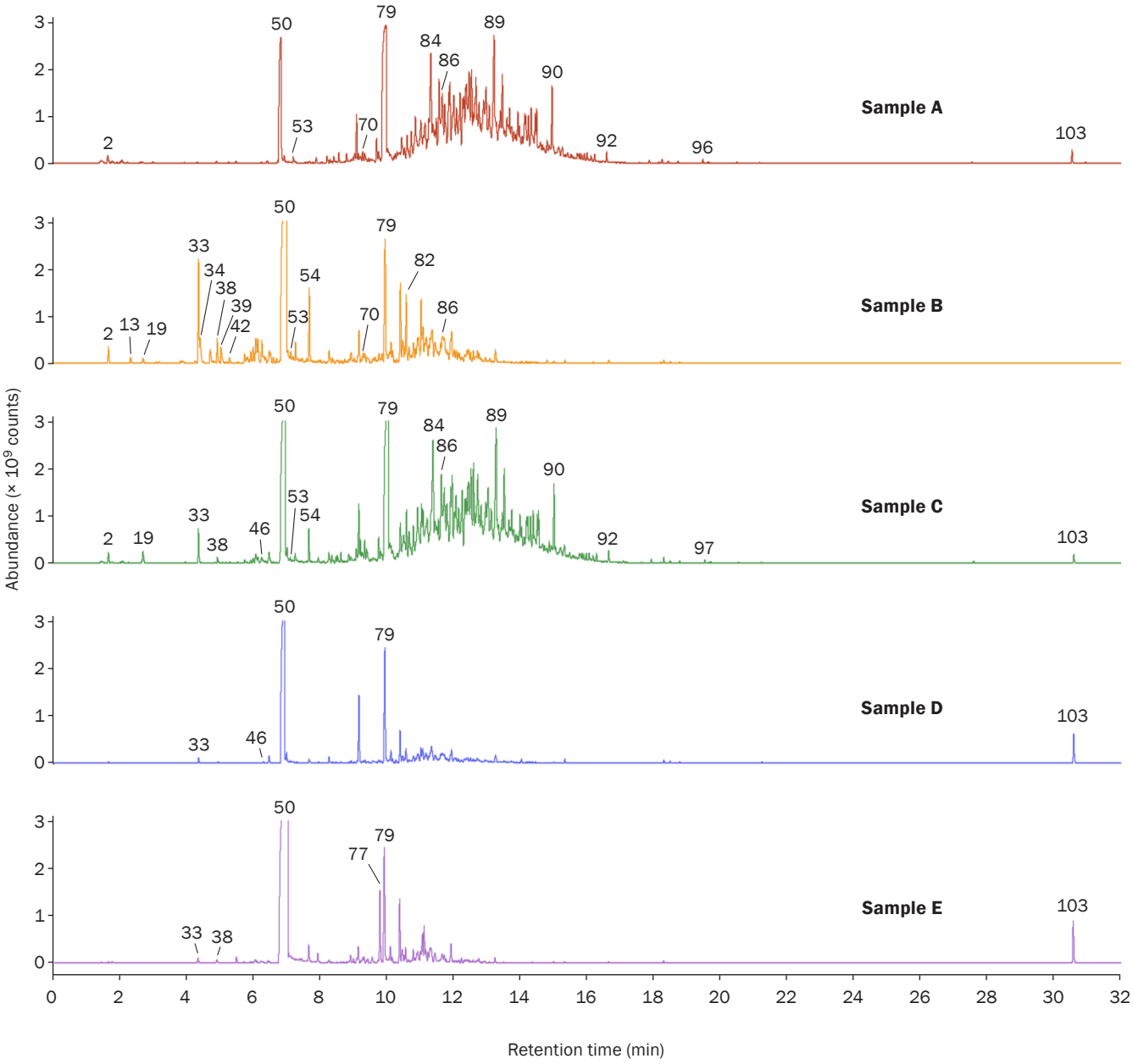
Ion source:	300°C
MS transfer line:	280°C
Full scan range:	m/z 35–350

Data analysis:
TargetView™ GC–MS software (Markes International) was used to selectively remove unwanted background noise from the chromatograms, and so improve the identification of analytes during subsequent automated comparison against a target library of ~540 components typical of polymeric materials. It also generated peak-area information that allowed semi-quantitation in terms of toluene equivalents. An example of the capabilities of TargetView for the analysis of polymers and other consumer goods is provided in Application Note 090.

Results and discussion

1. VOC profiles

Figure 4 shows analysis of Samples A–E. The large number of compounds released is immediately apparent, as is the presence (in various forms) of a broad hydrocarbon/oil-like response in all the samples.



2	Acetone	38	Hexanal	53	2-Butoxyethanol	82	Acetophenone	92	n-Tetradecane
13	2-Methylpropan-1-ol	39	n-Octane	54	Cumene	84	n-Undecane	96	Diethyl phthalate
19	Cyclohexane	42	n-Butyl acetate	70	n-Decane	86	1,2,4,5-Tetramethylbenzene	103	Bis(2-ethylhexyl) phthalate
33	Toluene	46	Ethylbenzene	77	o-Cymene	89	n-Dodecane		
34	Pentan-1-ol	50	Cyclohexanone	79	2-Ethylhexan-1-ol	90	n-Tridecane		

Figure 4: TD–GC–MS chromatograms of RMD samples A–E.

2. Supply line cleanliness

The presence of the broad hydrocarbon response in Samples A–E initially made us suspect that the air supply or connecting tubing might be contaminated. This possibility was eliminated by placing a sorbent tube immediately downstream of the air supply line, without any sample in position. The near-zero response (Figure 5) indicates that the hydrocarbon profile is a real feature, and that it is emanating from the RMD.

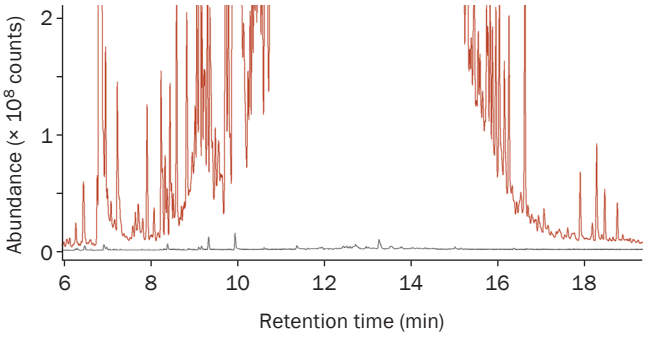


Figure 5: Expansion of the TD–GC–MS chromatogram of Sample A (red trace), and of air passed through the sampling line without any sample in position (grey trace).

3. Compound listings

In order to identify the compounds contained in Samples A–E, the chromatograms were screened against a 540-component library of compounds typically encountered in polymeric consumer goods and construction materials. Table A1 (see Appendix) provides a full listing of compound masses, and the most abundant components are shown in Figure 6.

Two compounds dominate the profiles of all five samples: cyclohexanone (#50) is used as a binding agent for polymer fittings, while 2-ethylhexan-1-ol (#79) is a precursor in the synthesis of phthalate plasticisers. The large number of other compounds present includes solvents, such as dichloromethane (#5, now declining in use as a binding agent, but present in all five samples), methyl ethyl ketone (#10, sometimes used in conjunction with cyclohexanone, and found in Samples B and D), and toluene (#33, present in all five samples).

Phthalates were also present in all five samples, with diethyl phthalate (#96) and bis(2-ethylhexyl) phthalate (#103) being confidently identified. The latter was the least volatile of the components, eluting as the last peak. A specification for phthalate-free medical tubing is available, but these results show that at least some manufacturers are not yet producing phthalate-free products.

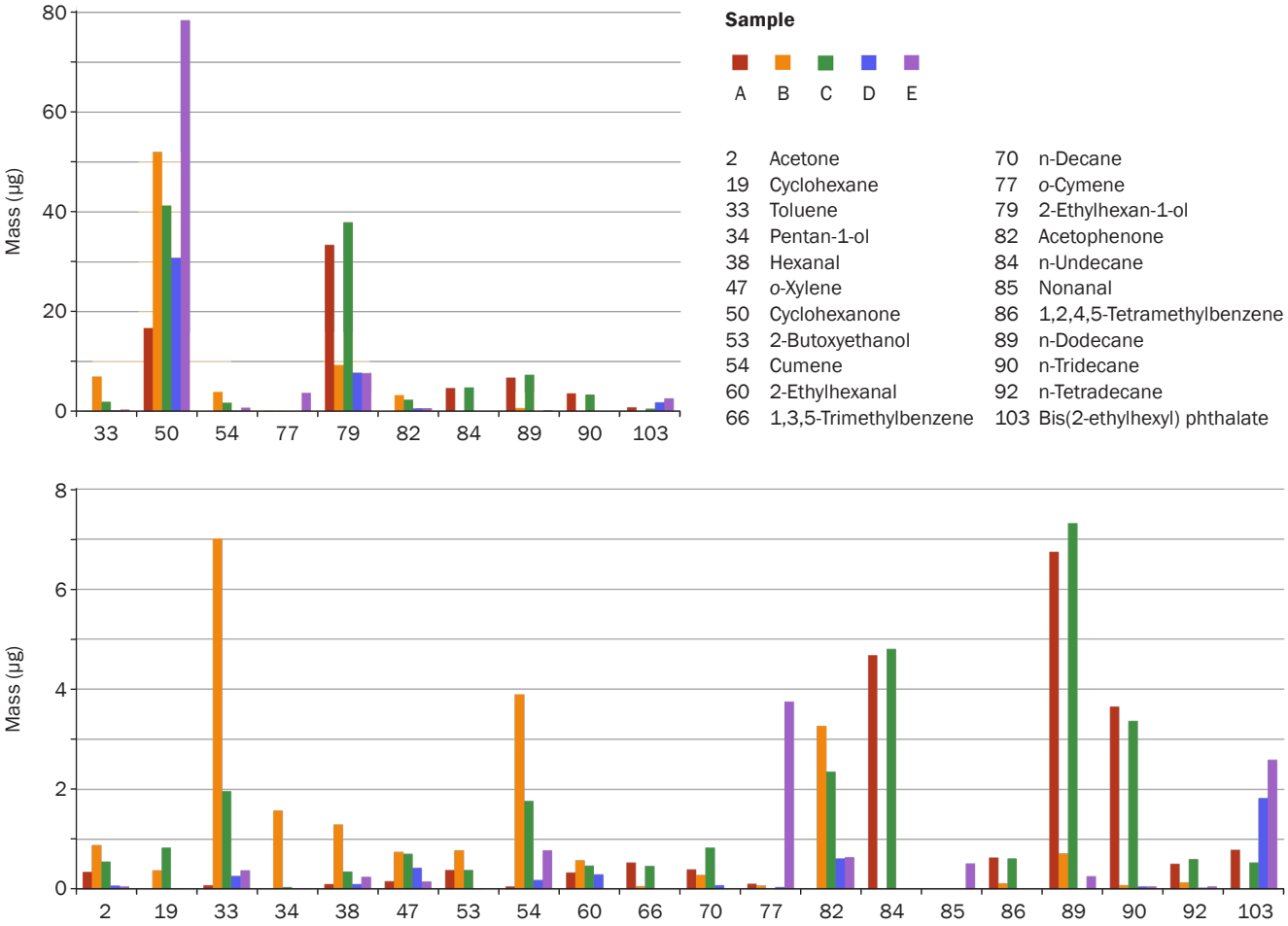


Figure 6: Top: Responses of the 10 compounds with masses above 2000 ng (2 µg) in any of the samples. Bottom: Responses of the 20 compounds with masses above 500 ng (0.5 µg) in any of the samples, excluding the two most abundant compounds (2-ethylhexan-1-ol and cyclohexanone).

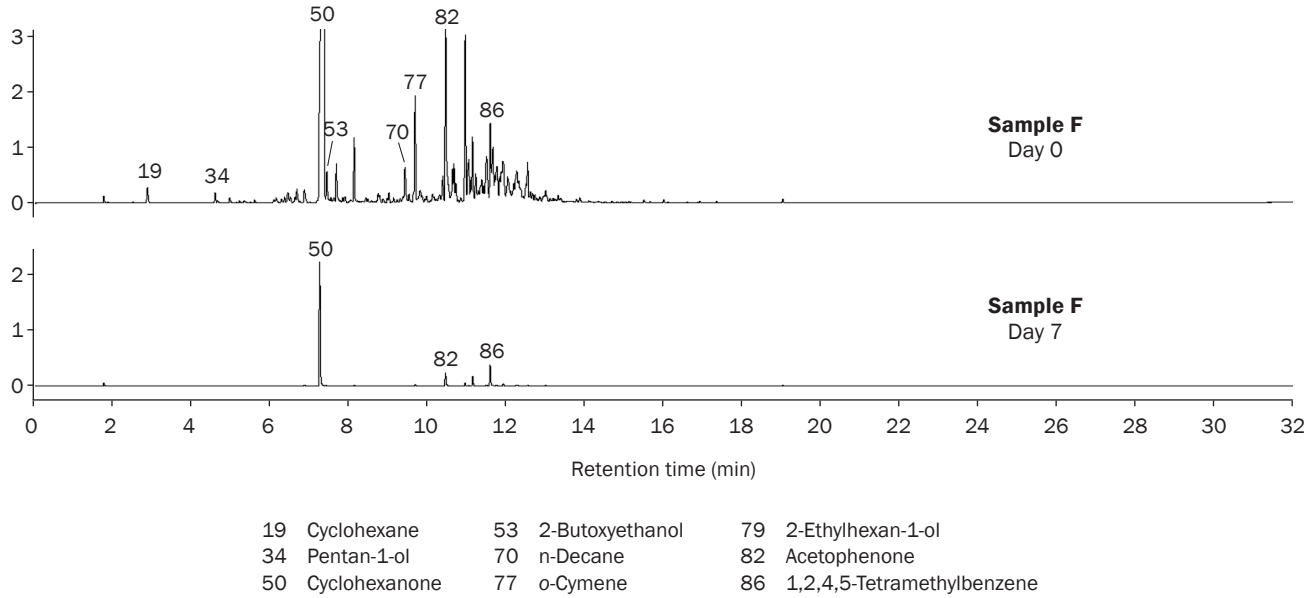


Figure 7: TD–GC–MS chromatograms of Sample F, on day 0 and day 7.

4. Time-course study

Sample F, a nasal cannula, was chosen for an investigation into the decay of volatiles over a period of 7 days, using the same 1-hour sampling protocol as for Samples A–E. The profiles at 0 and 7 days are shown in Figure 7, and decay profiles for cyclohexanone and toluene are plotted in Figure 8.

Overall, the profiles are very similar to the plots (for 30+ days) shown in the documentation for ISO 18562, and serve to illustrate the high degree of off-gassing in the initial 24 hours of use, followed by an extended period of decaying emissions.

5. TVOC values and exposures

ISO 18562-3 is primarily concerned with the "dose to the patient of a substance or sum of substances" within three exposure categories, which are: 'Limited' (≤24 h), 'Prolonged' (≥24 h and <30 days) and 'Permanent' (≥30 days). The method advises deriving allowable limits using acceptable toxicological databases to calculate tolerable intake (TI) values, but if no toxicity data is available then a threshold of toxicological concern (TTC) can be used instead.

In all three categories, the TTC levels for adults are 360 µg/day for the first 24 hours, falling to 120 µg/day subsequently. For other categories of patients the method indicates how the values should be adjusted – for example, the adult-to-neonate adjustment is 1/140, which reduces the TTC value to ~2.5 µg/day.

ISO 18562-1 specifies default breathing volumes that are used to calculate the dose to a patient in any 24-hour period. These are 0.21 m^3 (neonate), 2.0 m^3 (infant), 5.0 m^3 (paediatric) and 20 m^3 (adult), equating to rates of 0.15, 1.38, 3.47 and 13.8 L/min (lpm), respectively.

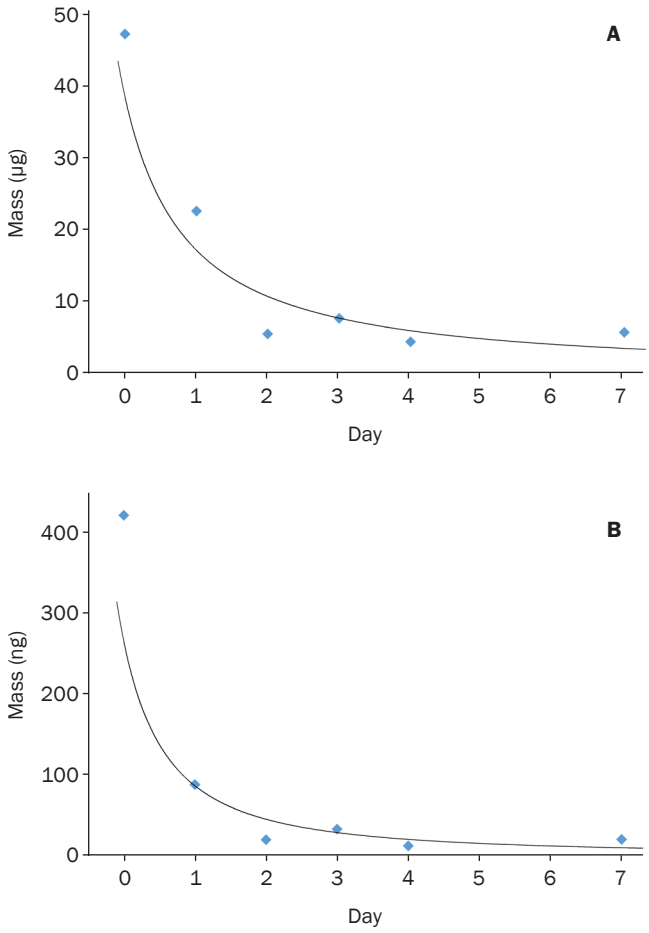


Figure 8: Decay profiles for (**A**) cyclohexanone and (**B**) toluene from Sample F over a period of 7 days (samples were not taken on days 5 and 6). Power-law trendlines have been added.

The sampling time of 1 hour and sampling rate of 0.1 L/min used in the current study means that the results are of greatest relevance to the 'Limited' (≤24 h) category and to neonatal breathing volumes. To assess how Samples A–E perform within this category, total VOC (TVOC) values were determined, both by summing the responses for all the identified library components and by integrating the entire chromatogram (Table 2).

To gain an idea of exposures that might result from a longer period of use, the TVOC values obtained by integration of the entire chromatogram were used to derive cumulative exposure values for the first 24 hours of use (Table 3). The values obtained for 1 hour of use (75–430 µg) are comparable to the 360 µg/day TTC for adults, but well over the 2.5 µg/day TTC for neonates. For 24 hours of use, the values are in the range 1370–7000 µg, which exceeds three times the TTC for adults, and is over 500 times the TTC for neonates.

		A	B	C	D	E
Library components only	**Mass (µg)**	67.6	85.4	110.0	43.3	97.1
	Conc. (µg/m³)	11200	14226	18339	7211	16182
Entire chromatogram	**Mass (µg)**	371.2	171.9	429.0	75.2	122.5
	Conc. (µg/m³)	61869	28645	71506	12535	20418

Table 2: TVOC values for Samples A–E, determined for a sampling period of 1 hour, both for the identified components and by integration of the entire chromatogram. Values are calculated in terms of toluene equivalents.[9]

Exposure (h)	A	B	C	D	E
1	371	172	429	75	122
6	2112	976	2440	427	696
12	3946	1823	4558	797	1301
18	5501	2542	6355	1111	1813
24	6777	3131	7830	1369	2234

Table 3: Estimated TVOC exposures in µg over the first 24 hours of use of Samples A–E, based on integration of the entire chromatogram and a 50% 24-hour decay rate (as indicated from the decay profiles in Figure 8).

Conclusions

This study shows that the sorbent sampling tubes and TD–GC–MS analytical equipment used is versatile and fully compliant with the requirements of ISO 18562 (and of the cited method ISO 16000-6). In particular, the thermal desorption instrument used to pre-concentrate the vapours is highly sensitive and easily automated, and in combination with GC–MS is able to reliably identify compounds released from the gas pathways of respiratory medical devices. Although the focus of ISO 18562-3 is on VOCs, use of sampling tubes containing multiple sorbent beds, in conjunction with the versatility of Markes' thermal desorbers, enables compounds to be analysed across the full range of volatilities.

The results obtained on the samples tested show that some of the respiratory medical devices available on the market today emit a broad range of VOCs and SVOCs. Our results indicate that 2-ethylhexan-1-ol and cyclohexanone are the most abundant components in all the samples, but also that many less abundant compounds are present. In addition, a broad oil/hydrocarbon band of unknown origin was also observed. In the context of earlier work we have carried out into emissions from polymeric materials,[10] such emission levels indicate potential issues with manufacturing and/or packaging quality. The use of low flow rates, and the fact that the products were sampled immediately after being removed from the packaging, means that these results represent a 'worst-case scenario' for VOC emissions, but nevertheless one that may be typical of products used for the care of certain patients.

References and notes

1. ISO 18562: Biocompatibility evaluation of breathing gas pathways in healthcare applications.
   Part 1: Evaluation and testing within a risk management process, 2017, www.iso.org/standard/62892.html.
   Part 2: Tests for emissions of particulate matter, 2017, www.iso.org/standard/62893.html.
   Part 3: Tests for emissions of volatile organic compounds (VOCs), 2017, www.iso.org/standard/62894.html.
   Part 4: Tests for leachables in condensate, 2017, www.iso.org/standard/62895.html.
2. Key shortcomings of ISO 10993 are that it does not specifically address VOC emissions from the gas pathways within RMDs, and that it is based on an indirect assessment of chemical emissions using animal implantation. Results are derived from contact exposure from bone, tissue and dentine, leading to questionable findings and potential false negatives.
3. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, *Official Journal of the European Union* (L117), 2017, 60: 1, http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AL%3A2017%3A117%3ATOC.
4. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, *Official Journal of the European Union* (L311), 2011, 44: 67, http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32001L0083.

5. ISO 16000: Indoor air – Part 6: Determination of volatile organic compounds in indoor and test chamber air by active sampling on Tenax TA sorbent, thermal desorption and gas chromatography using MS or MS-FID, International Organization for Standardization, 2011, www.iso.org/standard/38203.html.
6. ASTM D5466: Standard test method for determination of volatile organic compounds in atmospheres (canister sampling methodology), ASTM International, 2015, www.astm.org/Standards/D5466.htm.
7. Although modern canister-based systems offer analysis of compounds up to C_{14}, it is important to note that adsorption on the interior surfaces of the canister (or partitioning into any water present) may compromise release of compounds above $C_{9/10}$. In the current study, recovery of a number of compounds would have been impossible, including the heavier hydrocarbons, alcohols and phthalates, and polycyclic aromatics such as phenanthrene. All these are routinely monitored without difficulties using tube-based techniques.
8. It should be noted that multi-bed sorbent tubes can only be analysed on TD systems operating in backflush mode. Backflush desorption of the sorbent tube and focusing trap uses a reverse flow of carrier gas to release the compounds in the opposite direction to which they were sampled. Less volatile components are thus quantitatively retained and released from weak sorbents in the front of the tube/trap, while more volatile components are quantitatively retained and released from stronger sorbents at the rear of the trap. Further information is available in Application Note 064.
9. Where response factors are known for individual compounds, VOC concentrations can be calculated, as described in ISO 16000-6. When this is not the case, concentrations of individual components (or TVOC values) are approximated using the response factor of toluene, to give masses as toluene equivalents (known as 'semi-quantitation').
10. See, for example, Markes International Application Notes 059 (car trim materials), 065 (PVC foam, leather and paint), 103 (adhesives, flooring materials and a glazing spacer), 110 (glass sealant), 113 (PU foam) and 130 (spray polyurethane foam).

Trademarks

Applications were performed under the stated analytical conditions. Operation under different conditions, or with incompatible sample matrices, may impact the performance shown.

Appendix

No.	Target compound	t_R (min)	A		B		C		D		E	
			Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)
1	Ethanol	1.63	–	–	–	–	–	–	–	–	7.83×10^{7}	24.0
2	Acetone	1.69	1.13×10^{9}	345	2.89×10^{9}	883	1.80×10^{9}	551	2.27×10^{8}	69.5	1.74×10^{8}	53.3
3	Isopropanol	1.72	–	–	–	–	–	–	5.81×10^{7}	17.8	3.83×10^{7}	11.7
4	*tert*-Butanol	1.80	–	–	4.11×10^{7}	12.6	2.33×10^{8}	71.4	–	–	1.87×10^{8}	57.2
5	Dichloromethane	1.82	2.18×10^{8}	66.8	1.63×10^{7}	4.99	4.15×10^{7}	12.7	9.37×10^{7}	28.7	1.26×10^{8}	38.4
6	Methylhydrazine	1.83	1.69×10^{7}	5.18	–	–	–	–	–	–	–	–
7	Carbon disulfide	1.85	1.19×10^{8}	36.3	–	–	6.34×10^{7}	19.4	9.32×10^{6}	2.85	–	–
8	Propene	1.98	–	–	9.10×10^{5}	0.28	–	–	5.15×10^{5}	0.16	–	–
9	Acetic acid	2.11	7.42×10^{8}	227	–	–	–	–	–	–	–	–
10	Methyl ethyl ketone (Butan-2-one)	2.13	–	–	8.94×10^{7}	27.3	–	–	1.58×10^{6}	0.48	–	–
11	n-Hexane	2.14	1.15×10^{8}	35.1	–	–	–	–	–	–	4.69×10^{7}	14.3
12	Ethyl acetate	2.24	–	–	1.94×10^{7}	5.93	–	–	1.47×10^{7}	4.48	9.38×10^{6}	2.87
13	2-Methylpropan-1-ol	2.37	–	–	1.42×10^{9}	435	–	–	–	–	–	–
14	1,2-Dichloroethane	2.54	–	–	–	–	–	–	1.51×10^{6}	0.46	–	–
15	But-2-enal	2.54	–	–	–	–	1.20×10^{7}	3.68	–	–	–	–
16	1,2-Dichloroethane	2.55	–	–	–	–	–	–	–	–	2.55×10^{6}	0.78
17	1-Hydroxypropan-2-one	2.65	1.28×10^{8}	39.3	–	–	3.90×10^{7}	11.9	–	–	–	–
18	Benzene	2.69	1.52×10^{8}	46.4	–	–	2.13×10^{8}	65.1	3.46×10^{7}	10.6	4.64×10^{7}	14.2
19	Cyclohexane	2.74	–	–	1.22×10^{9}	373	2.73×10^{9}	836	1.16×10^{7}	3.55	–	–
20	Butan-1-ol	2.78	–	–	–	–	–	–	2.39×10^{6}	0.73	4.97×10^{7}	15.2
21	3-Methylbutan-2-one	3.00	1.57×10^{7}	4.81	–	–	–	–	–	–	–	–
22	2,2,4-Trimethylpentane	3.04	2.17×10^{8}	66.5	2.92×10^{8}	89.3	–	–	–	–	–	–
23	Pentanal	3.12	–	–	2.86×10^{8}	87.6	–	–	1.94×10^{7}	5.94	4.58×10^{7}	14.0
24	n-Heptane	3.22	1.75×10^{7}	5.36	–	–	–	–	–	–	4.70×10^{6}	1.44
25	Propanoic acid	3.23	6.60×10^{7}	20.2	–	–	–	–	–	–	–	–
26	Glycidol	3.40	8.23×10^{7}	25.2	–	–	–	–	–	–	–	–
27	Methyl methacrylate	3.41	–	–	8.99×10^{7}	27.5	–	–	4.48×10^{6}	1.37	–	–
28	n-Propyl acetate	3.47	–	–	4.77×10^{6}	1.46	–	–	–	–	–	–
29	Methylcyclohexane	3.65	–	–	1.05×10^{7}	3.20	–	–	–	–	1.29×10^{7}	3.96
30	Methyl isobutyl ketone	3.94	–	–	–	–	7.24×10^{7}	22.1	–	–	7.55×10^{6}	2.31
31	Propylene glycol	3.95	1.31×10^{8}	40.1	–	–	7.70×10^{7}	23.6	–	–	–	–
32	Pyridine	3.99	1.56×10^{8}	47.8	–	–	2.53×10^{8}	77.4	–	–	–	–
33	Toluene	4.36	2.52×10^{8}	77.1	2.29×10^{10}	7017	6.41×10^{9}	1961	8.78×10^{8}	269	1.23×10^{9}	375
34	Pentan-1-ol	4.45	–	–	5.14×10^{9}	1572	1.25×10^{8}	38.3	1.49×10^{7}	4.56	2.62×10^{7}	8.00
35	Cyclopentanone	4.72	–	–	–	–	–	–	5.36×10^{6}	1.64	–	–
36	*N*,*N*-Dimethylformamide	4.76	2.20×10^{7}	6.72	–	–	4.06×10^{7}	12.4	5.50×10^{7}	16.8	–	–
37	Oct-1-ene	4.85	1.08×10^{8}	33.0	–	–	–	–	–	–	–	–
38	Hexanal	4.94	3.44×10^{8}	105	4.22×10^{9}	1293	1.16×10^{9}	354	3.47×10^{8}	106	8.04×10^{8}	246
39	n-Octane	5.08	–	–	1.37×10^{8}	42.0	–	–	2.40×10^{7}	7.33	–	–
40	Tetrachloroethene	5.21	1.76×10^{6}	0.54	8.81×10^{7}	26.9	2.62×10^{7}	8.01	7.47×10^{6}	2.29	–	–
41	Furfural	5.23	3.03×10^{6}	0.93	–	–	2.71×10^{5}	0.08	2.68×10^{6}	0.82	–	–
42	n-Butyl acetate	5.33	–	–	1.09×10^{9}	332	1.18×10^{8}	36.2	1.16×10^{8}	35.6	–	–
43	1-Methoxy-2-propyl acetate	5.87	7.59×10^{7}	23.2	–	–	–	–	–	–	–	–
44	Chlorobenzene	5.94	6.62×10^{6}	2.03	–	–	1.15×10^{7}	3.53	5.34×10^{6}	1.63	8.60×10^{6}	2.63
45	2-Methylpropanoic acid	6.10	1.42×10^{7}	4.34	1.11×10^{7}	3.38	–	–	1.33×10^{7}	4.06	9.29×10^{5}	0.28
46	Ethylbenzene	6.28	1.65×10^{8}	50.5	9.99×10^{8}	306	5.17×10^{8}	158	3.10×10^{8}	94.8	2.30×10^{8}	70.3
47	*o*-Xylene	6.46	5.31×10^{8}	162	2.44×10^{9}	747	2.31×10^{9}	706	1.42×10^{9}	433	5.02×10^{8}	154
48	Vinyl acetate	6.47	1.04×10^{8}	31.7	2.26×10^{7}	6.91	–	–	–	–	–	–
49	Di-n-butyl ether	6.77	4.59×10^{8}	141	–	–	–	–	–	–	–	–
50	Cyclohexanone	6.86	5.47×10^{10}	16738	1.70×10^{11}	51989	1.35×10^{11}	41310	1.01×10^{11}	30845	2.56×10^{11}	78428
51	Styrene	6.92	1.86×10^{8}	56.9	–	–	2.43×10^{8}	74.3	5.39×10^{7}	16.5	–	–
52	n-Heptanal	7.09	7.08×10^{7}	21.7	–	–	1.97×10^{8}	60.3	–	–	–	–

Table A1: Compound identities, peak sums and masses (as toluene equivalents) found in Samples A–E.[9] *(Continued on next page)*

No.	Target compound	t_R (min)	A		B		C		D		E	
			Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)	Peak sum (TIC)	Mass (ng)
53	2-Butoxyethanol	7.24	1.26×10^{9}	384	2.54×10^{9}	777	1.25×10^{9}	381	3.54×10^{7}	10.8	–	–
54	Cumene	7.65	1.74×10^{8}	53	1.27×10^{10}	3898	5.77×10^{9}	1765	6.05×10^{8}	185	2.55×10^{9}	781
55	1,4-Dichlorobut-2-ene	7.67	–	–	–	–	–	–	1.52×10^{7}	4.65	–	–
56	Hexylene glycol	7.72	3.51×10^{8}	107	–	–	–	–	–	–	–	–
57	Indene	7.78	–	–	1.27×10^{7}	3.90	–	–	2.08×10^{6}	0.64	7.70×10^{6}	2.36
58	*trans*-Hept-2-enal	7.79	–	–	–	–	1.69×10^{8}	51.8	–	–	–	–
59	α-Pinene	7.92	8.90×10^{8}	272	–	–	–	–	1.89×10^{8}	57.8	1.35×10^{9}	412
60	2-Ethylhexanal	8.24	1.09×10^{9}	333	1.88×10^{9}	574	1.54×10^{9}	472	9.76×10^{8}	299	–	–
61	Camphene	8.28	–	–	–	–	–	–	–	–	1.33×10^{8}	40.7
62	n-Propylbenzene	8.28	2.99×10^{8}	91.4	9.93×10^{7}	30.4	2.53×10^{8}	77.3	4.76×10^{7}	14.56	2.31×10^{7}	7.06
63	Benzaldehyde	8.34	5.36×10^{8}	164	6.32×10^{8}	193	1.17×10^{9}	358	1.37×10^{8}	41.9	1.81×10^{8}	55
64	*m*-Ethyltoluene	8.45	1.24×10^{9}	379	3.20×10^{8}	97.9	–	–	1.82×10^{8}	55.6	–	–
65	*o*-Ethyltoluene	8.50	–	–	–	–	–	–	–	–	7.01×10^{7}	21.5
66	1,3,5-Trimethylbenzene	8.60	1.74×10^{9}	532	1.88×10^{8}	57.5	1.53×10^{9}	469	–	–	–	–
67	β-Pinene	8.83	4.78×10^{8}	146	–	–	4.14×10^{8}	127	–	–	1.23×10^{8}	37.6
68	α-Methylstyrene	8.96	–	–	9.73×10^{8}	298	4.07×10^{8}	125	7.82×10^{7}	23.9	–	–
69	Phenol	9.12	–	–	–	–	4.95×10^{8}	151	1.47×10^{8}	45.0	3.54×10^{8}	108
70	n-Decane	9.31	1.30×10^{9}	396	9.34×10^{8}	286	2.73×10^{9}	836	2.58×10^{8}	79.1	–	–
71	1-(2-Methoxy-1-methylethoxy)propan-2-ol	9.35	2.08×10^{8}	63.7	–	–	1.75×10^{8}	53.6	–	–	–	–
72	*p*-Dichlorobenzene	9.56	–	–	4.92×10^{7}	15.0	–	–	–	–	–	–
73	2-Methylaziridine	9.57	–	–	–	–	–	–	3.91×10^{6}	1.20	3.01×10^{7}	9
74	2-Methoxypropan-1-ol	9.60	1.63×10^{8}	49.9	–	–	1.41×10^{8}	43.1	–	–	–	–
75	3-Carene	9.62	–	–	1.51×10^{8}	46.1	8.35×10^{8}	256	2.47×10^{8}	75.5	8.53×10^{8}	261
76	*p*-Isopropyltoluene	9.84	–	–	–	–	3.88×10^{8}	119	–	–	–	–
77	*o*-Cymene	9.85	3.75×10^{8}	115	2.32×10^{8}	70.9	–	–	1.23×10^{8}	37.5	1.23×10^{10}	3749
78	Dimethyl butanedioate	9.91	–	–	7.29×10^{7}	22.3	–	–	–	–	–	–
79	2-Ethylhexan-1-ol	10.00	1.09×10^{11}	33385	3.04×10^{10}	9312	1.24×10^{11}	37883	2.55×10^{10}	7797	2.52×10^{10}	7708
80	1,4-Dichlorobenzene	10.05	–	–	–	–	6.16×10^{6}	1.89	1.98×10^{6}	0.61	–	–
81	Cyclopropylbenzene	10.07	–	–	5.22×10^{7}	16.0	–	–	5.07×10^{7}	15.5	–	–
82	Acetophenone	10.61	–	–	1.07×10^{10}	3268	7.69×10^{9}	2353	2.01×10^{9}	616	2.09×10^{9}	640
83	Nitrobenzene	10.96	6.78×10^{8}	208	–	–	6.76×10^{8}	207	–	–	–	–
84	n-Undecane	11.35	1.53×10^{10}	4679	–	–	1.57×10^{10}	4804	–	–	–	–
85	Nonanal	11.37	–	–	–	–	–	–	–	–	1.68×10^{9}	514
86	1,2,4,5-Tetramethyl-benzene	11.72	2.07×10^{9}	635	4.00×10^{8}	122	2.01×10^{9}	615	–	–	–	–
87	2-Ethylhexyl acetate	12.28	–	–	–	–	–	–	–	–	5.35×10^{8}	164
88	Naphthalene	12.99	–	–	–	–	–	–	–	–	8.61×10^{7}	26.3
89	n-Dodecane	13.24	2.20×10^{10}	6744	2.32×10^{9}	709	2.39×10^{10}	7323	–	–	8.42×10^{8}	258
90	n-Tridecane	14.98	1.19×10^{10}	3654	2.57×10^{8}	78.6	1.10×10^{10}	3366	1.81×10^{8}	55.3	1.63×10^{8}	49.8
91	(Cyclohex-3-enyl)benzene	15.63	–	–	1.15×10^{7}	3.52	–	–	–	–	–	–
92	n-Tetradecane	16.62	1.66×10^{9}	508	4.45×10^{8}	136	1.96×10^{9}	599	8.97×10^{7}	27.5	1.64×10^{8}	50.2
93	Longifolene	16.93	6.78×10^{7}	20.8	7.77×10^{7}	23.8	7.97×10^{7}	24.4	–	–	–	–
94	Butylated hydroxy toluene	18.44	–	–	4.25×10^{6}	1.30	–	–	4.11×10^{7}	12.6	–	–
95	Dibenzofuran	18.52	–	–	8.97×10^{5}	0.27	2.39×10^{6}	0.73	9.98×10^{5}	0.31	3.48×10^{6}	1.07
96	Diethyl phthalate	19.49	5.87×10^{8}	180	1.27×10^{6}	0.39	4.78×10^{8}	146	–	–	–	–
97	n-Hexadecane	19.64	1.84×10^{8}	56.4	9.46×10^{7}	29.0	2.00×10^{8}	61.1	–	–	–	–
98	Phenanthrene	20.59	–	–	–	–	1.89×10^{6}	0.58	–	–	–	–
99	2-Chloroacetophenone	22.56	2.92×10^{7}	8.95	6.56×10^{5}	0.20	4.09×10^{7}	12.5	1.12×10^{6}	0.34	1.44×10^{6}	0.44
100	Cyclododecane	23.36	7.58×10^{7}	23.2	–	–	–	–	–	–	1.22×10^{8}	37.4
101	Decan-1-ol	23.42	–	–	–	–	2.30×10^{7}	7.02	–	–	–	–
102	Di-n-butyl phthalate*	24.32	1.59×10^{6}	0.49	–	–	6.29×10^{5}	0.19	4.28×10^{5}	0.13	9.58×10^{5}	0.29
103	Bis(2-ethylhexyl) phthalate	30.54	2.58×10^{9}	789	–	–	1.74×10^{9}	533	5.95×10^{9}	1822	8.46×10^{9}	2589
Total number of compounds			**59**		**52**		**57**		**54**		**47**	

Table A1 *(Continued from previous page)* * Due to the nature of the mass spectrum, the identification of this compound was tentative.