# Development of an SI-traceable transmission curve reference material to improve quantitation and comparability of PTR-MS~~proton transfer reaction mass spectrometry~~ measurements

David R. Worton[1], Sergi Moreno[1,#], Kieran O'Daly[1], Rupert Holzinger[2]

[1] National Physical Laboratory, Hampton Road, Teddington, TW11 0LW, United Kingdom

[2] Institute for Marine and Atmospheric Research, IMAU, Utrecht University, Utrecht, the Netherlands

*Correspondence to*: David R. Worton (dave.worton@npl.co.uk)

[#] Now at World Meteorological Organization (WMO), 7bis Avenue de la Paix, C.P. 2300
CH-1211, Geneva 2, Switzerland

**Abstract.** Since its inception more than two decades ago proton-transfer-reaction mass-spectrometry (PTR-MS) has established itself as a powerful technique for the measurements of a wide range of volatile organic compounds (VOCs) with ~~providing~~ high time resolution and low detection limits and ~~, high sensitivity measurements~~ without the need for any sample pre-treatment. As this technology has matured and its application become more widespread there is a growing need for accurate and traceable calibration to ensure measurement comparability. As a result of the large number of VOCs detectable with PTR-MS it is impractical to have a calibration standard or standards that cover all observable compounds. However, recent work has demonstrated that quantitative measurements of uncalibrated compounds are possible provided that the transmission curve is accurately~~sufficiently~~ constrained. To enable this, a novel traceable multi-component gas reference material containing 20 compounds spanning ~~that spans~~ a mass range of ~~the molecular weight range of~~ 32 to 671 has been developed. The~~is~~ development and ~~the~~ compositional evolution of this reference material ~~are~~ is described along with an evaluation of ~~the~~ its accuracy and stability. This work demonstrates that for the majority of components the accuracy is < 5 % (most < 3 %; < 10 % for hexamethylcyclotrisiloxane (D3-siloxane) and 1,2,4-trichlorobenzene (1,2,4-TCB)) with stabilities of > 2 years (> 1 year for acetonitrile, methanol and perfluorotributylamine (PFTBA)).

## 1 Introduction

Proton-transfer-reaction mass-spectrometry (PTR-MS) is a technique that allows simultaneous measurements of multiple volatile organic compounds (VOCs) in real-time (≤ 1 s) with low detection limits ~~high sensitivity~~ (pmol mol$^{-1}$) and without

any sample pre-treatment (Lindinger et al., 1998; Hansel et al., 1999). Most VOCs, with the exception of alkanes with less than five carbon atoms, have proton affinities larger than water ($691 \pm 3$ kJ mol$^{-1}$) and are therefore detectable with PTR-MS. Also, because most VOCs have proton affinities below 900 kJ mol$^{-1}$ there is minimal excess energy following proton transfer resulting in minimal fragmentation. For these reasons it is a very convenient measurement technique for a wide range of applications. ~~OAs a result, o~~ver the last two decades PTR-MS has ~~developed to~~ become an important and widely applied ~~tool~~method for VOC measurements that has resulted in major advances in the field of atmospheric sciences (De Gouw and Warneke, 2007; Park et al., 2013; Yuan et al., 2017). It has also been applied in the medical sector ~~and food and beverage fields~~ for the detection of VOCs to d~~iagnose~~ ~~etect~~ diseases or disease states (Beauchamp et al., 2013) and in the food and beverage industry for characterising flavour and odour (Biasioli et al., 2011).

Multiple manufacturers now produce and commercially sell PTR-MS instruments globally that differ in the production and detection of ions including different types of mass spectrometer. Therefore, as its application becomes more widespread, and more datasets are generated there is an increasing need for accurate calibration and measurement comparability. Additionally, as part of the European funded Aerosols, Clouds and Trace Gases Infrastructure (ACTRIS) project (https://www.actris.eu/) there is an interest to establish PTR-MS as a technique for long-term monitoring of VOCs, which emphasises the need for a robust metrological infrastructure to control and assure the quality of data produced by monitoring stations performing these measurements. However, the lack of traceable reference materials to calibrate PTR-MS instruments presents challenges in the pursuit of obtaining comparable results and is an obstacle to ~~for~~ long-term studies. Primary~~Gas~~ reference materials (PRMs) prepared by gravimetry in high pressure cylinders ~~like those produced~~ by national metrology institutes (NMIs) underpins the accuracy (trueness) and comparability of measurement data through~~provide the~~ ~~necessary~~ traceability to the international system of units (SI). Traceability has been demonstrated as a critical component for chemical measurements that ensures the comparability, stability and coherence in measurements providing ~~ensuring~~ confidence in measurement results~~that data is accurate and comparable~~ (Brown and Milton, 2007). ~~These primary reference materials (PRMs)~~ produced by ~~the~~ NMIs represent the highest point in the traceability chain and the accuracy and international comparability is ensured through key comparisons organised within the Consultative Committee on Amount of Substance Gas Analysis Working Group (CCQM-GAWG) and in regional comparisons organised within the Regional Metrology Organisations (RMOs), e.g., EURAMET (Europe).

As a result of the ~~large number of potential~~numerous VOCs detectable with PTR-MS it is impractical to have a calibration standard or standards that cover all observable compounds. However, since the conception of PTR-MS, there has been awareness for the potential of this technique to provide quantitative measurements for compounds without the need for specific calibration materials (Hansel et al., 1999). The basis for this is that the amount fraction of compound R ([R]) can be determined from (Taipale et al., 2008):

$$[R] = \frac{1}{k\Delta t} \times \frac{I(RH^+)}{T(RH^+)} \times \left(\frac{I(H_3O^+)}{T(H_3O^+)}\right)^{-1} \qquad \text{Eq. 1}$$

Where k is the proton transfer reaction rate coefficient, $\Delta t$ is the reaction time, $I(RH^+)$ and $I(H_3O^+)$ are the observed ion count rates for the protonated ion of compound R ($RH^+$) and the hydronium ion ($H_3O^+$), respectively. $T(RH^+)$ and $T(H_3O^+)$ are the transmission efficiencies for $RH^+$ and $H_3O^+$ ions, respectively. The transmission coefficients are predominantly mass dependent, but they can also vary in time (De Gouw et al., 2003; Ammann et al., 2004; Steinbacher et al., 2004). Proton transfer reaction rate coefficients can be measured and/or predicted using quantum methods (Zhao and Zhang, 2004). If specific rate coefficients are agreed within the community for specific compounds and are widely used this would negate the role of different rate constants on measurement comparability (Table S1, Supporting Information). The reaction time and observed ion count rates are all measured parameters leaving just the transmission coefficients as variables required for quantitative measurements without specific calibrations. Cappellin et al. (2012) demonstrated the quantitative properties of one type of PTR-MS instrument by assuming a theoretical transmission based on the duty cycle of the time-of-flight mass analyser. However, for newer generation instruments that employ advanced ion optics to improve sensitivity, it is necessary to determine the mass-dependent transmission experimentally as the transmission of the system diverges from theory at low masses. Deviations can also occur at high masses due to poor tuning and/or ageing of the ion detection system (Müller et al., 2014).

There are several highly cited publications that explore best practices in PTR-MS measurements (e.g., Blake et al., 2009; De Gouw and Warneke, 2007; Yuan et al., 2017), including methods to calibrate and retrieve the mass dependent transmission (Taipale et al., 2008). However, many of these methods are slow and labour intensive and as a result calibrations and transmission curve retrievals are not performed frequently enough. This has limited the application of PTR-MS to mostly short campaign-scale intensive deployments and only a few groups have utilised PTR-MS for long-term studies (Holzinger et al., 2006; Taipale et al., 2008). However, rRecent work by Holzinger et al., (2019) has demonstrated: (i) a new method to retrieve the mass-dependent transmission from fast calibrations that should enable more frequent calibrations and (ii) the validity of a simple reaction kinetics approach to that a simple reaction kinetics model can accurately quantify measurements of uncalibrated compounds from different PTR-MS instruments with an accuracy of ≤ 30 % predict the sensitivities of different PTR-MS instruments provided the transmission curve was sufficiently constrained (Holzinger et al., 2019). provided the transmission curve is accurately constrained. This permits the quantification of measurements of uncalibrated compounds with an accuracy of ≤ 30 %. A prototype PRM, -0917a reported in this work, to constrain the transmission curve was initially developed by the National Physical Laboratory (NPL) and employed for the PTR-MS intercomparison campaign at the CESAR observatory in the central Netherlands (Holzinger et al., 2019), this is NPL PRM A574 reported in this work. Following this comparison exercise improvements to the composition were recommended needed to include additional compounds in the mass-to-charge (m/Q) 150 – 400 Th range to provide a more robust retrieval of the mass-dependent transmission.

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95   In this paper, the development and compositional evolution of ~~an NPL~~ PRMs and certified reference materials (CRMs) specific

96   for constraining the PTR-MS transmission curve ~~is~~ are described, including an evaluation of the accuracy through comparisons

97   validating the gravimetric preparation of various different PRMs~~mixtures~~ of similar composition and an assessment of their

98   long-term stabilities. For details on how to use the RMs to constrain the PTR-MS transmission curve the reader is directed to

99   H


## 2 Experimental methods

### 2.1 Gravimetric preparation of primary reference materials

102   The ~~NPL primary reference materials (~~PRMs~~)~~ were prepared at four distinct timepoints (September 2017, December-January

103   2018, August 2019 and August 2021) and the compositions evolved over this timeframe (Table 1) due to improvements in the

104   preparation and validation techniques (e.g., 1,2,4-trichlorobenzene; 1,2,4-TCB) or due to requests from the PTRMS

105   community for inclusion of new components (e.g., dimethyl sul~~f~~phide; DMS). All the ~~NPL~~ PRMs were prepared

106   gravimetrically in accordance with ISO 6142-1:2015 (ISO, 2015) from pure components. All pure components were purity

107   analysed in accordance with ISO 19229 (ISO, 2019). Table S2~~1~~ (Supporting Information) provides the sources and purities

108   for each component and shows that all chemicals with the exception of perfluorotributylamine (PFTBA) were ≥ 98 % pure.

109   Table S2 (Supporting Information) also shows the boiling points and vapour pressures for all compounds. All components

110   were liquids at room temperature and pressure, with the exception of propane (gas) and hexamethylcyclotrisiloxane (D3-

111   siloxane; solid). As a solid under room temperature and pressure conditions, D3-siloxane needed to be dissolved into a solvent

112   to enable its addition to the cylinder. Further details are given in the Supporting Information ~~(see details in the Supporting~~

113   ~~Information~~Supplementary text: Preparation of D3-siloxane reference materials).

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115   All ~~NPL~~ PRMs were prepared in 10 L aluminium cylinders (Luxfer) with a proprietary passivation treatment (Spectraseal™,

116   BOC) and BS341 no. 15 outlet diaphragm valves (Ceodeux). Cylinders were evacuated using an oil free pump (Scrollvac

117   SC15D, Leybold Vacuum) and turbo molecular pump with magnetic bearing (Turbovac 340M, Leybold Vacuum) to a pressure

118   of $< 3 \times 10^{-7}$ mbar. Individual compounds were added to the evacuated cylinder via a transfer vessel (capped $^1/_8$" diameter

119   tube, with a nominal volume of 1 mL, Swagelok, electro-polished stainless steel). The transfer vessel was weighed against a

120   tare vessel matched for size and shape before and after each addition into the evacuated cylinder (Mettler-Toledo XP2004S).

121   The ultra-high purity nitrogen balance gas (BIP$^+$, Air Products) was added via direct addition to the cylinder, through purged

122   $^1/_{16}$" tubing (Swagelok, electro-polished stainless steel). For the vast majority of compounds, they were initially produced as

123   binary parent mixtures at amount fractions > 10 μmol mol$^{-1}$ (typically at nominally 50 μmol mol$^{-1}$) though some were produced

124   as ternary or quaternary mixtures containing two or three compounds together in the same parent mixture. A full breakdown

125   of the 50 parent mixtures used to prepare~~for each of~~ the six ~~NPL~~ PRMs developed in this work are shown in Table 2. Aliquots

126  of each of these parent mixtures were added by direct addition to an evacuated cylinder to produce a final mixture containing

127  all 16 to 20 VOCs at nominal amount fractions of 1 µmol mol$^{-1}$ in a balance of nitrogen. (Lee et al., 2022)

**Table 1.** Overview of composition (name, formula, CAS#), and the protonated monoisotopic molecular ion (MH+), and any major fragment ions, formed following protonation in $H_3O^+$ mode) for 20 compounds included in the of the PRM and CRM PTRMS transfer curve reference materials, including the analytical technique used to validate, sources and purities of the pure chemicals and the key comparisons through which the traceability to the international community is derived.

| Compound[a] | Formula | CAS # | m/Q[Th] | | Traceability (Reference, if applicable) |
|---|---|---|---|---|---|
| | | | protonated | fragments | |
| methanol | CH₃OH | 67-56-1 | 33.033 | - | EURAMET-1305 OVOCs (Worton et al., 2022), CCQM-K174[b] |
| acetonitrile | CH₃CN | 75-05-8 | 42.034 | - | CCQM-K174[b] |
| acetaldehyde | CH₃CHO | 75-07-0 | 45.033 | - | CCQM-K174[b] |
| Propane[d] | C₃H₈ | 74-98-6 | not detected- | - | CCQM-K111 (Veen et al., 2017) |
| ethanol | C₂H₅OH | 64-17-5 | 47.049 | - | CCQM-K93 (Brown et al., 2013), EURAMET-1305 OVOCs (Worton et al., 2022), CCQM-K174[b] |
| acetone | CH₃OCH₃ | 67-64-1 | 59.049 | - | EURAMET-1305 OVOCs (Worton et al., 2022), CCQM-K174[b] |
| DMS | C₂H₆S | 75-18-3 | 63.026 | - | CCQM-K94 (Lee et al., 2016), CCQM-K165 (Lee et al., 2022)[c] |
| isoprene | C₅H₈ | 78-79-5 | 69.070 | 41.039 | EURAMET-886 (Grenfell et al., 2008; Grenfell et al., 2010) |
| MVK | C₄H₆O | 78-94-4 | 71.049 | - | CCQM-K174[b] |
| MEK | C₄H₈O | 78-93-3 | 73.065 | - | CCQM-K174[b] |
| benzene | C₆H₆ | 71-43-2 | 79.054 | - | CCQM-K10.2018 (Cecelski et al., 2022) |
| toluene | C₇H₈ | 108-88-3 | 93.07 | - | CCQM-K10.2018 (Cecelski et al., 2022) |
| m-xylene | C₈H₁₀ | 108-38-3 | 107.086 | - | CCQM-K10.2018 (Cecelski et al., 2022) |
| 1,2,4-TMB | C₉H₁₂ | 95-63-6 | 121.101 | - | EURAMET-886 (Grenfell et al., 2008; Grenfell et al., 2010) |
| 1,2,4-TFB | C₆H₃F₃ | 367-23-7 | 133.026 | - | - |
| 3-carene | C₁₀H₁₅ | 13466-78-9 | 137.132 | 81.070 | CCQM-K121 (Liaskos et al., 2018) |
| 1,2,4-TCB | C₆H₃Cl₃ | 120-82-1 | 180.937 | - | - |
| D3-siloxane[d] | C₆H₁₈O₃Si₃ | 541-05-9 | 223.064 | 207.033, 225.033[e] | EURAMET 1305 Siloxanes[d] |
| D4-siloxane[d] | C₈H₂₄O₄Si₄ | 556-67-2 | 297.082 | 281.051, 283.030,299.062[e] | EURAMET 1305 Siloxanes[d] |
| D5-siloxane[e] | C₁₀H₃₀O₅Si₅ | 541-02-6 | 371.101 | 355.070, 373.081[e] | EURAMET 1305 Siloxanes[b] |
| PFTBA | C₁₂F₂₇N | 311-89-7 | not detected | 651.961, 413.977 | - |

[a]Short names shown here but preferred full IUPAC names are: propan-2-one (acetone), (Methylsulfanyl)methane (dimethyl sulfide; DMS), 2-Methylbuta-1,3-diene (isoprene), but-3-en-2-one (methyl vinyl ketone; MVK), butan-2-one (methyl ethyl ketone; MEK), 1,2,4-trimethyl benzene (1,2,4-TMB), 1,2,4-trifluoro benzene (1,2,4-TFB), 3,7,7-trimethylbicyclo[4.1.0]hept-3-ene (3-carene), 1,2,4-trichlorobenzene (1,2,4-TCB), hexamethylcyclotrisiloxane (D3-siloxane), octamethylcyclotetrasiloxane (D4-siloxane), decamethylcyclopentasiloxane (D5-siloxane), and perfluorotributylamine (PFTBA). [b]Comparison in progress at the time of publication. [c]Not detectable in PTRMS in H₃O⁺ mode but included as an internal standard. [d]Further information on the mechanisms yielding product ions and fragments in Fig. S4 (Supporting Information). Comparison in progress at the time of publication. [e]Methyl/hydroxyl group switch.

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**Table 2.** Composition, hierarchies and parent cylinder IDs (dates prepared) for all components for the six ~~NPL~~ PRMs (~~0917a, 0917b, 1218, 0119, 0819 and 0821,~~A574, A578, A574, A578, A638, A643, 2819 and D961492) prepared in this work. The PRMs are identified by the date and year of their preparation (MMYY). As the first two were produced at the same time the suffices a and b and added to distinguish them. The colour scheme in the table headers is matched to that used in the figures throughout the paper.

| Compound | 0917a A574 (18/09/2017) | 0917b A578 (18/09/2017) | 1218 A638 (04/12/2018) | 0119 A643 (02/01/2019) | 0819 A581 (23/08/2019) | 0821 D961492 (31/08/2021) |
|---|---|---|---|---|---|---|
| methanol | A463 (13/02/2015) | | | | A410 (24/01/2013) | A602 (26/04/2018) |
| acetonitrile | A389R (11/02/2015) | | | | A403 (11/10/2012) | A670R (01/04/2021) |
| acetaldehyde | A400R (02/02/2015) | | | | A402 (11/10/2012) | 2832 (01/04/2021) |
| propane | D910381R (18/11/2014) | | | | NG561 (16/10/2014) | - |
| ethanol | A463 (13/02/2015) | | | | A410 (24/01/2013) | A602 (26/04/2018) |
| acetone | A463 (13/02/2015) | | | | VOC6 (05/05/2009) | A602 (26/04/2018) |
| DMS | - | | 2106 (21/02/2017) | | NG388 (13/09/2012) | 3073 (16/11/2020) |
| isoprene | D292194R (13/01/2011) | | | | VOC6 (05/05/2009) | D994138R2 (28/09/2020) |
| MVK | 2064 (24/06/2016) | | | | 2088 (24/06/2016) | 3070 (02/08/2021) |
| MEK | A389R (11/02/2015) | | | | A403 (11/10/2012) | 3070 (02/08/2021) |
| benzene | D910381R (18/11/2014) | | | | D842635R (13/10/2015) | D618317 (15/08/2018) |
| toluene | | | - | | | D600070 (19/03/2018) |
| m-xylene | D641688 (04/03/2010) | | D618307 (19/03/2018) | | D994171 (20/03/2013) | D618307 (19/03/2018) |
| 1,2,4-TMB | D442684 (02/03/2017) | | | D711530 (26/11/2018) | | D442684 (02/03/2017) |
| 1,2,4-TFB | A569 (11/09/2017) | | | | 2810 (21/08/2019) | D723197R (14/06/2021) |
| 3-carene | D090493 (18/11/2014) | | | D711532 (21/11/2018) ~~D711532 (21/11/2018)~~ | | |
| 1,2,4-TCB | | | D641970R (31/07/2018) | A568 (18/08/2017) | | D723197R (14/06/2021) |
| D3-siloxane | - | - | 2586 (07/11/2018) | 2693 (07/11/2018) | 2586 (07/11/2018) | 3134 (22/06/2021) |
| D4-siloxane | A582 (15/08/2017) | A567 (18/08/2017) | - | - | A582 (15/08/2017) | A629R (22/06/2021) |
| D5-siloxane | A582 (15/08/2017) | A567 (18/08/2017) | A629 (26/11/2018) | | A582 (15/08/2017) | A629R (22/06/2021) |
| PFTBA | | | | | - | D961497 (30/07/2021) |

Cylinder ID (Date Prepared)

## 2.2 Analytical methods

To perform the analytical~~-~~ validation a method was developed on a gas chromatograph (GC; Agilent Technologies 7890) instrument equipped with both a flame ionisation detector (FID) and electron ionisation (70 eV) mass spectrometer (Agilent 5975; GC-FID/MS system). Samples were introduced using a 6 port 2 position valve (VICI) and a fixed sampling loop (1 mL). The column effluent was split to both detectors simultaneously by using ~~, through the use of~~ a detector splitter plate (Agilent Technologies). Separation was achieved for all components using a DB-624 capillary column (J&W; 75m × 0.53 mm, df = 3 µm)~~, although 3-carene and 1,2,4-TMB were not baseline separated~~. The carrier gas was helium and the flow was held constant at 5 mL min⁻¹, with a temperature program starting at 30 °C held for 10 minutes, ramped at 10 °C min⁻¹ to 120 °C and held for 15 minutes before a final ramp of 50 °C min⁻¹ was applied to a final temperature of 200 °C, which was held for a further 10 minutes. The total run time was 46 minutes.

Low FID responses for methanol and acetaldehyde presented some analytical challenges ~~for validation work~~ because ~~as~~ the observed peaks were too small to achieve useable results due to poor reproducibility. As a result, another analytical method was developed on a second GC-FID instrument without an MS (Scion 456; Cryo-GC-FID system) that ha~~dd~~ a pre-concentration ~~loop~~ trap (15 cm of 1/8" tubing; 1 mL volume) packed with glass beads and cooled with liquid nitrogen that enabled trapping of larger volume samples yielding larger peaks and improved repeatability for ~~these~~ all three compounds. The pre-concentration trap was held at -185 °C for 2 mins during sampling prior to being heated to 200 °C and backflushed with carrier gas during the desorption cycle. Separation was achieved using a Rtx-624 capillary column (Restek; 105m × 0.32 mm, df = 1.8 µm). The carrier gas was hydrogen and the flow rate was held constant at 1 mL min⁻¹, with a temperature program starting at 30 °C held for 5 minutes, ramped at 25 °C min⁻¹ to 200 °C with a final hold of 25 minutes. The total run time was 42 minutes.

Figure 1 shows the chromatograms obtained from both instruments (cryo-GC-FID, blue; GC-MS/FID, red) and demonstrates that all compounds, with the exception of 1,2,4-trimethyl benzene (1,2,4-TMB) and 3-carene, and acetone and dimethyl sulfide (DMS), were baseline separated. The chromatogram in Fig. 1 shows a valley between the 1,2,4-TMB and 3-carene peaks and between the acetone and DMS peaks that provides sufficient separation to obtain robust and repeatable peak areas for all four compounds.

**Figure 1.** Chromatogram of ~~NPL~~ PRM 0819~~2819~~ showing separation of compounds in the GC-FID/MS (~~thin~~ red trace) and cryo-GC-FID (~~thick~~ blue trace).
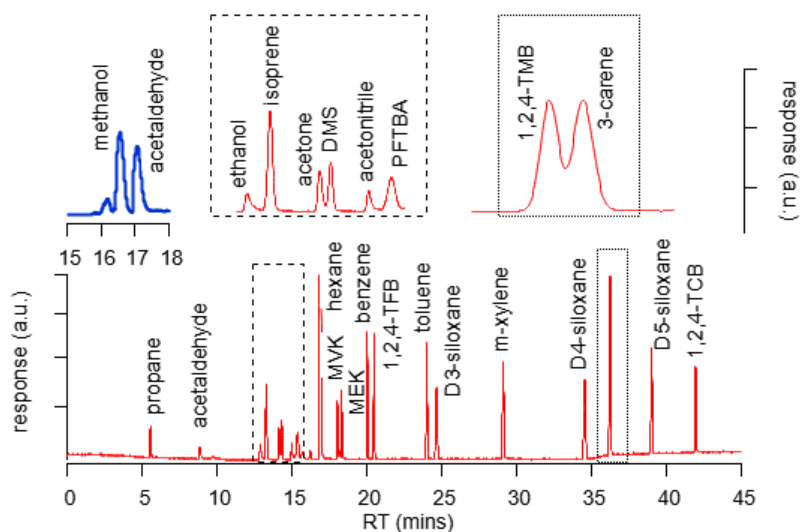


## 2.3 Stability assessment

Stability of all six ~~NPL~~ PRMs were assessed by tracking the ratios of the FID responses of each component relative to an internal reference that was present in every mixture and which is known to be stable (Rhoderick, 2010; Rhoderick and Lin, 2013; Worton et al., 2022). Propane was originally included as an internal tracer to monitor stability but as the PTR-MS in $H_3O^+$ mode cannot detect this compound it was replaced by benzene. Benzene is a good internal tracer with stability of > 2 years that has been well demonstrated relative to propane and hexane for this cylinder type at 5 µmol mol$^{-1}$ with an uncertainty of 0.5 % (Rhoderick et al., 2019). A similar performance would be expected at 1 µmol mol$^{-1}$ and is demonstrated in this work albeit with an uncertainty of 1 % (Fig. S1~~2~~, Supporting Information).

All the measurements used for the stability analysis were collected on the same GC-FID/MS instrument with the exception of methanol and acetaldehyde (Cryo-GC-FID). Both instruments remained unchanged throughout the entire time-period of the measurements, which spanned more than 4 years. The observed responses for each compound were corrected for differences in the gravimetric amount fraction and ratioed against the response of the internal reference compound benzene, that was present in every mixture. The uncertainties in the observed ratios included uncertainties for the gravimetric preparation and

9

176 the repeatability of the analyses. The combined standard uncertainties were multiplied by a coverage factor of 2 ($k=2$) providing

177 a coverage probability of 95 %. The observed ratios were normalised to the average response of all data for that compound to

178 enable comparisons between compounds with different FID responses. For this analysis ~~all~~ the data for all six ~~NPL~~ PRMs

179 were considered together to enable an understanding of stability across a longer time period than would be possible for a single

180 PRM. Least squares fit straight-line regressions were modelled to the temporal evolution of the data to determine if there was

181 any statistically significant change in amount fraction of any of the compounds in the ~~NPL~~ PRMs. The slopes from these

182 regression analyses were evaluated with an analysis of variance (ANOVA) test using the 'StatsLinearRegression' function in

183 IGOR pro 8.04 (Wavemetrics) (Zar, 1999; Snedecor and Cochran, 1989) to determine whether they were significantly different

184 to zero using an $F$-test, i.e., no drift in amount fraction during the measurement period (F < Fc).

185

## 2.4 Validation approach

187 Five ~~All 5 NPL~~ PRMs (0917a, 0917b, 1218, 0119, 0819, and 0821~~A574, A578, A638, A643, D961492~~) were validated against

188 ~~NPL~~ PRM 0819~~2819~~ with the exception of PFTBA and toluene that were only present in the most recent ~~NPL~~ PRM

189 (0821~~D961492~~). ~~NPL~~ PRM 0819~~2819~~ was used as the reference for all the validations because the parents used for the

190 preparation of this mixture were deliberately different from all other mixtures with the explicit goal of enabling the most robust

191 validation. All compounds were analysed on the GC-FID/MS system, with the exception of methanol and acetaldehyde (Cryo-

192 GC-FID). Toluene was validated by comparison against an existing ~~NPL~~ PRM containing BTEX (benzene, toluene, *m*-xylene,

193 *p*-xylene and *o*-xylene) components that was prepared gravimetrically at NPL in 2018 and had been independently validated

194 against other PRMs that were internationally compared as part of NPL's participation in key comparison CCQM-K10.2018

195 (Cecelski et al., 2022). These BTEX PRMs are known to be stable for more than 5 years and at the time of the comparisons

196 the BTEX PRM was less than 3 years old. PFTBA was validated against the gravimetric data used to make two independent

197 certified reference materials. The majority of the validation work took place between September and December 2020 with

198 one in 2019 and 2022, respectively, and three in 2021 (~~see~~ Table S1~~3~~, Supporting Information). As such there is an influence

199 of stability on the validation data as the ~~PTRMS NPL~~ PRMs differed in age at the time of validation.

200

201 Each comparison was conducted by running the ~~NPL~~ PRMs (0917a, 0917b, 1218, 0119, and 0821~~A574, A578, A638, A643~~

202 ~~and D961492~~) against ~~NPL~~ PRM 0819~~2819~~ in a repeating alternating pattern, ((AB)$_n$A)$_n$ where A represents ~~NPL~~ PRM

203 0819~~2819~~ and B one of the other PRMs (*j*) and with the number of repeats ranging between 3 and 5 (n = 3 to~~–~~ 5). The ratio in

204 response was determined by dividing B by the average response of the A's immediately before and after each analysis of

205 B.~~bracketing between the nearest neighbours T~~and t~~he average ratio was calculated for each compound based on the number

206 of repeats along with the associated standard deviation. The assigned analytical value for compound *i* in ~~NPL~~ PRM *j* ($x_{u,i,j}$)

207 was calculated by multiplying the average ratio by the gravimetrical amount fraction ($x_{s,i}$) of compound *i* in ~~NPL~~ PRM

208  08192819. The relative difference ($\Delta x$) between the assigned analytical value and the gravimetric value of compound $i$ in NPL

209  PRM $j$ was calculated from:

210

211  $$\Delta x\ (\%) = \frac{(x_{u,i,j} - x_{s,i})}{x_{s,i}} \times 100 \hspace{3cm} \text{Eq. } 21$$

212

213  The uncertainty in the relative difference combined the standard uncertainty in the repeatability in the analysis with the

214  gravimetric uncertainty. The combined standard uncertainty was multiplied by a coverage factor of 2 ($k$=2) providing a

215  coverage probability of 95 %.


216  **3 Results**

217  **3.1 Composition**

218  The PTR-MS transmissionfor curve reference material contains 20 different VOCs that span a wide range of molecular masses,

219  boiling points, vapour pressures (Table S2, Supporting Information) from 32 to 671 and a range of functional group classes

220  including alcohol, aldehyde, ketone, alkene, aromatic, halocarbon and siloxane (Table 2). With the PTR-MS technique, most

221  VOCs are entirely detected at their protonated mass, as well as a few compounds that partially fragment during protonation

222  (e.g. monoterpenes, siloxanes, and isoprene; see Table 1). The compounds were chosen by considering the needs of the PTR-

223  MS user community to cover the full range of mass-to-charge ratios (m/Q) encountered, their low fragmentation following

224  proton transfer and because many are of relevance in atmospheric measurements, which was the initial intended target end

225  user group. Other compounds were included as a consequence of the preparation method, that is the case for of $n$-hexane,

226  which is present included as the solvent diluent for D3-siloxane, and or propane, which was present in one of the parent

227  premixtures and was originally included as an internal tracer to monitor stability. The composition evolved over time, as shown

228  in Table 2, with DMS, 1,2,4-TCB, D3-siloxane, toluene and PFTBA being added at different times, and propane being removed

229  in the final iteration. For D4-siloxane there was a preparation error, and it was not added to either NPL PRM 1218A638 or

230  0119A643.

231

232  An amount fraction of nominally 1 µmol mol$^{-1}$ in a balance gas of nitrogen was selected as a compromise between preparation

233  complexity and mixture stability. This amount fraction enabled many components to be prepared from parent mixtures of

234  higher amount fraction ($\geq$10 µmol mol$^{-1}$), which substantially simplifies the preparation process. This amount fraction also

235  provided a reasonable starting point for stability of the wide range of function groups present in the mixture some of which are

236  known to have more limited stability at lower abundances fractions (nmol mol$^{-1}$) (Allen et al., 2018).

**3.2 Traceability to the International System of Units (SI)**

Traceability of the primary realisations to the international community through CCQM key comparisons or regional EURAMET comparisons provides confidence in the accuracy of the amount fractions for all components. SI traceability is important for underpinning long-term measurements as it provides a stable anchor point with which to reference all measurements to. Table 1 shows which comparisons underpin the traceability for each of the different components. All the components are underpinned by at least one CCQM or EURAMET comparison with the exception of 1,2,4-TFB, 1,2,4-TCB and PFTBA, for which there are currently no existing relevant comparisons.

**3.3 Hierarchies**

Table 2 shows all the parent mixtures and their preparation dates used to prepare all six for the preparation of all 6 NPL PRMs (0917a, 0917b, 1218, 0119, 0819, and 0821) and i. In total , 50 different parent mixtures were used to produce the 6 NPL PRMs (A574, A578, A638, A643, 2819, D961492). In general, parent mixtures were similar for PRMs 0917a, 0917b, 1218 and 0119A574, A578, A638 and A638 but were different to PRMs 0819 and 08212819 and D961492 providing independence and thus confidence in the validation work and in thus the preparations. There were a few exceptions. For m-xylene the parent used for PRMs 1218 and 0119A638 and A643 wasere the same as PRM 0821D961492 but different to 0917a, 0917b and 0821A574, A578 and D961492. For 1,2,4-TMB only two parent mixtures were used one for 0917a, 0917b and 0821A574, A578 and D961492 and another for 1218, 0119 and 0819A638, A643 and 2819. For 3-carene only two parents were used one for 0917a and 0917bA574 and A578 and another for 1218, 0119, 0819 and 0821A638, A643, 2819 and D961492. For D3-siloxane three parents were used, one for 1218 and 0819A638 and 2819, one another for 0119A643 and another for 0821D961492.

**3.4 PRM Validation**

Figure 2 shows the relative differences ($\Delta x$) determined from Eq. 1 for all compounds using all the validation data obtained from the 13 comparisons outlined in Table S13 (Supporting Information). In the majority of cases PRM 0819 was used as the reference to which all others are compared. It was chosen as such because at that time it was the newest PRM to be produced and was used to benchmark all the others that had already been made. Thus, PRM 0821 was also referenced to PRM 0819 to provide a link between all six PRMs. All the data shown in Fig. 2 is the FID data from the GC-MS/FID instrument with the exception of acetonitrile (MS data from the GC-MS/FID instrument), methanol and acetaldehyde (FID data from the cryo-GC-FID instrument). The MS data is used for acetonitrile because the FID data shows a larger more variability, which is likely attributed to the co-elution of an impurity in the FID that was present at different amount fractions in the different PRMs but we do not have an conclusive evidence to support this and additional work is needed to confirm. This variability is not observed in the MS data providing better precision (Fig. S12, Supporting Information).

268 In general, the data from Fig. 2 could be split into three groups. The first group consisted of propane, isoprene, benzene,
269 toluene, 3-carene, methanol, acetonitrile, acetaldehyde, *m*-xylene, 1,2,4-TMB, MEK where the spread in the validation data is
270 within 3 % and these represent components where NPL had substantial prior experience. The second group is acetone, DMS,
271 MVK and PFTBA where the spread in the validation data is within 5 % and these are relatively new components where
272 capabilities were developed more recently. Recognising the challenges in preparing PRMs containing siloxanes as a result of
273 their low~~er~~ vapour pressures and observing the recent improvements in preparation since 2019, the D4-siloxane and D5-
274 siloxanes can also be categorised as group 2 after excluding the earliest parent preparations used for 0917a~~A574~~ and
275 0917b~~A578~~ in 2017, which are inconsistent with more recent work as part of the EURAMET 1305 Siloxanes comparison (Van
276 Der Veen et al., 2022). The final group is comprised of D3-siloxane and 1,2,4-TCB where the spread in validation data is
277 within 10 % and these compounds represent those which the most challenging to prepare as a result of either unique phase
278 transition properties or ~~their~~ low vapour pressures, respectively. There is an observable bias of about 8 % between two groups
279 of mixtures; one group is 1218~~A638~~ and 0819~~2819~~ and the other is 0119~~A643and,~~ 0821~~D961492~~. This reflects differences
280 between the parent mixtures (2586, 2693 and 3134) that resulted from the challenges in preparation. Ethanol also sits with this
281 group in part due to the small size of the peak observed in the GC-MS/FID instrument and because of what looks like an outlier
282 (0119~~A643~~), suggesting some potential losses during preparation that were unique to this one ~~NPL~~ PRM.
283
284 All the FID and supporting MS data for all compounds are shown in Fig. S1~~2~~ (Supporting Information). No MS data was
285 available for toluene, 1,2,4-TCB or PFTBA because the relevant single m/Q ions had not been included in the MS single ion
286 monitoring method at the time of analysis and methanol where the MS signal was too small to provide a reliable response.
287 Figure S1~~2~~ shows very good agreement between the FID and MS validation with all components agreeing within the
288 uncertainties providing confidence in the validation results.
289
290 In addition to the observed bias in parent mixtures for D3-siloxane three other parent mixtures were also discovered to be
291 biased after re-analysis. The observed differences have been corrected for in Fig. 2 and Fig. S1~~2~~ (Supporting Information). For
292 methanol, one parent (A410) was confirmed to be 5.0 % high relative to the other parents (A463, A540 and A602) For MVK,
293 one parent (3070) was confirmed to be 6.3 % low relative to the other parents (2064 and 2088). For 1,2,4-TMB, one parent
294 D711530 was confirmed to be 6.0 % low relative to D442684 and other in-house standards of 1,2,4-TMB not used in this work
295 but used to prepare 30 component ozone precursor mixtures at NPL (Grenfell et al., 2010).
296
297

**Figure 2.** Relative difference ($\Delta x$) using the FID data (except acetonitrile, which uses the MS data) for all components in ~~the~~ ~~five different~~ of the PRM~~sprimary reference materials~~ (0917a, 0917b, 1218, 0119 and 0821~~A574, A578, A638, A643 and D961492~~) relative to PRM~~primary reference material~~ 0819~~2819~~ (solid symbols). The solid black line represents the average of these validations with the error bar representing the associated expanded uncertainty ($2\sigma$). For D4- and D5-siloxane the averages do not include the validations from 0917a~~A574~~ or 0917b~~A578~~. Methanol and acetaldehyde data are from the cryo-GC-FID instrument while all others are from the GC-FID/MS instrument. Open symbols represent the original data before correcting for biases observed in three of the parent mixtures (A410, 5 % low for methanol; 3070, 6.3 % low for MVK and D711530 6 % low for 1,2,4-TMB). PFTBA and toluene were only included in the most recently prepared PRM (0821~~D961492~~) and are not present in 0819~~2819~~. Their validation is described in the text. Supporting validation data from all the MS and FID measurements is shown in Fig. S~~1~~2 (Supporting Information).
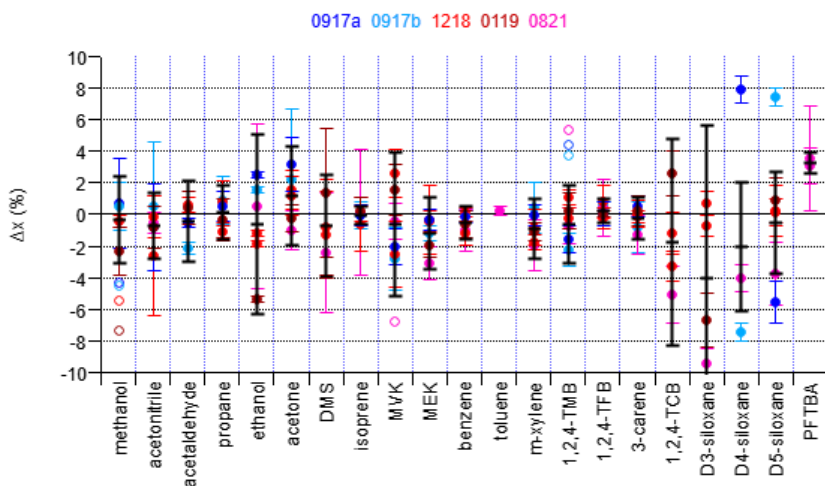


## 3.5 CRM Validation

To enable a more cost effective and timely delivery to end users a certified reference material (CRM) was also developed. In contrast to the PRMs the CRMs are not prepared by gravimetry but by the direct addition of multicomponent mixtures derived from the original pure liquids. Further details of the preparation method are given in the Supporting Information

315     (Supplementary text: Preparation and validation of certified reference materials). The amount fractions for the components in

316     the CRMs were assigned through analytical comparisons between each CRM and one or more of the PRMs. In this way,

317     preparation is quicker and more cost effective while maintaining the integrity of the values and their traceability. An additional

318     advantage of the CRMs is that because the solid D3-siloxane is dissolved in the other components no *n*-hexane is used which

319     avoids any potential interferences from the presence of reagent ions other than $H_3O^+$ like $O_2^+$ and $NO^+$. Initially with the

320     developed CRM preparation method it was possible to produce mixtures that had blend tolerances of 20 – 30 % (Fig. S3,

321     Supporting Information), which are suitable for end users but work is continuing to improve this with the aim of achieving

322     better than 10 % blend tolerances in the near future. The blend tolerances are just an indication of the repeatability of the

323     preparation process and do not reflect the uncertainties in the assigned value, which are between 3 – 10 % (compound

324     dependent). These uncertainties were dominated by the observed differences between the PRMs.

### 3.6 Stability

326     Figure 3 shows the stability data for four selected compounds; methanol, isoprene, D3-siloxane and PFTBA. These were

327     selected as representative examples of the different observed stability behaviours although the stability data plots

328     corresponding to all compounds are shown in Fig. S21 (Supporting Information). The trendlines from the least squares fit

329     straight-line regressions shown in Fig. 3 and Fig. S12 (Supporting Information) were used to determine the annual drift rates

330     shown in Table 3 and Fig. 4. From the ANOVA test there are statistically significant trends (F > Fc) for 10 of the compounds

331     (methanol, acetonitrile, acetaldehyde, ethanol, acetone, DMS, isoprene, MVK, benzene, D3-siloxane) but these trends are

332     small (< 2 % $yr^{-1}$) except for methanol, acetonitrile and PFTBA.

333

334

335     Methanol and acetaldehyde were the only two components that were measured on the cryo-GC-FID and hence the datasets are

336     more limited. A result is that there is no overlap between the three PRMs so any systematic differences between them may

337     result in an artificial bias, which may exacerbate any stability trend. More work is needed to confirm this. The stability data

338     for D3-siloxane reflects the observed validation bias and shows two clear trends; one for 1218 and 0819 and the other for 0119

339     and 0821. For the regression analysis and drift calculations these have been treated independently (Table 3).

340

341     All compounds, with the exceptions of methanol, acetonitrile and PFTBA, show trends similar to isoprene with good stability

342     and annual drift rates of < 3 % $yr^{-1}$ (Table 3). For acetonitrile the large spread in validation data (FID data; Fig. S2, Supporting

343     Information) leads to a noisy stability dataset that may play a role in the larger observed drift rate or this component maybe

344     less stable. As PFTBA was only included in the last PRM (0821) the stability data only represents about half a year and

345     extrapolating the current trend to 1 and 2 years results in a drift rate that is not accurate as interpolation of the data would

346     suggest no statistical change in amount fraction and minimal drift. More data is needed to confirm the longer-term stability

347     behaviour of PFTBA.
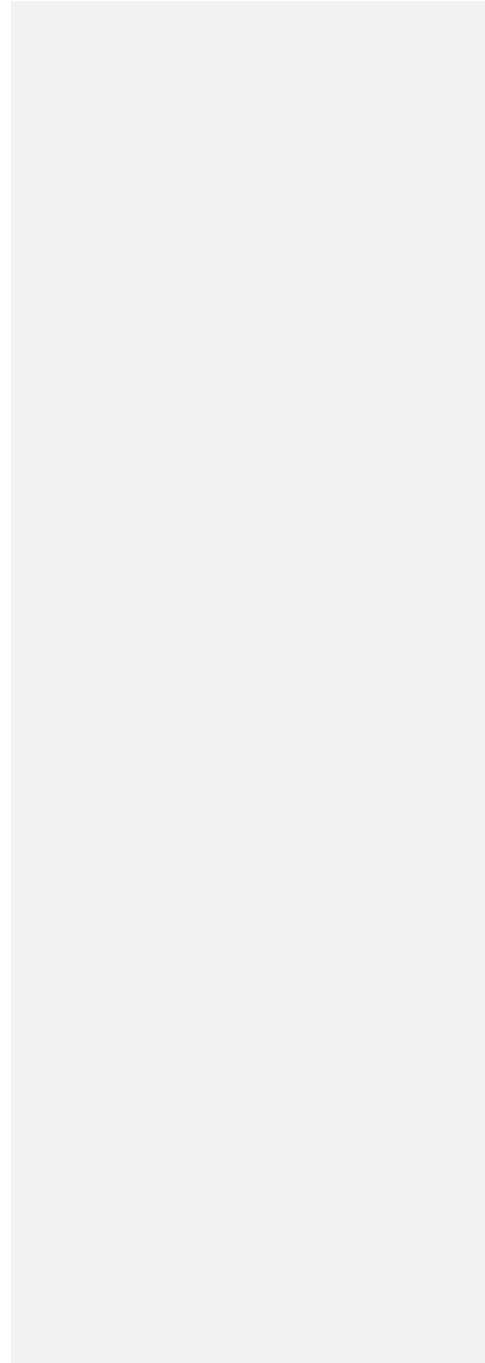
349  **Figure 3.** Stability of normalised response with time for four selected compounds relative to benzene, methanol (top left),
350  isoprene (top right), D3-siloxane (bottom left) and PFTBA (bottom right) for all six ~~NPL~~ PRMs (solid symbols). The open
351  symbols (methanol; top left) show the original data before being corrected for an observed 5.0 % bias in the parent mixture
352  (A410). The best fit curves from least squares straight line regression analyses are shown (solid black line) along with the 95
353  % confidence interval of the fits (shaded area). The slope, intercept and F-statistic data from the regression analyses are shown
354  in Table 3. Stability plots for all compounds are shown in Fig. S1~~2~~ (Supporting Information).

355
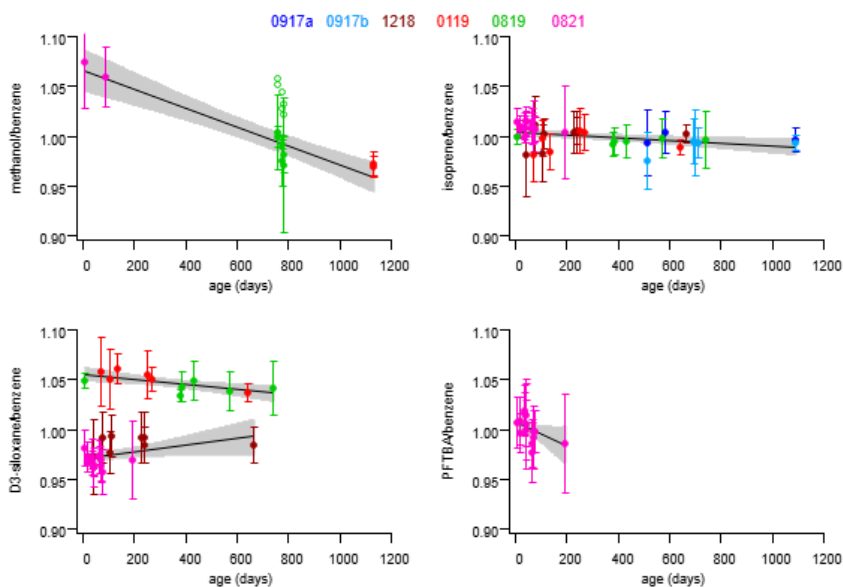


356

357

358  ~~Methanol and acetaldehyde were the only two components that were measured on the cryo-GC-FID and hence the datasets are~~
359  ~~more limited. A result is that there is no overlap between the three NPL PRMs so any systematic differences between them~~
360  ~~may result in an artificial bias, which may exacerbate any stability trend. More work is needed to confirm this. The stability~~
361  ~~data for D3-siloxane reflects the observed validation bias and shows two clear trends; one for A638 and 2819 and the other for~~
362  ~~A643 and D961492. For the regression analysis and drift calculations these have been treated independently (Table 3).~~

363

364  ~~All compounds, with the exceptions of methanol, acetonitrile and PFTBA, show trends similar to isoprene with good stability~~
365  ~~and annual drift rates of <3 % yr⁻¹ (Table 3). For acetonitrile the large spread in validation data (FID data; Fig. S1, Supporting~~

17

366  ~~Information) leads to a noisy stability dataset that may play a role in the larger observed drift rate or this component maybe~~
367  ~~less stable. Additional work is needed to confirm. As PFTBA was only included in the last NPL PRM (D961492) the stability~~
368  ~~data only represents about half a year and extrapolating the current trend to 1 and 2 years results in a drift rate that is not~~
369  ~~accurate as interpolation of the data would suggest no statistical change in amount fraction and minimal drift. More data is~~
370  ~~needed to confirm the longer-term stability behaviour of PFTBA.~~

371

372  Given the age differences between the different PRMs at the time of validation (233 – 709 days; Table S~~1~~2, Supporting

373  Information) it is not possible to deconvolute the contributions of stability and preparation to the observed validation

374  differences. However, Fig. 4 shows that for the majority of compounds there is good agreement between the observed average

375  validation data and the calculated drift for over 1 – 2 years, with the exception of methanol, acetonitrile and PFTBA, which

376  differ for the reasons discussed previously. These observations are consistent with the age differences of the different PRMs

377  at the time of validation indicating that stability was likely the major driver between the observed validation differences.

378

379

Table 3. Summary of the results of the least squares straight-line regression analysis for all stability data shown in Figures. 3 and Fig. S2 (Supporting Information). Results are shown for the slope (± 2σ), intercept (± 2σ), ANOVA test statistics (F and Fc) used to evaluate the presence of a statistically significant trend (F > Fc), the calculated annual drift (± 2σ) determined from the linear fit and the average of the validation data (± 2σ), also shown in Figure. 2.

| compound | slope (× 10⁻⁵) | intercept | F | Fc | Drift (%/yr) | Avg valid. (%) |
|---|---|---|---|---|---|---|
| methanol[a] | -9.539 ± 2.700 | 1.067 ± 0.021 | 57.005 | 5.318 | -3.48 ± 0.42 | -0.37 ± 2.77 |
| acetonitrile | -12.328 ± 6.128 | 1.036 ± 0.026 | 16.530 | 4.085 | -4.50 ± 0.94 | -0.72 ± 2.08 |
| acetaldehyde[a] | -5.345 ± 2.800 | 1.037 ± 0.022 | 19.699 | 5.318 | -1.95 ± 0.44 | -0.40 ± 2.53 |
| propane | 0.653 ± 5.393 | 0.997 ± 0.027 | 0.062 | 4.225 | 0.24 ± 1.97 | 0.16 ± 1.66 |
| ethanol | -7.841 ± 7.55 | 1.023 ± 0.032 | 4.405 | 4.085 | -2.86 ± 0.36 | -0.61 ± 5.64 |
| acetone | 3.462 ± 3.206 | 0.990 ± 0.013 | 4.765 | 4.085 | 1.26 ± 0.86 | 1.18 ± 3.08 |
| DMS | 2.441 ± 2.351 | 0.995 ± 0.007 | 4.473 | 4.149 | 0.89 ± 2.24 | -0.76 ± 3.22 |
| isoprene | -1.338 ± 0.975 | 1.004 ± 0.004 | 7.690 | 4.085 | -0.49 ± 1.17 | -0.04 ± 0.60 |
| MVK | -3.523 ± 2.564 | 1.010 ± 0.011 | 7.708 | 4.085 | -1.29 ± 0.94 | -0.61 ± 4.50 |
| MEK | 0.575 ± 1.967 | 0.998 ± 0.008 | 0.349 | 4.085 | 0.21 ± 0.36 | -1.23 ± 2.25 |
| Benzene[b] | 1.329 ± 0.983 | 0.996 ± 0.004 | 7.456 | 4.085 | 0.49 ± 0.18 | -0.48 ± 1.07 |
| Toluene[c] | -3.546 ± 4.536 | 1.002 ± 0.004 | 2.902 | 4.747 | -1.30 ± 1.66 | 0.19 ± 0.29 |
| m-xylene | 0.129 ± 2.034 | 1.000 ± 0.009 | 0.016 | 4.085 | 0.05 ± 0.74 | -0.87 ± 1.88 |
| 1,2,4-TMB | -0.870 ± 5.155 | 1.003 ± 0.022 | 0.116 | 4.085 | -0.32 ± 1.69 | -0.57 ± 2.42 |
| 1,2,4-TFB | -1.373 ± 1.448 | 1.004 ± 0.006 | 3.672 | 4.085 | -0.50 ± 2.05 | 0.27 ± 0.74 |
| +3-carene | -0.734 ± 4.631 | 1.002 ± 0.019 | 0.103 | 4.085 | -0.27 ± 2.84 | -0.25 ± 1.33 |
| 1,2,4-TCB | 4.512 ± 6.455 | 0.991 ± 0.018 | 2.027 | 4.149 | 1.65 ± 1.16 | -1.73 ± 6.56 |
| D3-siloxane[d] | -2.641 ± 1.740 | 1.056 ± 0.007 | 11.444 | 4.965 | -0.96 ± 0.29 | -4.02 ± 9.67 |
|  | 3.195 ± 3.220 | 0.970 ± 0.007 | 4.287 | 4.351 | 1.17 ± 0.56 |  |
| D4-siloxane[e] | 4.799 ± 4.300 | 0.988 ± 0.012 | 0.765 | 4.225 | 1.75 ± 0.74 | -2.03 ± 4.06 |
| D5-siloxane[e] | 2.066 ± 0.390 | 0.985 ± 0.026 | 1.833 | 4.085 | 0.75 ± 1.68 | -0.49 ± 3.27 |
| PFTBA[e] | -12.045 ± 13.440 | 1.007 ± 0.010 | 3.813 | 4.747 | -4.40 ± 1.66 | 3.31 ± 0.70 |

[a]The GC-FID data for methanol and acetaldehyde was too small to be quantified so this data is from the cryo-GC-FID data and is limited. [b]Benzene stability was determined relative to isoprene. [c]Toluene and PFTBA were only included in the most recent PRM so the assessment of stability is limited in its duration to only 200 days. [d]There was a clear bias between several of the PRMs caused by differences in the parent mixtures used so the trends were fitted to the two obvious groupings. [d]There was a clear bias between several of the PRMs caused by differences in the parent mixtures used so the trends were fitted to the two obvious groupings. [e]Data from 0917a and 0917bA574 and A578 wereas excluded from the regression analysis. [e]Toluene and PFTBA were only included in the most recent NPL PRM so the assessment of stability is limited in its duration to only 200 days.

**Figure 4.** Comparison of 1-year (filled grey squares) and 2-year (open grey squares) drift rates, calculated from the data in Table 3, with the average validation data (black bars) taken from Fig. 2. For D3-siloxane there are two datapoints for the drift correspond to the two regressions shown in Table 3. The error bars represent the associated expanded uncertainties, representing the 95 % confidence limit.
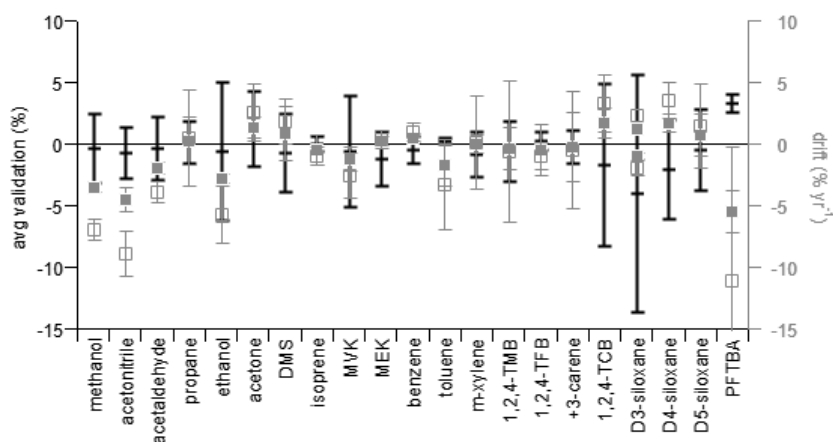


## 4 Conclusions

In this work the development of a new primary reference materials (PRMs) and certified reference materials (CRMs) for constraining the mass dependent transmission curve of PTR-MS instruments haves been described along with an evaluation of their validation and stability of the PRMs and the repeatability in preparation (blend tolerances) for the CRMs. Six of these PRMs have been prepared to date from a suite of 50 parent mixtures and these have been used to value assign more than 10 CRMs that have been disseminated to end users. In general, there is evidence of very good agreement for the majority of components that supports the robustness of the preparation and 2 years of stability. Challenges were observed in preparation for the least volatile compounds especially for D3-siloxane due to it being a solid at room temperature and pressure. More work is needed to better describe the long-term stability of methanol, acetonitrile and PFTBA. This work highlighted several challenges in analysis that could be resolved by the development of a new analytical method utilised a single instrument equipped with both a preconcentration trap and dual detector setup (MS and FID). This work demonstrates what is currently

409 possible with respect to composition, amount fraction, uncertainty and stability and provides an important reference to which

410 other gas standards that are in use with the PTR-MS can be compared and benchmarked to verify their accuracy to further

411 improve the comparability of PTR-MS measurement data.

412

413 In the short term (next 5 years) the implementation of an SI traceable transmission curve reference material, such as the one

414 described in this work, using a method similar to that described in Holzinger et al., 2019 is the most pragmatic approach to

415 directly address improving the accuracy of quantitation and comparability between different PTR-MS instruments and users.

416 This reflects the challenges and complications of rapidly developing a universally accepted calibration system based on pure

417 liquids that is SI traceable. The use of a SI traceable reference material to properly constrain the transmission curve provides

418 a readily applicable framework to ensure confidence in temporal and spatial data to support the use of PTR-MS in a broad

419 range of application areas. The use of the transmission curve reference material approach should be seen as a pre-requisite and

420 a complement to additional future efforts to provide alternative calibration efforts for specific target compounds where

421 uncertainties of better than 30 % are needed. Alternative approaches would certainly be necessary for those compounds that

422 are unsuitable for inclusion in high pressure gas standards possibly as a result of very low vapour pressures or other

423 complicating factors such as chemical compatibility with other compounds.

424

425 Future work to improve the uncertainty of individual components that have the greatest influence on the transmission curve fit

426 would have the biggest influence on the accuracy and repeatability of the transmission~~for~~ curve retrieval ~~fit~~ thereby~~us~~

427 maximising the impact of future improvements for the PTR-MS user community. For PTR-MS instruments that utilise time of

428 flight mass spectrometers the focus would be on improving the uncertainty of the largest molecular weight components

429 specifically the D3-, D4-, D5-siloxanes and 1,2,4-TCB, which represent the greatest challenges in preparation due to their low

430 vapour pressures.


431 **Data availability**

432 All data used to produce the figures in this paper are available on request.


433 **Competing interests**

434 The authors declare that they have no conflict of interest.

## Author contributions

DRW and RH conceptualized the work. DRW processed the data, produced the figures and tables and wrote the paper. RH provided inputs to define the composition of the PTR-MS reference material and contributed to the writing of the paper. SM developed novel methods for the preparation of primary and certified reference materials, planned and prepared all reference materials, conducted all the validation and stability data collection and contributed to the writing of the paper. KOD contributed to the preparation of reference materials, reprocessed some of the stability data and worked with SM to prepare the certified reference materials. ~~RH provided inputs to define the composition of the PTR-MS reference material~~ All authors ~~and~~ reviewed the paper.

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