Response to reviewer 2

The authors thank the reviewer for the positive response and thorough comments that have improved the manuscript. The point-by-point response is below. The reviewers' comments are numbered and are in black font, the authors responses are also numbered and in blue font to ease readability.

Comments from Reviewer

Worton et al. present a neat development of a state-of-the-art multicomponent gas standard and evaluates its accuracy and stability. The major application of the standard will find in constraining the transmission of PTR-MS instruments which in turn will help in more accurate quantification of uncalibrated compounds based on the proton transfer reaction theory. The standard looks extraordinary in its meticulousness of preparation, is SI-traceable and well characterized in terms of stability of the included compounds. An impressive achievement was to embrace complex chemical compositions varying many orders of magnitude in vapor pressures providing unprecedented mass range of 32 to 671 Da. While the manuscript is generally well written and will be useful probably beyond the PTR-MS community, it has a potential for further enhancements of its clarity. I made just a few relatively minor comments which hopefully can be addressed in the revised version.

General

R2.1 It is somewhat surprising that the paper assumes pre-existing knowledge from a general AMT reader about concepts such as mass spectrometer's transmission. I think it would be helpful for the novice PTR-MS audience as well as general community a paragraph or a section that explains the basics of transmission and then refer the reader for more details to Holzinger et al. (2019). Additionally, concepts used inconsistently (e.g. transmission curve and transfer curve) may unnecessarily increase readers' mental processing time.

Noted about inconsistent use of concepts. Transfer has been changed to transmission curve throughout the manuscript. The following text has been added to the manuscript in the introduction at line 55 to explain the basics of the transmission: "**The basis for this is that the amount fraction of compound R ([R]) can be determined from (Taipale et al., 2008):**

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

Where k is the proton transfer reaction rate coefficient, Δt 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 reasonably well 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, recent 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 quantify measurements of uncalibrated compounds from different PTR-MS instruments with an accuracy of ≤ 30 % provided the transmission curve is accurately constrained.”

R2.2 The inclusion of volatile cyclic siloxanes to gas standards is phenomenal but is not new and was already neatly conducted by other vendors with high reputation in the VOC community such as Apel-Riemer Environmental, Inc. who have been at the forefront of preparing those mixtures at a 5% accuracy confirmed by the GC measurement in about hundreds of PTR-MS papers (e.g. Tang et al., 2014; Werner et al., 2021). It is unclear how the NPL standard stands out because it does not compare other standards used by the community which seems like a lost opportunity for this otherwise excellent paper.

What is unique here is the SI traceable nature of the majority of components. To be able to demonstrate SI traceability through international key comparisons with other NMIs is key here. This ensures the accuracy of the components, which is of critical importance for both comparability and also for ensuring the accuracy (trueness) of the reference material remains constant with time. As NPL is not part of the PTR-MS community it is difficult for us to make comparisons to standards that are actively used in this community and we rely on end users to make those comparisons and report those results. We would certainly encourage the community to make those comparisons or to engage with us to provide us with their standards to make such comparisons.

R2.3 Although the paper shows exemplary progress for future transmission measurements, I think it could be made clear that the NPL standard is not trying to monopolize the gas standard transmission market. As the fair comparison with other standards has not been provided, a note mentioning that other standards can also be potentially appropriate and useful for transmission measurements would be reassuring.

Indeed this is not the intention. In the conclusion we have added some text that eludes to the use of other standards. The added text is: “**This work demonstrates what is currently possible with respect to composition, amount fraction, uncertainty and stability and provides an important reference to which other gas standards that are in use with the PTR-MS can be compared and benchmarked to verify their accuracy to further improve the comparability of PTR-MS measurement data.**”

R2.4 The reference list seems somewhat modest and generally not acknowledging the progress in overcoming challenges in transmission measurements and calibrations which have been widely used by the PTR-MS community for almost 3 decades. I encourage making a stronger connection to the

PTR-MS classic (e.g. Taipale et al., 2008) and recent literature (not only Holzinger et al., 2019) and further emphasizing the novelty and advancements that the new standard might offer.

We have added additional references and text in the introduction after line 55 to address this, see the response to R2.1 above which contains the added text.

Specific

R2.5 I agree that n-hexane was a relatively good choice for the D3 solvent, but the statement in the SI is misleading about n-hexane undetectability by PTR-MS: "because the proton affinity of n-hexane is less than water and therefore does not undergo proton transfer and is not detectable by PTR-MS when operating in the H3O+ mode.". What I want to remind is that there is no 100% pure H3O+ mode so all PTR-MS instruments operate in a more or less mixed ionization mode with the O2+ and NO+ being major impurities with relative proportions to H3O+ typically ranging from 1 to several percent (Amador-Munoz et al., 2016). For instance, for a 1% of the O2+ impurity, the detection limit for hexane would be expected only about 2 orders of magnitude higher than that for a VOC undergoing proton transfer. Therefore, if the n-hexane solvent is used in excess, there is no doubt that high signal will be observed on the charge transfer and hydride abstraction n-hexane ions. I therefore suggest it is clarified how the solvent may have affected the transmission measurements, interferences, and if the n-hexane signal on M86 and M85 and lower alkyl fragments (e.g. M71, M57, M43) may have been saturated.

Noted. The main point here is that provided the CRM is used to constrain the transmission curve then any interference from n-hexane is removed because for the CRMs the solid D3-siloxane is dissolved in the other components, which are all liquids, and so no n-hexane is needed. This point has been clarified by removing reference to the proton affinity in the D3-siloxane preparation section and by adding text in the supporting material (section: Preparation and validation of certified reference materials) to: "**While the proton affinity of *n*-hexane is less than water and therefore does not undergo proton transfer it is still detectable depending on amount fraction because of the presence of minor impurities of O_2^+ and NO^+ typically 1 – 3 % (Amador-Muñoz et al., 2016), which could cause interferences from signals resulting from the charge transfer and hydride abstract ions. Therefore, an additional advantage of the CRMs is that because the solid D3-siloxane is dissolved in the other components and no n-hexane is used so any potential interferences from the presence of n-hexane are avoided**.". Also, in the main text (section 3.5 CRM Validation) the follow has been added to point out the advantage of using the CRMs in the field as this problem is avoided: "**An additional advantage of the CRMs is that because the solid D3-siloxane is dissolved in the other components no *n*-hexane is used which avoids any potential interferences from the presence of reagent ions other than H_3O^+ like O_2^+ and NO^+**."

R2.6 L221 It seems greatly overemphasized that D3 is challenging because of its low vapor pressure. It may be counterintuitive but despite D3 being solid at the room temperature, its vapor pressure is actually high (11.6 mmHg at 25 C) and has a low boiling point of 131 C +/-8C at atmospheric pressure. It means that the D3 solid is unique and readily sublimes. I suggest changing "because of low vapor pressures" to "because of its unique phase transition properties" or something along those lines. I would also suggest to include some relevant properties such as boiling points and vapor pressures to the table.

Added the following text to clarify this: "The final group is comprised of D3-siloxane and 1,2,4-TCB where the spread in validation data is within 10 % and these compounds represent those which the most challenging to prepare as a result of **either unique phase transition properties** or low vapour pressures, **respectively.**" We have added a table in the Supporting Information (Table S2) that includes physical properties (boiling points and vapour pressures).

R2.7 TMB has a lower vapor pressure than D3 and D4. I do not think it is critical but it fits better the 3rd category. A table with vapor pressures and boiling points could be useful.

The groupings were based more on the agreement in the validation data. 1,2,4-TMB while it has a lower vapour pressure than D3- and D4-siloxanes, we have a great deal more experience in handling this chemical as it is used in our 30 component ozone precursor mixture that we have been preparing for more than 15 years. We have added a table (Table S2) of boiling points and vapour pressures to the supporting information.

R2.8 Figure 3 top right panel looks exactly as I would expect an outstanding standard to behave. However, I wonder about the reason for an unexpected slight instability of other compounds presented in the other panels. For instance, why is D3 (and acetone in SI Fig. S2) being generated over time and why are other compounds depleted if there are no oxidants in this relatively high concentration standard (1 ppm) and given the unique proprietary passivation of the cylinder that was promising a longer stability compared to a regular standard.

You need to be careful not to over interpret the trend data because they are based on multiple reference materials as any differences between them (as evidence from the validation data) may influence these as well as changes to the instrument over the long time periods involved. Differences between detector response between the different stability measurement points assumes that every compound behaves like benzene (the well behaved reference) but this is unlikely to be the case and slight differences will also influence the data and lead to artefacts in the data that may result in very small temporal trends. To address this it would be necessary to follow individual mixtures for longer periods of time. This was not possible in this work but is of interest going forward. The observed changes are within the observed differences observed in the validation work and demonstrate that these compounds are stability with the quoted uncertainties for at least 2 years currently.

R2.9 What was the regulator and type of surfaces used and could metal surfaces be an explanation for a less excellent stability of the compounds? Methanol stabilization on metal surfaces is a known issue that should not be confused with the excellent preparation of the standard. Only two years of stability is decent but maybe slightly less than absolutely outstanding and it would be nice to improve that aspect if not for this mixture maybe in the future.

We use only silconert-2000 (sulfinert) coated tubing and fittings (Restek Corporation) and use a custom minimum dead volume connector based on a variable restriction of a flattened 1/16" tubing to control the pressure drop and for flow control instead of a regulator, needle valve or mass flow controller. As such there is minimal surface interactions between the gas stream and what surfaces are contacted are passivated with silconert-2000 (sulfinert).

R2.10 PFTBA should be spelled out on its first use. It is a very interesting compound that would make sense to describe a little further to the curious audience.

Perfluorotributylamine has been spelled out on its first use in the abstract and in the introduction.

R2.11 Why were D6 and D7 siloxanes unincluded? This is surprising because their vapor pressure is still sufficiently high that can be seen even in the highly diluted atmosphere (e.g. Karl et al., 2018). At least adding D6 should have been feasible.

We had not considered these at this time. Thanks for the suggestion. The composition of the transmission curve standard is not fixed and addition of relevant or important compounds could be considered in the future. We would need to look at the physical properties of these two components to determine whether it is feasible to accurately add them to a high pressure gas cylinder at an amount fraction in the µmol/mol range, which is different to whether it could be present in the gas phase at atmospheric pressure and a lower amount fractions.

R2.12 It would be appropriate to discuss the effect of compound purity. For example, for a 98% purity, if the vapor pressure of compounds making up that 2% is orders of magnitude higher than the compound making up the 98%, the 2% might completely dominate the PTR-MS signal and potentially interfere with other compounds' protonated ions or fragments. I think it would be useful to show some PTR-MS data if you have analyzed the spectrum of the individual 98% pure compound – or if there is a different way to find out what exactly the impurities were?

I am not sure I really understand the comment that if the vapour pressure of impurities is much higher than the main compound then the impurities may dominate the PTRMS signal. It is the proton affinity and the amount fraction that would dictate the response in the PTRMS. Perhaps the reviewer is thinking about the headspace vapour diffusion method that they mention later. In this work, we have purity analysed all the liquids that we have used for the preparation of the PRMs and CRMs in accordance with ISO19229 and this is the origin of the purity data. We do not rely on the purity specified by the manufacturer. Following ISO19229 we look for critical and significant impurities. Critical impurities are those whose presence which would directly impact the amount fraction of other compounds in the mixture. For example, if methanol is present as an impurity in the ethanol then for the PTRMS mixture the methanol impurity would be critical because methanol is also present in the mixture. In this case the amount fraction of the methanol impurity is added to the amount fraction of the methanol that is directly added to give a total amount fraction of methanol in the mixture. This is done for all components. Significant impurities are those that would impact the uncertainty of the mixture by at least 10 % and in the case of the PTRMS could fragment and potentially interfere with other compounds. No impurities were present at 2 %. The major impurities are present at < 0.5 %, most < 0.1 %. As a result of the very small amounts of the pure materials used to prepare the final PRM or CRM mixtures the amount fraction of any impurities in the final mixtures are very small (nmol/mol) and once they are further diluted prior to introduction into the PTRMS instruments (large dilution ratios 40 – 500 used in Holzinger et al., 2019) these are even smaller (pmol/mol) meaning they have a negligible effect. Interferences are negligible. For example, even for impurities that are structural isomers, e.g., 1,2,3-TMB and 1,2,5-TMB (structural isomers of 1,2,4-TMB, which is present in the PRMs and CRMs) and are isobaric molecules so indistinguishable in PTR-MS change the amount fraction by less than < 0.05 %, which is significantly smaller than the assigned uncertainty of 3 %. This is evidenced by the fact that all major ions that are produced from a gas standard sample in the PTR-MS can actually be attributed to the target compounds in the standard.

R2.13 For the validation experiments how was the standard diluted for the GC and PTRMS measurements? I am missing the RH, the MFCs (and their materials of the seat and the seal, presumably Viton-free?). Were temperature and RH consistent in all measurements? I wonder if that could shed more light on the mechanism for the annual drifts for methanol, acetonitrile, acetone, and PFTBA.

For the validation experiment the mixtures were analysed directly at 1 umol/mol (ppm) of the GC-FID/MS and cryoGC-FID instrument, they were not diluted and no dilution system was used. The mixtures were not analysed by PTR-MS as part of the validation or stability work. We use only silconert-2000 (sulfinert) coated tubing and fittings (Restek Corporation) and use a custom minimum dead volume connector based on a variable restriction of a flattened 1/16” tubing to control the pressure drop and for flow control instead of a regulator, needle valve or mass flow controller. As such there is minimal surface interactions between the gas stream and what surfaces are contacted are passivated with silconert-2000 (sulfinert). The measurements were all conducted in a temperature controlled laboratory and relative humidity does not have any effect on the direct GC analysis of high pressure gas standards.

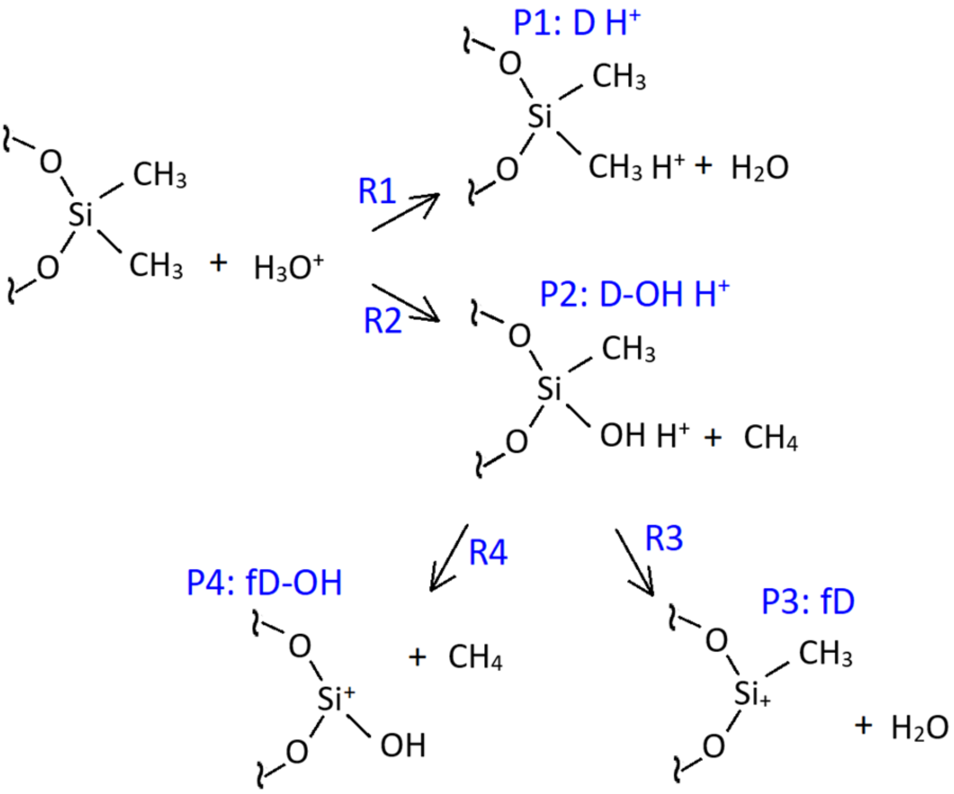
R2.14 I am not a huge fan of the long and overly specific titles. I wonder if it might be possible to simplify the title just a little bit. Specifically, it might be considered shifting the emphasis in the title from “comparability” to more generally on “improved quantification” which in my opinion could resonate even more broadly.

We have added “quantitation and” to the title before comparability. However, we think its still important to include comparability in the title because that is one of the main focuses of having SI traceability for this standard which is to ensure that measurements are true (accurate) thus ensuring all measurements are on a level playing field and improving the comparability, which is key for assimilating data from different sites and different groups into potential data products to be used by the wider community of researchers. To shorten the title we have abbreviated “proton transfer reaction mass spectrometry” to “PTR-MS”, which is commonly done in other PTR-MS publications in the literature.

R2.15 It would be valuable to add info on how processing of D3-D5 siloxane signals was done in your PTR-MS work. In the provided reference to Holzinger et al., 2019 it was not mentioned how the Si isotopes and the CH4-loss fragments were dealt with to reconstruct the transmission curve as the approach requires to sum up all the ions specific to the analyte. In addition, it is unclear what the proton transfer reaction constants were used for those siloxanes.

We have added the following information to the supporting information.

Figure S4. Fragmentation of cyclic siloxanes in PTR-MS



Calculation of product ion abundances from the outlined reaction mechansim:

Compound	Product ions			
	P1[a]	P2	P3	P4
D3-siloxane	m223.064*1.37	(m225.044– m223.064*0.13) *1.36	m207.033 * 1.36	(m209.012 – m207.033 * 0.12) *1.35
D4-siloxane	m297.083*1.52	(m299.062– m297.083*0.18) *1.51	m281.052 * 1.50	(m283.031 – m281.052 * 0.18) *1.49
D5-siloxane	m371.101 *1.69	(m373.081 – m371.101 *0.24) *1.68	m355.071 * 1.67	(m357.050 – m355.071 * 0.23) *1.66

[a] Correction for stable isotopes.

These assume that for D3-siloxane (209.012 / 209.030 and 225.044 / 225.061 Th are unresolved), D4-siloxane (299.062 / 299.080 and 283.031 / 283.049 Th are unresolved) and D5-siloxane (373.081 / 373.099 and 357.050 / 357.067 Th are unresolved). Note, that P4 is typically not detected for D3 and D5.

R2.16 Overall, it was extremely enjoyable to read through this seminal work, but I think the conclusions and take-home messages could be even further expanded. For example, as a community should we invest more in the gas standards that can last for at least 2 years or would a properly designed and SI-traced liquid stock solution for dynamic calibration in the proper cal. box could allow even more thorough calibrations including compounds which are challenging or impossible to prepare in gas standards such as organic acids, and with the formulations that can span monoisotopic masses at least until 1000 Da.

This is an interest point. To address this, we have added the following text to the conclusion of the manuscript: "**In the short term (next 5 years) the implementation of an SI traceable transmission curve reference material, such as the one described in this work, using a method similar to that described in Holzinger et al., 2019 is the most pragmatic approach to directly address improving the accuracy (trueness) of quantitation and comparability between different instruments and users. This reflects the challenges and complications of rapidly developing a universally accepted calibration system based on pure liquids that is SI traceable. The use of a SI traceable reference material to properly constrain the transmission curve provides a readily applicable framework to ensure confidence in temporal and spatial data to support the use of PTR-MSs in a broad range of application areas. The use of the transmission curve reference material approach should be seen as a pre-requisite and a complement to additional future efforts to provide alternative calibration efforts for specific target compounds where uncertainties of better than 30 % are needed. Alternative approaches would certainly be necessary for those compounds that are unsuitable for inclusion in high pressure gas standards possibly as a result of very low vapour pressures or other complicating factors such as chemical compatibility with other compounds.** "

Technical

R2.17 Introduction: "with high sensitivity (pmol mol-1). ". Should be changed to something like "ultralow detection limits" (sensitivity is not the same as detection limit).

Corrected to "low detection limits".

R2.18 L136 remove space before percent.

Done.

R2.19 Entire ms: Ensure consistency with spelling of sulfide/sulphide (either sulfide or sulphide).

These have all been corrected to sulfide.

R2.20 L95 Provide VICI valve model (and if it contained Viton seals that can potentially obfuscate methanol stability).

The body of the valve (model: A3C6WT) is silconert-2000 (sulfinert) coated and the rotor is Valcon T (polyimide/PTFE/carbon composite) so no viton seals.

R2.21 319-321 the use of transmission and transfer curves in one sentence can be rather confusing for some readers.

Transfer has been changed to transmission curve throughout the manuscript.

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