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# Non-Contact Detection of Thiodiglycol Vapors and Associated Degradation Products Using Atmospheric Flow Tube Mass Spectrometry

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**Abstract**:

Thiodiglycol (TDG) is a synthetic precursor and an environmental degradation product of sulfur mustard (HD). Consequently, its presence can be indicative of illicit preparation or historical presence of chemical weapons, but its lower toxicity lends itself to use as an HD simulant for testing and method development. Detection of TDG vapor often proves elusive with existing techniques exhibiting undesirably high detection limits in the gas phase (>ppm). Moreover, traditional approaches to detecting TDG vapor rely upon non-specific approaches that do not provide the certainty afforded by mass spectrometry. Using atmospheric flow tube mass spectrometry (AFT-MS), which has previously demonstrated the capacity to detect parts-per-quadrillion levels of vapor, we evaluate the capacity of this approach for non-contact residue analysis based upon TDG vapor sampling and nitrate clustering chemistry. Furthermore, we discuss challenges with ambient vapor detection using the AFT-MS system and associated observations related to TDG degradation into 2,2'-sulfonyldiglycol from exposure to ambient conditions with vapor detection being possible even after 7-weeks of sample aging.

**Keywords**: Atmospheric Flow Tube; Mass Spectrometry; Non-Contact Residue Analysis; Thiodiglycol; Thiodiethanol; Sulfur Mustard; HD; Chemical Warfare Agent Simulants; Environmental Monitoring

## Introduction

Preemptive detection and advanced forensic methods are essential to mitigate the production, transport, and deployment of chemical weapons. Consequently, trace detection of chemical warfare agents (CWAs) remains a valuable segment of defense-related analytical chemistry research. A range of different analytical technologies have been applied to the task of CWA detection including Raman spectroscopy, [1] standoff FT-IR spectroscopy, [2] electrochemical gas sensors, [3] and atmospheric pressure ionization mass spectrometry approaches, [4, 5] with the most selective of these methods using mass spectrometry for the final stage of analyte analysis. With respect to the mass spectrometric techniques, several ambient sampling and ionization approaches have been applied to trace vapor detection of various CWAs, CWA simulants, and related species. Secondary electrospray ionization (SESI-MS), [4, 5] direct analysis in real time (DART-MS), [6] selected ion flow tube mass spectrometry (SIFT-MS), [7] gas chromatography mass spectrometry (GC-MS), [8] and atmospheric flow tube mass spectrometry (AFT-MS) [9–11] have all been used to demonstrate some form of trace CWA-related vapor detection. Of these, AFT-MS has been shown to be readily applicable to realistic conditions for non-contact vapor detection particularly in applications requiring rapid sample screening.

The essential concept behind the efficacy of atmospheric flow tube mass spectrometry is the use of extended reaction times to enhance analyte sensitivity through ion-analyte collisions. [12, 13] Within a flow tube apparatus a dielectric barrier discharge or similar ion source is commonly located at the sampling entrance that generates a low-density plasma of reactant ions. Assisted by a modest vacuum pull, sample vapors in close proximity to the AFT entrance are drawn into the reactant ion-containing flow tube. During the transit through the tube driving by bulk flow of gas, an extensive number of ion-neutral collisions occur which allow the most probable ion chemistry to reach an equilibrium state. When clustering is thermodynamically favored, the target ion-analyte cluster is readily detected using mass spectrometry. The increased *m/z* of the reactant ion-analyte cluster can assist in maximizing signal to noise ratio as these products are

often observed at higher *m/z* values beyond the background commonly generated in air from DBD processes. The AFT-MS approach has been effectively demonstrated for sub-parts-per-trillion analyte vapor detection for nitrated explosives, [12–16] salt-based explosives, [17] amine-based drugs, [18] and organophosphorus CWA simulant compounds. [9–11] This trace detection method has been proven effective for both negative and positive ion monitoring. Here we describe yet another category of analytes that can be observed, monitored, and even quantified with AFT-MS: organosulfur CWA breakdown products. To the best of our knowledge, the work presented in this article is the first report of thiodiglycol (TDG) clustering with nitrate anions. Furthermore, the use of AFT-MS permitted the development of a non-contact sampling method for residue analysis permitting vapor detection with real-time performance.

While the detection of the target CWA in any screening and forensic application is ideal, degradation due to environmental factors is not uncommon. It is for this reason that the present effort also included an evaluation of common TDG degradation products. A primary breakdown product of the CWA sulfur mustard, or HD, is TDG, which can be further oxidized first to 2,2'-sulfinyldiglycol (TDO) and then to 2,2'-sulfonyldiglycol (TDOO) following a sufficient amount of time present in ambient conditions. TDG residues of as little as 1 µg could elicit measurable signals from headspace vapor by simply inserting the residue samples within the sampling inlet. Furthermore, a subset of the TDG residue samples was analyzed following ~7 weeks of aging, undisturbed in a laboratory environment. Though detection of TDG following this sample aging period was not realized, the common oxidation products TDG were readily observed in the vapor phase.

## Experimental

***Chemicals and Sample Preparation.*** All thiodiglycol, sometimes referred to as thiodiethanol, solutions and residue samples were prepared from a neat liquid TDG stock source of ≥99% purity (Sigma Aldrich; St. Louis, MO, USA). Similarly, LC-MS grade methanol was used as the solvent in all TDG solutions made for the experiments

outlined here. Methanol was selected specifically as the solvent because of its miscibility with TDG and high vapor pressure, allowing for minimal sample drying times. Concentrated stock solutions of TDG in methanol were first prepared from neat TDG and were diluted further to yield to the appropriate concentrations for deposition and analysis. Calibration standards and quality control (QC) samples were prepared from dilution of separate concentrated stock solutions.

A series of three calibration curves were prepared for non-contact detection of vapor from trace TDG residues. All TDG residue samples were prepared by the deposition of 5 μL of TDG solution at the appropriate concentration to glass microscope slide covers (25 mm by 25 mm). The same volume of solution was used to produce the samples in an effort to simplify the range of experimental variables impacting the observed signals. The applied TDG residues were left to dry undisturbed for a minimum of 2 hours to ensure that the solvent was completely evaporated. The first set of calibration standards were made in replicates of three per applied analyte mass and covering masses 1, 2, 5, 10, 20, 50, and 100 μg of TDG and QC samples of 3 and 30 μg. These initial samples were prepared with the TDG solution deposited approximately in the center of each glass cover slip with minimal manipulation of the solution following analyte deposition. However, it should be noted that the solution spread could easily vary by travel of the liquid from interaction with the glass surfaces. This original set of TDG residue calibration samples in the range of 1-100 μg were kept covered and undisturbed in a darkened room without direct exposure to sunlight for approximately seven weeks. The 1-100 μg calibration standard and accompanying QC samples—of which three replicate residues were prepared per TDG mass—were analyzed twice per replicate for a total of six measurement values for a particular TDG mass. In select instances within the 10 μg, 50 μg, and QC 30 μg sets, a single sample was analyzed in triplicate to verify signal stability, but only the first two values out of the three measurements were used for subsequent data processing and calibration curve calculations. This decision was made to realize consistency in the data processing across all sample concentrations. It is worth noting that inclusion of all data points obtained for each concentration did not alter the resulting calibration curves in any statistically meaningful fashion. Calibration fits

and error analysis was performed using Igor Pro (Wavemetrics; Lake Oswego, OR, USA).

After witnessing a degree of signal variation between sample slides for the same mass of TDG applied, two additional calibration curves were prepared to examine the relative impacts on signal variability and QC accuracy. This was accomplished through calibration curves covering 1 to 20 µg TDG residue masses. One set of calibration and QC samples was made where a single residue sample was prepared per analyte mass, but each was analyzed with AFT-MS using four replicate instances to characterize variability from the instrumental method alone. Another set of calibration and QC samples was prepared where each TDG residue mass to be measured was made as five replicate residues each on different glass slides, wherein each separate sample would be analyzed with AFT-MS only once. The intent behind this set of residue replicates was to isolate the degree of reproducibility in sample signal resulting from calibration standard residue sample preparation alone. Finally, to make a simple assessment of residue surface area's relation to resultant analyte ion signal, a set of four standards were prepared with the same deposited TDG mass but deliberately different spreads of analyte so as to vary the residue surface area. The resulting residue surface areas were approximated to be 0.3, 1.2, 1.5, and 2.8 $cm^2$.

***AFT-MS System and Sampling.*** All experiments were performed using an atmospheric flow tube mass spectrometry system that approximated the design previously reported, [9–14, 17, 19] but with some modifications made to the sampling inlet for facilitating surface residue analysis (Figure 1). In brief, an Agilent 6410A triple quadrupole mass spectrometer (Agilent Technologies; Santa Clara, CA, USA) was fitted with a custom ion inlet housing to permit the introduction of ions from a ~60 cm, 1-inch inner diameter copper tube with a dielectric barrier discharge (DBD) ion source fitted to the other end. A house vacuum pull of approximately 1 L/min was applied to the inlet housing so that reactant ions and other species could be drawn toward the mass spectrometer inlet. The DBD source used here was a simplified version of a four-bulb design previously reported. [10, 11, 19] To circumvent the difficulty of fitting four individual DBD sources

into two brass tees where electrical arcing can easily occur between sources or between the DBD source and the tube, this updated design combines the four individual sources into one large DBD ion source with voltage supplied by a single pair of electrical leads. Along with the benefit of reducing the potential for arcing, the large DBD source ran on 15 V, and required only 80 mA of current in comparison to the previously reported 0.1 A when the DBD bulbs were powered separately. As illustrated in Figure 1, a small section of additional copper tubing with a 4 cm by 2 cm slit in the side was added at the front flow tube inlet. A light flow of purified nitrogen gas (99.9%, ~1 L/min) was directed along the long axis of the flow tube, as well. This created an area where residue samples on glass slides could be inserted under consistent conditions and where analyte signal could be enhanced due to the added nitrogen carrier gas.

Samples of TDG residue on glass cover slips were held in the sampling slit at the front of the flow tube for analysis. Using tweezers, the samples were held horizontally for 10-15 seconds at an indentation located at the center of slit used to mark the insertion location. The headspace vapors coming from the residue samples were monitored by selected ion monitoring of the predominant reactant ion at *m/z* 125, $HNO_3 \bullet NO_3^-$, as well as TDG•$NO_3^-$ (*m/z* 184), TDO•$NO_3^-$ (*m/z* 200), and TDOO•$NO_3^-$ (*m/z* 216) as appropriate. The dwell time used for observing each ion was 200 ms.

## Results and Discussion

***Thiodiglycol Ionization and AFT-MS.*** Prior publications regarding trace MS analysis of TDG, such as the vapor analysis using DBD ionization by Wolf et al. [4] and $Ni^{63}$ ionization by Crawford et al., [20] predominantly monitored protonated TDG. Unfortunately, the apparent proton affinity of TDG is likely quite low relative to the numerous possible interfering species that may be present in any given laboratory environment due to off-gassing, such as amines. [21–24] This is substantiated by Midey et al., who reported a computationally-derived proton affinity of 833 kJ/mol for the sulfur atom on TDG. [25] The comparatively low proton affinity of TDG minimize the probability that any given TDG molecule can preferentially abstract protons for sufficient ionization

within a complex environment (e.g. ionized air in the field). Additionally, monitoring the intact protonated TDG species can be challenging even with a soft ion source like DBD because the loss-of-water fragment ion is readily formed. [4] Prior work by Morrison and Clowers postulated that the presence of hydroxyl groups on alkylphosphonic acids may facilitate cluster formation with nitrate, [11] and exploring the possibility of nitrate interaction with TDG was the route taken to circumvent the difficulty in protonation resulting from the low TDG proton affinity and potential fragmentation from instability of the protonated species. As shown in Figure 2, a low but measurable signal of ~7000 cps for TDG adducted with nitrate (*m/z* 184) can be observed from sampling the vapor from a container of neat TDG with the lid slightly cracked. By contrast, a signal for protonated TDG was nearly undetectable (data not shown) and thus was not pursued for this experiment.

***Non-Contact Vapor Detection and Quantifying Dried Thiodiglycol Residue.*** For semi-quantitative evaluation of trace vapor concentration from minute residues of TDG, a sampling approach with the AFT-MS was devised where the TDG is deposited on small glass coverslips. These coverslips could then be held within the partially open flow tube that has both a vacuum pull and a light flow of nitrogen over the sample to assist the mass transport through the flow tube. The headspace vapor from the TDG residues is then conveyed down the flow tube for ionization and mass analysis. With a saturated vapor pressure for TDG at 298 K of 0.49 mTorr, and under the typical ambient pressure of ~690 Torr at Washington State University in Pullman, WA the maximum vapor concentration of TDG is ~3 ppm. However, in the dynamic vapor sampling environment of an atmospheric flow tube system, the very low mass TDG residues cannot create a saturated system. Correspondingly, the levels of TDG vapor detected are well within the realm of sub-ppm levels in the vapor phase. Combined with the rapid analysis times and sample clear-out characteristics, the AFT-MS system can realize impressive levels of detection.

While the exact vapor concentrations produced by each sample mass is challenging to determine under the conditions used, it is feasible to approximate TDG residue mass by

simple vapor sensing with appropriate calibration curves. A sample mass range covering 1-100 µg and the two quality control samples of 3 µg and 30 µg underwent non-contact analysis to yield the ion current traces displayed in Figure 3. The instrumental response to the non-equilibrium vapor sampling from the deposition of TDG ranging from 1-100 µg is shown in Figure 4. The mean analyte masses for the quality control samples as found by the calibration curve had a reasonable initial degree of accuracy for non-contact detection ($5 \pm 5$ µg for the 3 µg QC, $34 \pm 19$ µg for 30 µg QC). However, the signal variability and resulting precision issues indicate the need to further investigate the primary sources contributing to signal differences between replicate samples for the same applied residue mass. Stated differently, the individual residue replicates prepared as calibrants for a particular residue mass appeared to have an outsized contribution to the sample errors. As detailed below, there are a range of factors, including surface area, that contribute to this variability. However, it is important to note that the signals presented in Figure 3 were derived from the TDG vapor produced by the dried standards. The rapid modulation of the signal when the sample slides were inserted into the sampling apparatus further emphasizes the potential of this technique for use as a rapid screening tool where absolute quantitation is not the primary figure of merit driving future action.

***Sources of Signal Variability for Trace Residue Analysis.*** At the outset of the outlined experiments, it was anticipated that the total solution volume was one parameter that would contribute to signal variability. To mitigate this factor solution volumes were maintained at 5 µL for all TDG masses applied. However, the ion current obtained between sample replicates for the same mass displayed more variation than anticipated (Figures 3 and 4). One probable source of signal fluctuation could be from the residue sample preparation and its relation to the surface area covered by each dried samples. Variations in dried surface area could easily impact the amount of non-equilibrium vapor generated during sample analysis with the AFT-MS. Even taking care to maintain consistent analyte solution application, the unpredictability of localized analyte clustering after solution deposition rendered this a difficult task. Furthermore, the issues associated with dried sample area compound as analyte quantity increases;

the smaller analyte masses (1 µg up to ~20 µg) are spread more uniformly as the solution is applied to the glass slide and create a larger surface area per analyte quantity. It is worth noting that at higher TDG concentrations visible microdroplet formations were noticed after the primary solvent deposited had evaporated. Over time, these smaller droplets, presumed to consist primarily of the target analyte, evaporated, but the variability of this process further contributes to challenges in absolute quantitation. Non-uniform sample drying was apparent when the total mass of TDG exceeded 20 µg. Additionally, this observation corresponds to deviations from signal linearity at higher sample masses.

To assess the contributions of sample preparation on the variability of sample response, two additional calibration curves and corresponding QC samples were prepared and analyzed using slightly differing approaches. The TDG mass range used for the two subsequent curves was 1-20 µg to reduce the influence of residue droplets clustering together at the higher masses. A first curve was produced by four replicate analyses of a single residue sample per applied TDG mass (Figure 5a), which was intended to identify variation due to the instrument response. The second curve—consisting of five replicate residue samples prepared for each analyte mass all measured once—was evaluated to reveal any precision issues due to physically applying analyte solution on to the glass coverslips (Figure 5b). As can be seen in Figure 5, the sample set producing the curve in Figure 5a exhibited noticeably lower signal variation for the calibration standard measurements, while the sample set from Figure 5b had standard deviations that were roughly double that of the standard deviations from the Figure 5a curve. Furthermore, a marked difference in both precision and accuracy is evident when the QC samples are compared. The QC samples were prepared as 1.3 and 13 µg TDG residues, which were also the analyte masses obtained from the curve in Figure 5a with percent relative standard deviations of ±8% and ±7%, respectively. In contrast, the Figure 5b curve yielded QC masses of -1 ± 0.9 µg and 11 ± 3 µg for the quality control residues prepared at 1.3 and 13 µg, respectively. Compounding upon the precision issue is one of sensitivity; it certainly should be noted that the signal magnitudes for the 20 µg samples in Figure 5 are roughly on order with that observed for the 100 µg TDG

signals shown in Figures 3 and 4. The ability to create calibration samples that yield consistent signals as a function of analyte quantity is the foundation of calibration curves and any discrepancies must be scrutinized.

A final, rough assessment of analyte surface area's influence on analyte signal was made by deliberately varying the spread of TDG after depositing the solution on glass coverslips. A set of 10-μg TDG residues were made by applying the solution in one of four distinct patterns to ensure that each sample varied in analyte surface area from the others. The mean TDG signals from these four samples were plotted as a function of approximate residue surface area in Figure 6a. The areas were approximated in Igor Pro as a proportion of the total slide area based upon the sample images shown in Figure 6b. As anticipated, the smallest surface area sample (~0.3 $cm^2$) yielded the lowest signal for the TDG-nitrate adduct, while the highest signal was obtained for the greatest residue surface area (~2.8 $cm^2$). Moreover, the upper and lower bounds of residue area of differ by a factor of 9, largely correlating with the roughly 7-fold change in signal between the two samples. The samples with intermediate values for residue surface area produced signals with overlapping standard deviations, although this appears reasonable because the rough estimation of residue areas for those two samples differ by only ~20%, or ~0.3 $cm^2$. Overall, the data presented in Figure 6a appear to confirm the relationship between analyte residue surface areas and resulting signals observed via AFT-MS instrumentation.

***Assessing Further Degradation of CWA Hydrolysis Products.*** The environmental degradation kinetics of CWA species such as sulfur mustards have been reasonably well documented, [26–28] while the corresponding simulants or degradation products for those same CWAs have not had their decomposition timelines as thoroughly scrutinized. However, there are a few references of note regarding the subsequent degradation of the sulfur mustard hydrolysis product, thiodiglycol. Lee and Allen report having observed no more than 4% loss of TDG in aqueous solution due to decomposition over the course of two weeks, [29] but our approach in long term dried residue sample degradation may not necessarily be directly comparable to the Lee and

Allen aqueous samples. Because Lee and Allen did not report any kind of substantial loss of TDG concentration at their longest time point (2 weeks) without a soil catalyst present, it was assumed that significantly longer than two weeks' exposure to ambient conditions would be necessary for any kind of TDG loss to be identified. While the initial sulfur mustard CWA may be presumed to be more reactive than its degradation products due to the chloride versus hydroxide leaving groups, the remarkable persistence of sulfur mustard as influenced by humidity was described by Mizrahi et al. [28] Mizrahi et al. found that sulfur mustard kept in an environment of certain dry soils could require in excess of 50 days before any spectral differences indicating degradation were visible. The Lee and Allen results as well as observations by Mizrahi et al. indicated that, to ensure any kind of TDG decomposition had taken place in time for a second round of analysis of the 1-100 µg TDG residues, a minimum of roughly 50 days would likely need to pass before our TDG residues could degrade without altering the ambient conditions. With this in mind, the group of TDG residue samples used as the initial set of 1-100 µg calibration standards was kept loosely covered and without disruption in a dark, dry, and room temperature location for 7 weeks, or about 50 days.

After the thiodiglycol residue samples on glass were allowed to sit for 7 weeks, the standard samples of 1 µg through 100 µg were retrieved for subsequent analysis via SIM mode with AFT-MS. In anticipation of TDG degradation through oxidation the target *m/z* values monitor SIM was expanded. In addition to the primary nitrate-nitric acid reactant ion at *m/z* 125 and the nitrate adduct of TDG at *m/z* 184, the adducts of nitrate with 2,2'-sulfinyldiglycol (*m/z* 200; TDO) and 2,2'-sulfonyldiglycol (*m/z* 216; TDOO) were evaluated. A survey of the species observed in one of the three 100 µg TDG residue samples after 7 weeks of aging is shown in Figure 7a. Observation of the degradation products in the samples with the highest masses helped constrain the *m/z* list used for subsequent evaluation of signals from samples with smaller deposited masses. TDO and TDOO nitrate adducts were monitored in addition to the TDG nitrate adduct because these species largely retain the overall structure of TDG and were anticipated to be ionized through interacting with nitrate much like TDG. Somewhat unexpectedly, no signal for the thiodiglycol adduct with nitrate was visible, thereby indicating that a

substantial portion of the 100 µg residue sample had likely transformed into its degradation products and left only TDG in an amount that could not be detected by the AFT-MS system. The first oxidation product TDO also was not observable from analyzing the aged 100 µg sample, but TDOO resulting from a second oxidation [30, 31] did yield a signal from insertion of the sample into the flow tube sampling inlet. Starting with the smallest sample that could produce an identifiable signal for TDOO, the aged residue samples for 5 to 100 µg of initially deposited TDG were analyzed using SIM on ions at *m/z* 184 and 216 (Figure 7b).

As an added confirmation that a chemical change had occurred in the residues, we prepared a fresh TDG residue sample for visual comparison with an aged TDG sample. Figure 7c shows the sharp contrast in appearance of the newly deposited residue (Figure 7c (i)), which was allowed to dry for two hours, with the 7-week-old sample (Figure 7c (ii)). While the new residue maintains the appearance of the thiodiglycol liquid, the aged residue had a white, dried, and crystalline appearance, which fits a general description of 2,2'-sulfonyldiglycol at room temperature as a white solid. [32] It should be noted that the TDOO was certainly not the sole degradation product present and that a range of species including but not limited to 1,4-dithiane, 1,4-thioxane, and divinyl sulfone could have been simultaneously present in the aged residues. [33] However, the very observation of TDOO within the residues after visibly extensive degradation of TDG is, itself evidence that AFT-MS is a versatile and sensitive approach for non-contact trace detection. Furthermore, these observations also demonstrate the possible application of AFT-MS detection of other organosulfur CWA simulant species, organosulfur pesticides, and related compounds.

## Conclusion

Along with the established use of AFT-MS for trace analysis of vaporized explosives, [12, 13] AFT-MS can be used as a method for non-contact detection of vapor emanating from dried residues on a solid surface. The initial AFT-MS experiments by Ewing et al. established relationship between observed ion current and analyte concentration that

approximated linearity. However, the task of precisely generating vapors from solid analytes proves more challenging due to the non-equilibrium vapor concentrations. While the vapor detection trends from 1-100 μg TDG residues could be considered linear based upon the $R^2$ >0.9, there are clear deviations from linearity that occur that are dependent, at a minimum, on sample volume applied, sample mass, and surface area. Another extremely relevant aspect that constrains the linear dynamic range of the AFT-MS approach is the concentration the reactant ion species. In the present case, the nitrate anion was generated from laboratory air which yields a largely constant level of $NO_3^-$ generated from the existing DBD source. Under these conditions it is not surprising that as the concentration of the target analyte increases the chemical reservoir of $NO_3^-$ is diminished. Ideally, an increase in the reactant ion current (i.e. $NO_3^-$ ) would aid in expanding the dynamic range of the system in future instrumental iterations and such conditions may be realized by incorporating an auxiliary source of $NO_x$. Under such conditions any dependence upon reactant ion concentration, which was not controlled or varied under the present effort, could be minimized. Given the distinct dependence of analyte signal upon residue surface area as clarified by Figure 6, the evolution of method development for non-contact, quantitative detection of trace analytes in any state other than uniformly dispersed vapor will necessitate a rigorous examination of factors outside of sample quantity that influence AFT-MS signal. Regardless of the challenges of applying AFT-MS for non-contact quantification, these results for TDG show that AFT-MS is well-suited for trace-vapor sensing application wherein the presence or absence of analyte necessitates action. When placed in the context of CW agent monitoring applications, absolute quantitation at high concentrations is rarely the primary concern. The present effort evaluating the range of factors impacting AFT-MS response to residual TDG illustrates that challenges for absolute quantitation persist, however, the near real-time response for trace vapors even after sample aging signifies the potential of AFT-MS as a versatile, rapid screening tool.

## Author Contributions

All authors contributed to experimental design. KAM conducted all of the laboratory experiments with supervision and consultation with BHC. All authors have given approval to the final version of the manuscript.

## Conflicts of Interests

There are no conflicts of interest to declare

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**Figures.**

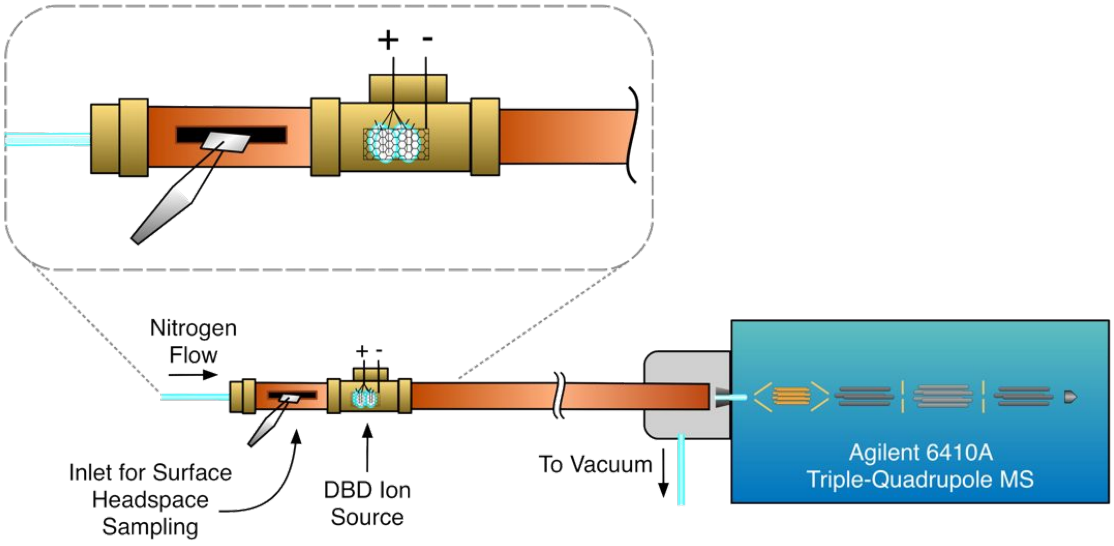


**Figure 1.)** The system used for analyzing vapor from dried thiodiglycol residues was a modified atmospheric flow tube-mass spectrometry setup where an orthogonal sampling slot was created to allow for gas flow over inserted glass coverslips. Additionally, the four-bulb dielectric barrier discharge ion source was made to be more compact and require lower current by combining all four dielectric bulbs with a single pair of electrical leads.

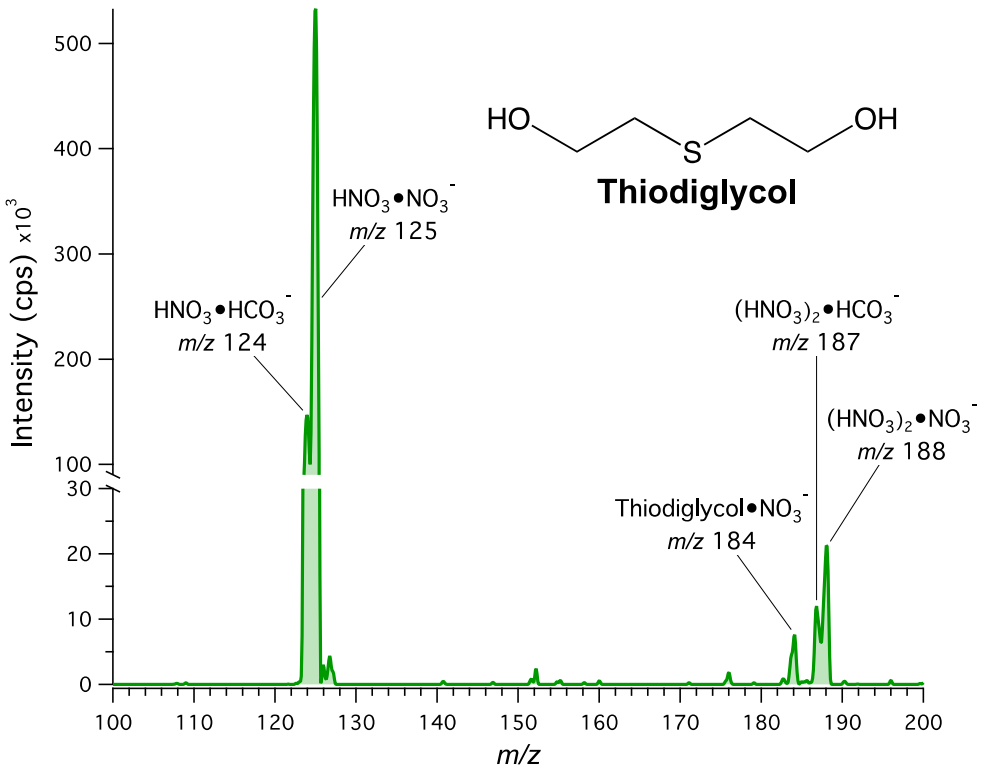


**Figure 2.)** The targeted CWA simulant species thiodiglycol is observed at *m/z* 184 as a nitrate adduct within AFT-MS mass spectra, along with reactant ions $HNO_3 \bullet HCO_3^-$, $HNO_3 \bullet NO_3^-$, $(HNO_3)_2 \bullet HCO_3^-$, and $(HNO_3)_2 \bullet NO_3^-$.

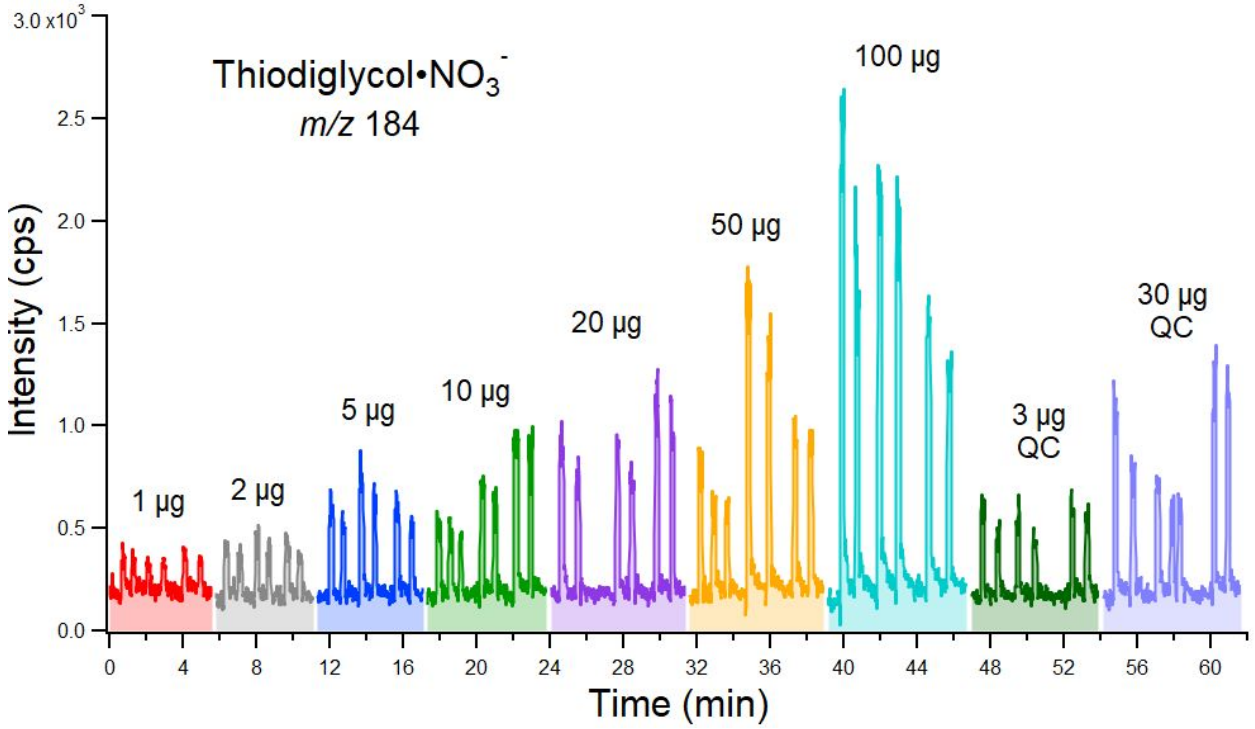


**Figure 3.)** Measurements of non-equilibrium vapor obtained from the deposition of 1-100 µg calibration standards. An overall upward trend in signal is observed as the dried analyte mass increased. For clarity, all measurements for a single concentration were obtained in a single experimental campaign including multiple slides containing dried TDG. The data for each concentration range was obtained over the period of ~5 min.

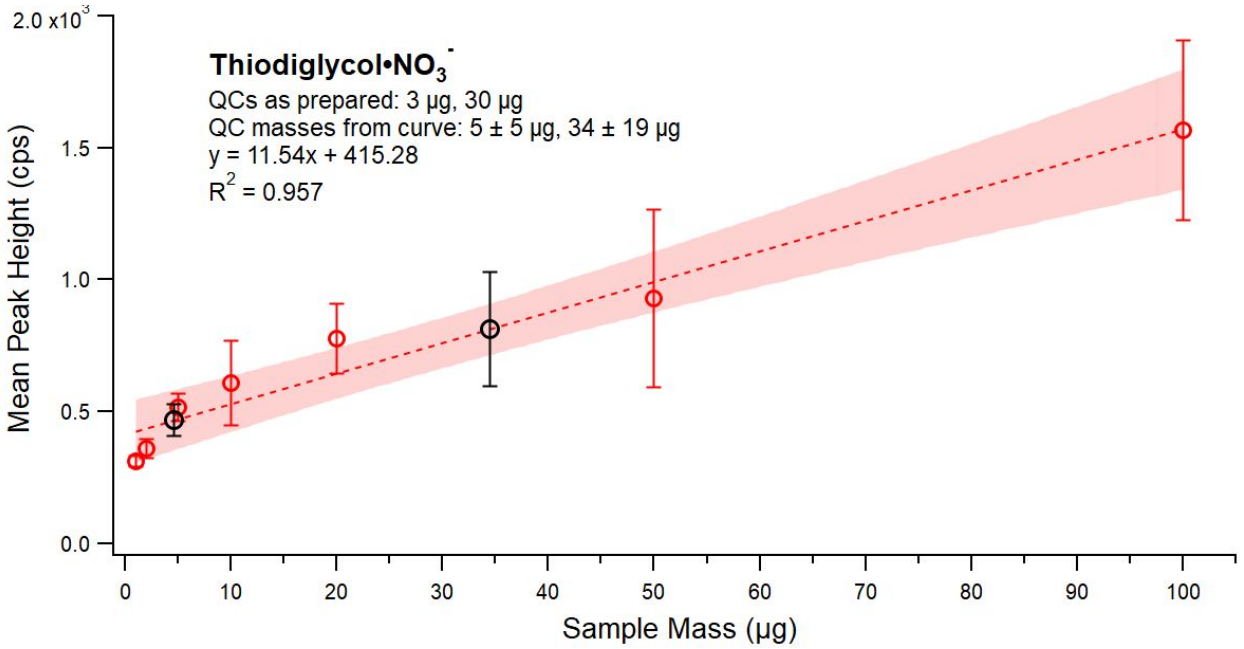


**Figure 4.)** The calibration curve for vapor detection from thiodiglycol surface residues from deposition masses ranging from 1-100 µg. While there is a greater degree of signal variation and correspondingly lower precision for the QC masses, this experiment provides a viable proof-of-concept of using AFT-MS for non-contact trace TDG residue detection.

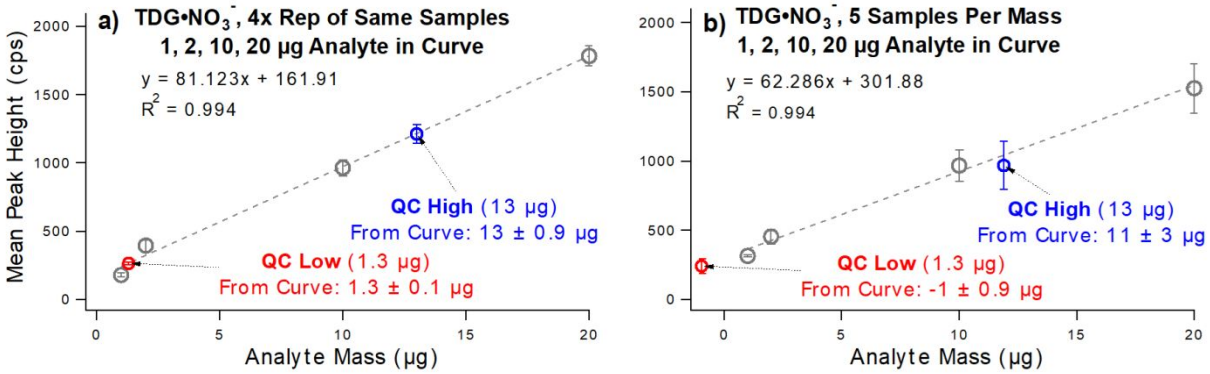


**Figure 5.)** To investigate two possible sources of signal variation for TDG detection by AFT-MS, two additional calibration curves and QC detection experiments were performed on a higher precision analyte mass range where **a)** only a single sample per analyte mass was measured four times and **b)** five replicate samples were prepared for analysis per TDG mass and measured only once. While the two curves yielded the same $R^2$, four replicate measurements of a single sample per mass **(a)** produced enhanced QC precision and accuracy over single replicate analysis of five separate samples per analyte mass **(b)**.

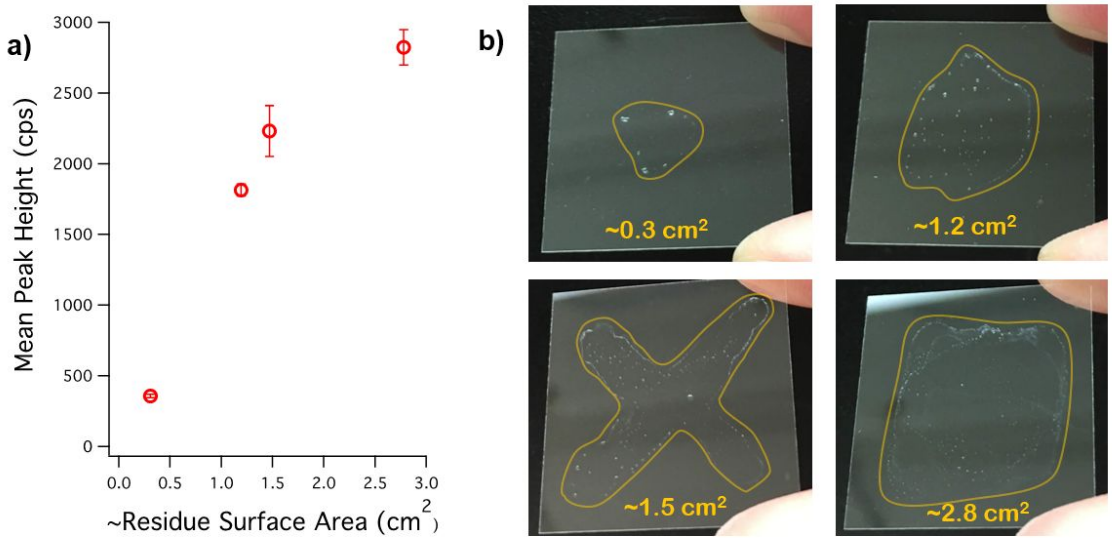


**Figure 6.) a)** Comparison of ion current signal for replicate analysis of thiodiglycol from samples of constant concentration (2 µg/µL) and deposited volume (5 µL) for a total of 10 µg but varying in deliberate analyte residue spread. **b)** Photos depicting the slides with differing sample areas highlighted and approximated surface areas indicated below the residue.

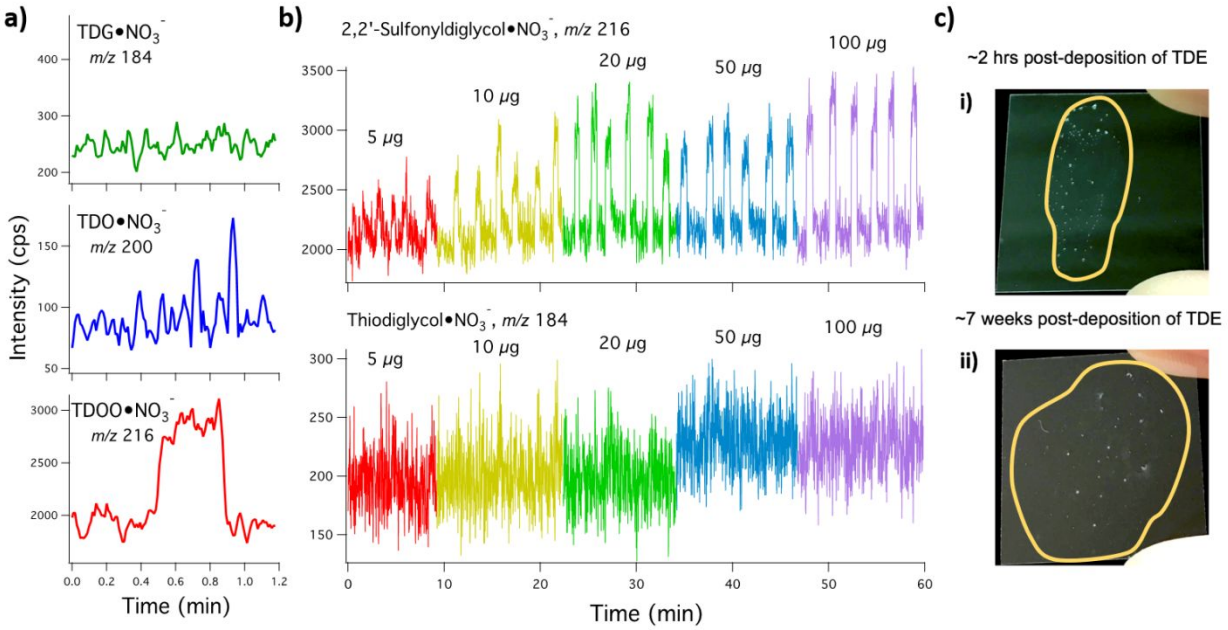


**Figure 7.) a)** As a preliminary assessment of the aged thiodiglycol residues, one of the 100 µg residue samples was analyzed using SIM on *m/z* 184, 200, and 216, which correspond to the nitrate adducts with thiodiglycol (TDG), 2,2'-sulfinyldiglycol (TDO), and 2,2'-sulfonyldiglycol (TDOO), respectively. **b)** Non-contact vapor detection profiles of 1-100 µg TDG residue samples after 7-weeks of aging. **c)** A visual comparison of a 10-µg TDG residue merely two hours after sample deposition with a 7-week post-deposition 10-µg TDG residue reveals the transformation of an analyte that is liquid at room temperature (i) to degradation products that are crystalline solids at room temperature (ii).