

CARCINOGENIC BENZENE: AN ALTERNATE METHOD TO ASSESS EXPOSURE
AMONG MARITIME WORKERS

by

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DEDICATION

First, this thesis is dedicated to my beautiful wife, Erica Heredia Maisonet. Without your love and encouragement, I would have never been able to complete this thesis or excel academically. Second, to my three sons, Anthony, Caleb, and Sebastian, who are my greatest achievements and continually remind me of what's important in life. Continue chasing your dreams, make the life you want to live, and always stay connected with God and family.

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ABSTRACT

Carcinogenic Benzene: An Alternate Method to Assess Exposure Among Maritime Workers

Miguel A. Maldonado, Master of Science in Public Health, 2022

Thesis directed by: Captain Michael E. Stevens Jr., Ph.D., Division Director for Occupational and Environmental Health Sciences, Department of Preventive Medicine and Biostatistics

Background:

Environmental and occupational exposure to benzene poses a risk to the Coast Guard and other maritime workers such as those who load/unload containers, dock workers, ship crews, cargo inspectors, and customs officers. Airborne occupational exposures to benzene are understudied in the maritime industry. Benzene is classified as a known human carcinogen by the International Agency for Research on Cancer and the U.S. Environmental Protection Agency.

Objective:

This project investigated whether diffusion-based, passive air sampling for benzene with a radial sampler with subsequent thermal desorption and analysis by GC/MS shows good agreement with an established conventional method and results produced by a ‘gold standard’ reference instrument. A performance evaluation was conducted using a Radiello® radial sampler when performing a 15-minute air sampling experiment for benzene under controlled laboratory conditions. A level of agreement assessment was performed between the Radiello® results,

conventional Assay Technology 566 OVM axial badges, and a direct-reading reference instrument.

Methods:

Generation of the laboratory-controlled atmosphere of benzene was carried out in a dynamic flow chamber controlled by a Miller-Nelson HCS-501 flow, temperature, and humidity control system. Benzene concentrations ranging between 0.50 and 2.5 ppm were generated, verified, and monitored with a Gasmeter DX4040 Fourier Transform Infrared Spectrometer (FTIR). The Radiello® and Assay Technology OVM samplers were exposed to each benzene atmosphere for 15 minutes. The radial samples were analyzed using a thermal desorption technique, while axial samplers were analyzed using a conventional solvent desorption technique.

A series of one-way Analysis of Variance tests comprised of device and concentration factors were used to compare the mean difference between the Radiello®, OVM, and reference instrument approaches. The relative standard deviation was used to investigate the precision and the relative percent error was used to investigate the accuracy of the samplers. A Bland-Altman analysis investigated the agreement and correlation between the results of the Radiello®, OVM, and direct-reading reference instrument.

Results:

This study determined the level of agreement, precision and accuracy between two passive samplers when exposed to low benzene concentrations and a 15-minute sampling time. Although the OVM showed the best level of agreement in Scenarios 2 (1.25 ppm) and 3 (2.50 ppm), the OVM analytical method could not quantify benzene at the lowest target concentration

at Scenario 1 (0.50 ppm). The Radiello® was able to quantify benzene in all scenarios but with a lesser level of agreement and 40% relative error. The Radiello® and OVM demonstrated good precision based on the relative standard deviation values.

Conclusions:

The Radiello® combined with thermal desorption shows superior sensitivity. The OVM combined with solvent-based desorption is not a viable option for low concentrations and short sampling times. At this point, no recommendation can be made to the Coast Guard for the deployment of the Radiello® to determine short-term personal exposures to benzene. It is recommended that a future study reevaluate its performance at the proposed STEL of 0.10 ppm and a greater variety of temperatures and relative humidity levels that Coast Guard inspectors encounter in the field.

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CHAPTER 1: INTRODUCTION

1.1 STATEMENT OF PURPOSE

The purpose of this study was to identify the most effective means of passive personal sampling for short-term exposure of U.S. Coast Guard personnel to benzene. This was performed by evaluating the precision, accuracy and level of agreement between a radial diffusive sampler analyzed by thermal desorption techniques and an axial diffusive sampler analyzed by conventional solvent desorption techniques. The samplers were compared by passively sampling benzene concentrations in a dynamic flow chamber under laboratory conditions.

Volatile organic compound (VOC) emissions in air such as benzene are inherently abundant in the maritime environment, and concentrations vary depending on the vessel, operation, facility, or shipping container contents. U.S. Coast Guard inspectors examine various marine platforms and facilities that handle petroleum cargoes and freight shipping containers to verify compliance with applicable regulations and international conventions. Environmental and occupational exposure to benzene poses a risk to the Coast Guard population, and research into these specific risks is understudied. To the best of our knowledge, as of March 2022, no published studies or data have evaluated occupational exposures of the Coast Guard population to benzene. ACGIH classifies benzene as an A-1 confirmed human carcinogen and can cause hematological effects, leading to aplastic anemia and the development of leukemia.

Utilizing passive samplers to conduct short-term (15-minute durations) personal sampling of airborne benzene enables the Coast Guard to ensure compliance with Short-Term Exposure Limit (STEL) occupational exposure limits. Passive samplers feature several desirable properties,

including intrinsic safety, ease of use, and minimal training requirements for the wearers and operators. Additionally, passive samplers preclude the use of expensive and cumbersome active sampling pumps. Passive air sampling devices contain a specific sorbent bed to collect organic vapors via diffusion from the surrounding air instead of through active air movement across its sorbent bed using a battery-powered pump. Specific samplers can be desorbed using heat instead of solvents, which features additional benefits, such as higher sensitivity and the ability to be used 100-200 times before the sorbent requires replenishing. This study will evaluate the performance of a radial sampler with a Carbograph 4 sorbent capable of being thermally desorbed and a traditionally used axial passive badge using conventional solvent desorption. The study involves each sampler type performing a 15-minute passive sampling of various BTEX concentrations in a dynamic flow chamber under controlled laboratory conditions. The results of the sampling analyses will then be evaluated based on the level of agreement of each sampler type with a gold standard reference instrument.

The overall project is intended to investigate whether passive sampling of benzene with a radial sampler analyzed by thermal desorption would show enough promise in the lab to warrant a field study in work environments typically encountered by Coast Guard personnel.

1.3 RESEARCH QUESTIONS AND SPECIFIC AIMS

This research aimed to determine if the USCG's efforts to best manage occupational exposure to hazardous VOCs like benzene could be enhanced. To test this aim, this research evaluated the performance of a traditionally used axial passive sampling device and method (subsequently desorbed using a solvent and analyzed using gas chromatography-mass spectrometry (GC/MS)) relative to results produced from using a radial passive sampling device and method (utilizing thermal desorption and analysis by GC/MS).

1.3.1 Research Question

What is the level of agreement, precision, and accuracy between a conventional axial diffusive sampler (Assay Technology 566 Organic Vapor Monitor) and a radial diffusive sampler (Radiello® C-RAD145) when used to passively sample a range of airborne concentrations of benzene under laboratory conditions?

1.3.2 Specific Aims

1. Determine sampler accuracy, precision, and agreement relative to a direct reading, 'gold standard' reference instrument method at pre-determined benzene concentrations, temperature, sampling time, and relative humidity.
 - Benzene evaluation range: Concentrations will be at 0.20 x STEL, 0.50 x STEL and 1.0 x STEL.
 - The specific concentrations of interest have been summarized in Table 1.

Table 1: Benzene concentrations of interest (4).

Concentrations of Interest				
Chemical	2019 ACGIH TLV	1/5 x STEL	1/2 x STEL	1 x STEL
Benzene	0.5 ppm	0.50 ppm	1.25 ppm	2.5 ppm

Specific parameters for this study included:

- Temperature: Room temperature at 21 °C (69.8 °F). The temperature was generated and maintained by the Miller-Nelson HCS-501-200.
- Relative humidity (R.H.): 70% R.H. (Humidity Ratio of 76.4 grains of moisture per pound of dry air). R.H. was generated and maintained by the Miller-Nelson HCS-501.
- Sampling time of interest: 15-minutes

2. Perform a series of one-way Analysis of Variance tests comprised of device and concentration factors to compare the mean difference between the Radiello[®], OVM, and Gasmeter reference instruments.
3. Perform a Bland-Altman analysis to investigate the agreement and correlation between the Radiello[®], OVM, and direct-reading reference instrument:
 - a. Radiello[®] C-RAD145 (radial diffusive sampler) vs. FTIR Reference
 - b. Assay Technology 566 OVM (axial diffusive sampler) vs. FTIR Reference
 - c. Radiello[®] C-RAD145 vs. Assay Technology 566 OVM.

1.3.3 Sampling Plan

Three different scenarios (groups) of sampling media were compared. Scenarios 1, 2, and 3 were conducted at the same exposure time, relative humidity, and temperature when evaluating a concentration range of benzene. (Table 2).

Table 2: Sampling plan for Scenarios 1, 2, and 3.

Sampling Plan			
	Scenario 1	Scenario 2	Scenario 3
Concentration of Interest	1/5 x STEL	1/2 x STEL	1 x STEL
Exposure Time	15 minutes	15 minutes	15 minutes
Relative Humidity	70% RH	70% RH	70% RH
Temperature	21 °C	21 °C	21 °C
Number of Assay Technology 566 O.V.M. Samples	26	26	26
Number of Radiello [®] C-RAD145 Samples	26	26	26

CHAPTER 2: LITERATURE REVIEW

2.1 HISTORY OF BENZENE

Early use of benzene in the industrial setting traces back to the later part of the 19th century. Benzene was an excellent solvent for rubber latex which quickly made its way worldwide into the rubber industry to make rubber-coated waterproof fabrics, bicycle and automobile tires, and molded rubber products (47). Several young women from a canning factory in Baltimore suffered from weakness, hemorrhage, pancytopenia, and aplastic anemia. These workers were exposed to benzene while handling the rubber solution, when spreading the rubber over the fabric or pouring it into molds, and finally, during the drying of the product. The volatility of benzene is one of the critical chemical attributes that allowed it to evaporate, leading to excessive worker exposure. Benzene-based rubber cement was also used before metallic seals were developed in the canning industry. This same rubber cement was used in shoe manufacturing, leading to similar exposures (47). The production of benzene during this time was also ramped by the need to produce more toluene to manufacture explosives for World War I. After the war, there was increased use in glue manufacturing, artificial leather, hat manufacturing, printing, paint, adhesives, dry cleaning, automobile assembly, petroleum products, and blending of motor fuels (29). Cases of aplastic anemia, known as benzene poisoning, soon skyrocketed as expansion in its use increased through the 19th century. Some of these employees were diagnosed with benzene poisoning within a few weeks of initial employment, with a few dying within months. These employees' exposure levels ranged from 200-1000 ppm of benzene (29).

2.2 EXPOSURE TO BENZENE

2.2.1 Indoor and Environmental Exposure

Benzene sources and concentrations are very diverse and can vary significantly according to the indoor or outdoor environment. Of the various VOCs, benzene is one of the most significant contributors to air pollution and the fifth leading risk factor for premature mortality globally (25). Vehicular exhaust and industrial emissions are considered the most significant contributors resulting from the combustion of fossil fuels, evaporation at gas station pumps and tanks, or accidental spills (15; 48). Consumer products add to indoor emissions through tobacco smoke, home/building heating systems, solvents, adhesives, and industrial equipment (48). Indoors, benzene can volatilize from household cleaning products, fabric/leather treatments, and automotive products (15). Vapor pressure explains why benzene is found in the air. Benzene has a high vapor pressure at normal temperatures ($\sim 20^{\circ}\text{C}$), which relates to the tendency of molecules wanting to escape from the liquid or a solid-state. Household cleaning products absorbed onto items such as carpets, glass, pillows, flooring, and wallcovering can result in persistent background levels after cleaning.

2.2.2 Common Jobs with Occupational Exposures in the Maritime Community

Approximately 500 million freight containers are shipped annually between countries worldwide (49). Approximately 90% of all international freight is shipped by container ships, representing about 50,000 commercial merchant ships (49). Globalization of trade is expected to grow as more giant container ships are constructed, such as the Ultra Large Container, capable of transporting 24,000 Twenty-Foot Equivalent Units (20-foot-long containers). Depending on the consumer products being transported, items in these shipping containers may off-gas hazardous

chemicals, including benzene (44). Many international countries with large shipping ports located in Rotterdam, Netherlands; Hamburg, Germany; Gothenburg, Sweden; and Australia have a growing interest in understanding the occupational exposures to the various chemicals in containerized cargoes (44). Previous studies examining potential exposure risks from containerized cargoes have focused on fumigants, while others have concentrated on fumigants and off-gassing hazardous chemicals. In one study, Baur et al. (2009) investigated 2,113 containers arriving at the second-largest container terminal in Hamburg, Germany. They determined that 1,478 (70%) containers were contaminated with toxic chemicals above the chronic reference exposure levels (RELs), and 761 (36%) exceeded the higher acute reference exposure thresholds (13). Benzene contamination was four times greater than for fumigants. RELs used were based on the Office of Environmental Health Hazard Assessment (OEHHA) (Acute 27 $\mu\text{g}/\text{m}^3$; Chronic 3 $\mu\text{g}/\text{m}^3$) (13). Budnik et al. (2017) also found that the mean amounts of benzene analyzed container air were 698-fold higher when compared to the OEHHA chronic RELs (16). These exposures present an inhalation hazard to workers entering a shipping container through the entire supply chain management of the container. The exposed population could include personnel who pack and unload the container, dock workers, vessel crews, cargo inspectors, and customs officers.

In 2019, the U.S. imported 9.14 million barrels per day (MMb/d) of petroleum from 90 countries. This petroleum includes crude oil, hydrocarbon gas liquids, refined gasoline, diesel fuel, and biofuels (54). During this same year, the U.S. exported 8.4 MMb/d to 190 countries (54). Chemical and oil tankers transport the various chemicals needed by consumers worldwide. Several studies had evaluated VOC exposure risks associated with transporting fossil fuels and chemicals to determine the occupational exposures to compounds like benzene since the only existing data available before these studies were based on a predictive statistical analysis (32).

Research studies employing passive sampling devices have included measuring airborne concentrations and monitoring benzene on several tanker ships. The airborne concentrations measured aboard these vessels showed that cargo vapors produced during the transportation, loading/offloading, and tank cleaning operations created an atmosphere with concentrations surrounding the vessel and in some machinery spaces within the vessel ranging from 1.92 to 76.4 $\mu\text{g}/\text{m}^3$ (32). A nested case-reference study by Nilsson (1998) investigated the risk of cancers that affect the blood, bone marrow, and lymph nodes on deck crews on tankers exposed to cargo vapors. They found an increased risk of lymphatic and hematopoietic malignancies (Mantel-Haenszel odds ratio (OR) 2.6) with a significant exposure-response relationship among seamen exposed to benzene (42). The ORs were increased for lymphoma (OR 3.2), multiple myeloma (OR 4.0), and leukemia (OR 1.6), but the increase was only significant for non-Hodgkin's lymphoma (OR 3.3) (42).

Another study by Višnja *et al.* (2021) evaluated a low and high exposure group to airborne occupational exposure in a petrochemical plant. Compared to the European Union's occupational exposure limit (OEL) of 3.25 mg/m^3 , the High Exposure Group showed a benzene max concentration ten times higher than the OEL value (range 3.18-32.11 mg/m^3 ; mean 10.1 mg/m^3) (55). The Low Exposure Group showed a range of 0.07 to 1.18 mg/m^3 and a mean of 0.30 mg/m^3 (55). The exposed populations across these three studies identified the potential for significant exposures to workers and crews across the entire petrol supply chain from the refinement to its transportation on board a vessel.

2.2.3 Occupational Exposures in the Coast Guard

The U.S. Coast Guard is a federal agency responsible for navigation and vessel inspection laws, regulations, and international conventions governing marine safety. Coast Guard marine

inspectors perform inspections for safety, security, and environmental protection on the U.S. and foreign-flagged commercial vessels to verify compliance with safety of navigation, firefighting, seaworthiness, propulsion, structural integrity, lifesaving, the safety of navigation, and cargo handling systems. The Coast Guard is also tasked with inspecting a percentage of the 11 million maritime containers that arrive at U.S. seaports sourced from diverse overseas countries (22). In 2020, the Coast Guard inspected approximately 33,626 containers spread across 30 different Coast Guard units in the U.S. and its territories. Another statutory mission of the Coast Guard is to inspect waterfront facilities for safety and security requirements to prevent accidents that could lead to death, injury, spills, or a disruption of the maritime transportation system (53).

Benzene is inherently abundant in the maritime environment, and concentrations can vary depending on the type of vessel, operation, facility, or shipping container contents. U.S. Coast Guard marine inspectors board various marine platforms and facilities that handle petroleum cargoes and containers to verify compliance with applicable regulations and international conventions. As of January 2022, no published studies or data have evaluated Coast Guard marine inspectors or facility inspectors for benzene exposure. However, other countries have published studies that evaluated occupational exposures to containerized cargoes and the occurrence of off-gassing chemicals (12; 13; 16; 44; 49; 50). Several studies by Prezant (2018), Budnik *et al.* (2017), Svedberg *et al.* (2017), Baur *et al.* (2015), and Baur *et al.* (2010) showed a high percentage of containers contaminated with fumigants and industrial solvents at concentrations above chronic or acute exposure levels based on OEHHA RELs, Australian Workplace Exposure Standards, and NIOSH recommended occupational exposure limits. Concentration levels varied by the types of cargoes/consumer products confined inside the shipping containers. Studies by Nilsson *et al.* (1998), Saani *et al.* (2002), Jacobs *et al.* (2010), and Višnja *et al.* (2021) evaluated workers on tank ships and facilities that handle chemicals and

petroleum products. These studies found an atmosphere of airborne benzene concentrations surrounding the vessel contributed by the transportation, loading/offloading, and tank cleaning operations. Occupational exposures at petrochemical plants showed significant benzene emissions exceeding European OELs.

2.3 POTENTIAL HEALTH IMPACTS

The International Agency for Research on Cancer classified benzene as a carcinogen (Group 1) (30). Additionally, the Environmental Protection Agency (EPA) has classified benzene as a Group A carcinogen (known human carcinogen) and can cause hematological effects, leading to aplastic anemia and the development of leukemia (56).

The toxicological profile for benzene discusses that acute occupational exposure (5-10 minutes) to high concentrations of benzene vapors 700 to 3,000 ppm may cause narcosis: headaches, dizziness, drowsiness, confusion, tremors, and loss of consciousness. It is also an eye and skin irritant. Brief exposure to benzene in the air in the range of 10,000 to 20,000 ppm can also cause death. Chronic exposure to benzene (365 days or more) can cause acute myeloid leukemia, lymphocytic leukemia, non-Hodgkin's lymphoma, and multiple myeloma. Chronic exposure will reduce red and white blood cells from bone marrow, resulting in aplastic anemia. In addition, there is also a reduction in B-cell and T-cell proliferation (56). A total of 186 studies of varying references evaluated acute inhalation effects (14 days or less) in humans and animals. A summary of the chemical toxicokinetic and health effects has been provided in Table 3.

Table 3: Summary of individual chemical toxicokinetic and health effects.

Component	ADME	Mode of Action	Target Organs
Benzene (56)	- Absorption: Lung, GI - Distribution: Wide – all tissues - Metabolism: - Liver by CYP2E1 - Bioactivated (2 pathways) - Excretion: - Bile & urine (metabolites) - Breath (benzene)	- General anesthetic effects of lipophilic solvents - Decrease in bone marrow cellularity - Metabolites may induce oxidative DNA damage	- Central Nervous System - Hematologic - Cancer
ADME = Absorption, Distribution, Metabolism, and Excretion CYP2E1 = Catalase and cytochrome P450 2E1			

2.4 PUBLIC HEALTH /MILITARY HEALTH RELEVANCE

Coast Guard marine inspectors, under normal circumstances, typically do not spend more than eight hours a day conducting vessel or container inspections. Also, while on a vessel, the inspector typically doesn't spend more than fifteen minutes in one area since the inspection scope requires them to be mobile. On average, inspecting an individual container does not typically take an inspector more than five minutes. Focusing on 15-minute STELs could better characterize an inspector's exposure profile and help identify areas of a ship or the specific containers that contributed the highest exposures.

Characterizing benzene concentrations encountered during a routine container or vessel inspection could also demonstrate the need for additional administrative controls or personal protection equipment.

Sampling methods that accurately measure personal exposures are essential to characterize benzene exposures accurately to Coast Guard personnel.

A literature review found no studies specific to benzene STELs using a radial diffusive sampler with thermal desorption and GC/MS as the analytical method to evaluate occupational exposures.

Although solvent extraction is more commonly used over thermal desorption, it does have its drawbacks. Major drawbacks to this approach include the relatively large amounts of solvent used to desorb the compound(s) of interest off the sampling media and the minimal amount of diluted sample delivered into the analytical system, typically one microliter. This decreases

analytical sensitivity due to the increased solvent background when performing chromatography (45). The investigator would thus need to sample for a more extended period to collect enough mass to detect the analyte of interest. Another major drawback of using liquid solvents is the hazard potential to human health and the environment related to the use of liquid solvents and the generation of solvent waste. On the other hand, thermal desorption is an excellent alternative to solvent extraction since the whole sample is analyzed, providing a higher degree of sensitivity.

2.5 OCCUPATIONAL EXPOSURE LIMITS

The 8-hour permissible exposure levels (PEL) and short-term exposure limits (STEL) established by the Occupational Safety and Health Administration (OSHA) for benzene are 1 ppm and 5 ppm, which represent the legal limits for occupational exposures. The Coast Guard has kept exposures as low as possible and has adopted limits set out by a professional organizations such as the American Conference of Governmental Industrial Hygienists (ACGIH). Threshold Limit Values are health-based values created by committees that review published and peer-reviewed literature. ACHIG recommends a Threshold Limit Value (TLV) for an 8-hour time-weighted average (TWA) of 0.50 ppm and a short-term exposure limit (STEL) of 2.50 ppm. The TWA average is a concentration of a hazardous substance in the air averaged over an 8-hour workday and a 40-hour work week to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effects (5). The STEL is a 15-minute exposure that shouldn't be exceeded at any time during the workday. The STEL is the concentration to which it is believed that nearly all workers can be exposed continuously for a short period of time without suffering from irritation, chronic or irreversible tissue damage, dose-rate-dependent toxic effects, or narcosis (5).

The National Institute for Occupational Safety (NIOSH) recommended exposure level (REL) for time-weighted average is 0.10 ppm and a STEL of 1.0 ppm (31). The OELs for the individual chemicals that make up benzene are outlined in Table 4. This study focused on the ACGIH STEL of 2.50 ppm associated with benzene and a concentration range of 0.50 to 2.50 ppm. The ACGIH 2022 Notice of Intended Changes recently proposed an adjusted TLV TWA of 0.02 ppm and a STEL of 0.10 ppm.

Table 4: Occupational exposure limits for ACGIH, NIOSH, and OSHA (11).

Occupational Exposure Limits		Benzene (ppm)
ACGIH	TLV	0.5
	STEL	2.5
NIOSH	REL	0.1
	IDLH	500
	STEL	1
OSHA	PEL	1
	Ceiling	None
	STEL	5
ACGIH= American Conference of Governmental Industrial Hygienists		
NIOSH= National Institute for Occupation Safety and Health		
OSHA= Occupational Safety and Health Administration		
TLV = Threshold Limit Value (8-hour work shift time-weighted average)		
STEL= Short Term Exposure Limit (15 minutes)		
REL= Recommended Exposure Limit (10-hour work shift time-weighted average)		
IDLH= Immediately Dangerous to Health or Life		
PEL = Permissive Exposure Limit (8-hour work shift time-weighted average)		
Ceiling: The maximum exposure limit, which cannot be exceeded for any length of time		

2.6 ACTIVE AND PASSIVE SAMPLING APPROACHES

Several methods have been used to monitor entire work shifts or specific, shorter duration tasks where the potential for workplace chemical exposures exists. These methods include: conventional sorbent-based active (pumped) sampling, passive sampling, and direct-reading

instruments such as Fourier transform infrared spectrometry (FTIR)-based instrumentation. It should be noted that the adjective "passive" and "diffusive" are synonymous (14).

Standard methods to monitor benzene for workers' exposures involve using battery-powered air sampling pumps, which pull sampled air through specific sampling cartridges at specified sampling rates (typically in L per min). Depending on the analyte(s) of interest, these cartridges contain charcoal or other sorbents. After the work shift, these sorbents are desorbed in the laboratory using different methods. A common methodological approach is to desorb using carbon disulfide). Following desorption, a microliter amount of the diluted liquid sample (containing solvent and analyte) is injected into an analytical system, typically a gas chromatograph equipped with a flame ionization detector. NIOSH method 1501 is an example. Another methodological approach includes high-temperature thermal desorption utilizing NIOSH method 2549, which utilizes mass spectrometry for analysis (NIOSH method 2549) (31).

FTIR (NIOSH Method 3800, 2002) also offers many advantages, such as continuous monitoring and measurement of peak exposures with instantaneous data logging capabilities (31). However, these systems are larger/heavier, more expensive, and sensitive to humidity and background interference, creating challenges when monitoring Coast Guard inspectors who are constantly mobile on vessels, containers, or oil terminals.

Conventional methods to passively or actively sample benzene components offer good accuracy and precision. Accuracy refers to the correctness of a measurement and is synonymous with the term "validity." On the other hand, precision refers to the consistency of measurement and is synonymous with the term "reliability" (21). However, each type of sampling offers several well-established advantages and disadvantages. Active sampling does offer the advantage of allowing for flow rate variability. Since the pump has a variable speed, it can be adjusted to collect enough analyte mass for detection by the analytical instrument if the chemical is present

in appreciable amounts in the sampled airborne environment. Hundreds of sampling and analysis methods have been validated and published by NIOSH and OSHA, using active sampling (57).

Some disadvantages associated with active sampling may deter from picking this type of method. For example, active sampling with pumps and charcoal tubes is not always user-friendly. Active sampling requires heavy pumps that are bulky and cumbersome for workers to wear and the pumps also require trained personnel to operate and monitor them. Coast Guard inspectors often work in areas with minimal space while inspecting a vessel or container, making it difficult for those wearing pumps to move around in these spaces. Due to the nature of the various types of spaces inspectors encounter, crawling and climbing through very tight areas inside a packed container or in between rows of piping on a vessel could present a challenge with active sampling and possibly cause crimping of the sampling tube or damage to the pump. The pump and calibrator's high initial investment cost makes this setup more costly.

Brown 1993 describes a diffusive sampler as a device that takes a sample of vapor or gas from the atmosphere at a rate controlled by a physical process. This physical process is known as diffusion through a static air layer or permeation through a membrane that does not rely on active movement (pumped) of air through the sampler. This diffusion and permeation can best be described by Fick's First Law of diffusion, which relates the mass uptake rate by the sampler to the concentration gradient, the time of exposure, and the sampler area exposed to the pollutant atmosphere. Validation of the uptake rates also considers real-world parameters such as non-steady-state sampling, the effects of fluctuating concentrations, sorbent saturation, wind velocity, turbulence at the sampler surface, temperature, and pressure (14). Passive sampling is particularly suited to monitor personal exposure to benzene in the various maritime platforms such as liquid cargo ships (crude, product, chemical, liquefied gas carriers, oil rigs, tank barges), dry cargo ships (bulk, container, reefer, roll-on/roll-off) and specialized cargo ships (passenger,

heavy-lift, tugs). It is less obtrusive for workers, reduces the potential for sample loss due to an equipment malfunction, and can be used by personnel not familiar with heavy active sampling pumps or with minimal training (43).

Axial diffusive samplers are the most commonly used, commercially available passive sampling device. These were also the first type of sampler to offer a diffusion path parallel to the sorbent axis (15) (Figure 1). Since these devices are planar or axial in shape, they offer lower sampling rates and limited sampling capacity. As a result, sensitivity can be affected due to analyte back-diffusion due to the low sampler capacity of axial samplers (48). In 1996, a newer version of a diffusive sampler known as the Radiello® C-RAD145 was released by Fondazione Salvatore Maugeri (Padova, Italy) and consisted of a radial, cylindrical diffusive body, which houses a cylindrically shaped sorbent (Figure 2) (18). Designing a sampler with a larger surface area for absorbing analytes offers an increased sampling area relative to axial diffusive samplers. The diffusive axial sampler used in this study includes the Assay Technologies 566 Organic Vapor Monitor (O.V.M.), Assay Technology, Livermore, CA), and the radial type of diffusive sampler used consists of the Radiello® C-RAD145. With passive sampling, the radial diffusive sampler offers the best option for low to high concentrations with short duration sampling since the radial design allows for a sizeable diffusive area relative to the adsorbing surface while still maintaining a small diffusive surface between the diffusive membrane and the adsorbent (15; 48).

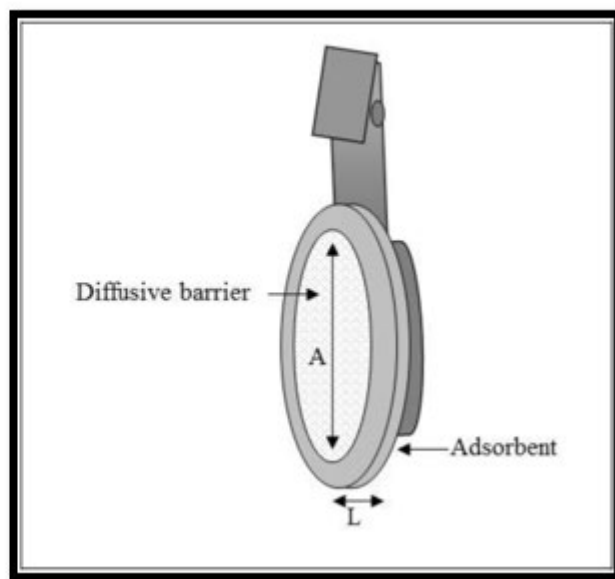


Figure 1: An axial diffusive sampler: The Assay Technology 566 OVM sampler with an inert charcoal wafer and 76-hole sampling grid (17; 38).

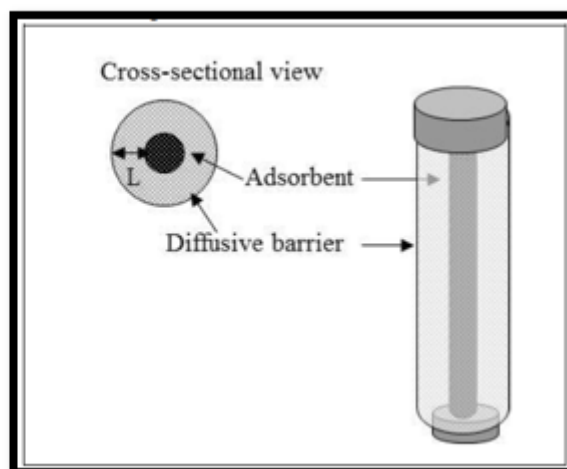


Figure 2: A Radial Diffusive Sampler: Radiello® C-RAD145 sampler with the yellow diffusive body packed with Carbograph 4 adsorbent (18; 38)

The impact of Radiello®'s utilization of thermal desorption for analysis was included in the performance evaluation of this study by comparing it to a traditional passive method employing solvent desorption. Thermal desorption (TD) is a simple, sensitive, and selective

technique that can produce a representative exposure measurement for short-term sampling (51). TD is compatible with automated sampler analysis and provides a more cost-effective approach since the sorbent can be reused up to 100 times. TD also avoids sample preparation steps that require toxic, flammable solvents, such as carbon disulfide, to desorb the analyte of interest from the sorbent. These solvents can create potential exposure or fire hazards in the lab. Solvent desorption can result in lower extraction efficiency versus thermal desorption since dilution effects can result in a 1000-fold reduction in the mass available for analysis relative to thermal desorption (19; 51). Analysis by thermal desorption eliminates these problems, as the analyte of interest is driven out of the sorbent by heat, and virtually all collected molecules are made available for analysis. Ramirez *et al.* (2010) conducted a study comparing solvent and thermal desorption for 90 volatile organic compounds, including benzene. Their study identified a higher level of performance with TD that allowed for shorter sampling periods and provided more precise data (45). In the period sampled during the study, solvent desorption was able to detect and quantify only 18 of the 90 VOCs, while TD could detect and quantify 50 VOCs. Benzene was one of the analytes which showed the highest difference in the values obtained by both methods. For instance, sampling showed target benzene compounds of Day 1: $1.40 \mu\text{g}/\text{m}^3$ (solvent desorption) vs. $2.53 \mu\text{g}/\text{m}^3$ (TD), Day 4: $3.60 \mu\text{g}/\text{m}^3$ (solvent desorption) vs. $17.15 \mu\text{g}/\text{m}^3$ (TD), Day 8: $1.30 \mu\text{g}/\text{m}^3$ (solvent desorption) vs. $9.18 \mu\text{g}/\text{m}^3$ (TD) (45).

2.7 PASSIVE SAMPLING THEORY

A passive sampler is a device used to collect various types of chemicals in the air through a diffusion process. These samplers can be used in an indoor workplace or outdoor environment for personal or environmental monitoring. They are also manufactured to be effective based on

the analyte of interest and are classified as axial or radial diffusive samplers. Using a passive sampler for long-term monitoring of eight hours or more will produce an average concentration over the measured period. A short-term sampling of four hours or less can allow for more accurate characterization of peak exposures that may not be detectable with long-term sampling. The problem with long-term monitoring is the potential to underestimate the potential acute toxic effects.

Fick's First Law of diffusion allows for the free flow of analytes from the sampled medium (high concentration) to a collecting medium (low concentration) (26). This flow continues until equilibrium is reached, and the amount of analyte on this medium depends on the concentration and the exposure time (26). The equation associated with Fick's Law is described by *Equation 2.1* and *Equation 2.2* (18). The focus of this study evaluated a fifteen-minute exposure time at concentrations ranging from 1/10th to one times the STEL.

$$Q = D * K \quad (2.1)$$

Q = Sampling Rate (L/min)

D = Diffusion Coefficient of a Given Analyte (mm²/s)

K = Geometric Constant of the Sampler

$$K = S/L \quad (2.2)$$

K = geometrical constant of the sampler

S = diffusive surface (mm)

L = distance between the diffusive surface and adsorbing surface (mm)

The sampling rate (Q) of a diffusive sampler depends on a diffusion coefficient (D) and the geometric constant of the sampler (K) (*Equation 2.1*). The diffusion coefficient (D) remains constant for the analyte of interest. The best way to improve the sampling rate (Q) is to maximize the geometrical constant (K) (*Equation 2.2*). The geometrical constant is calculated as a ratio of the diffusive surface and the distance between the diffusive surface and the adsorbing surface.

Figure 3 shows the surface area of a diffusive sampler. The diffusive surface (S) is "transparent," allowing gaseous molecules to cross it along path L, which is parallel to the axis of the cylindrical box. The molecules are then absorbed and "trapped" by the adsorbing surface (A) (18).

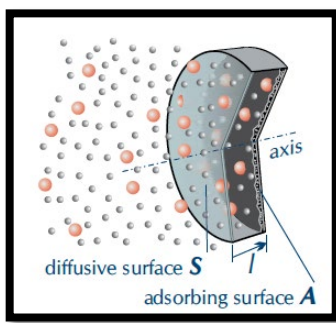


Figure 3: Axial sampler adsorbing and diffusive surfaces (18).

The radial design of the Radiello[®] allows for improving the geometrical constant (K). The geometrical constant is based on a ratio of the diffusive surface area to the diffusion path. Figure 4 shows the cylindrical surface of the Radiello[®] versus the diffusive surface of a traditional axial sampler. The Radiello[®]'s cylindrical outer surface allows for a much larger adsorbing and diffusive surface when compared to the axial sampler. The radial design allows for an exponential increase in uptake rates (~27.7 mL/min) compared to traditional passive samplers (~9.69 mL/min), which offer shorter sampling times and consistent sampling rates (18).

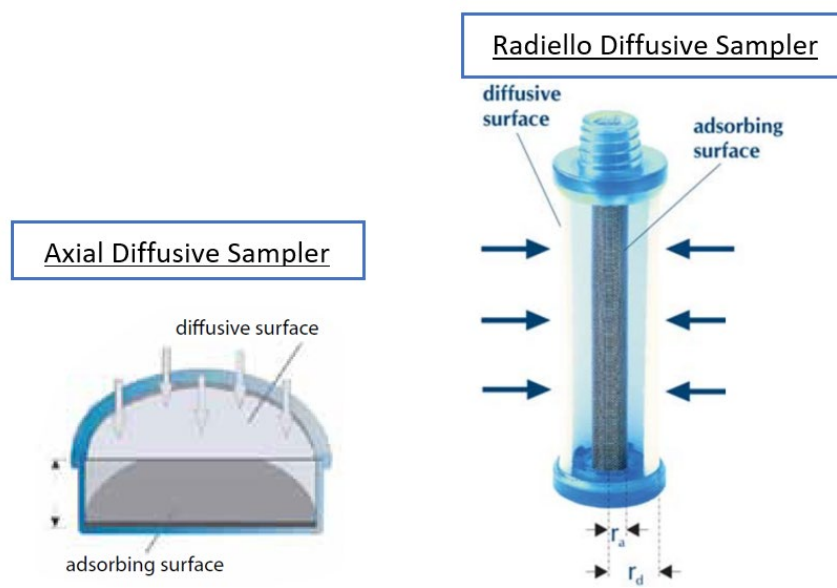


Figure 4: Axial diffusive sampler (566 OVM) and a radial diffusive sampler (Radiello®) (18).

2.8 PASSIVE SAMPLERS: RADIELLO® AND OVM

Standard diffusive type samplers include Radiello®, Perkin Elmer tubes, SKC 575, 3M OVM 3500, ORSA-5 Draeger, and Assay Technology 566 OVM (11). The Radiello® diffusive sampler is dependent on the adsorbent and its diffusive body selection. The adsorbent selection is critical since it is directly tied to its performance. Depending on which sorbent and diffusive bodies are chosen, the analysis technique (solvent or thermal desorption) also depends on this selection. An optimum adsorbent should be stable, reusable, easily desorbed, selective, and maintain a constant uptake rate during the sampling period (11). This uptake rate can be influenced by the chemical factors and environmental conditions it could encounter, including temperature, relative humidity, wind velocity, concentration level (sorbent capacity), and sampling time. While some decrease in uptake rate may occur over time, this amount is hardly appreciable unless sampling for many hours or days or in extremely high concentrations, as the

capacity of the sampler becomes a factor. Diffusive samplers are typically validated under laboratory and field conditions considering these environmental and chemical factors. The temperature has the most significant effect on diffusivity. Also, the material's porosity (diffusive body) can change with temperature variations. Variations with relative humidity had minimal effects on sampling rates due to the hydrophobic nature of the Carbograph 4 (11).

The Intituti Clinici Scientifici Maugeri (Pavia PV, Italy) manufactures two versions of the Radiello[®] for detecting volatile organic compounds (VOCs). One version uses a white diffusive body with 530 ± 30 mg activated charcoal. VOCs are trapped by adsorption, and recovery is made through the use of carbon disulfide. The validated uptake rate for benzene at 25 °C (298 K) was 80 mL/min. The second version of the Radiello[®] has a yellow diffusive body with 350 ± 10 mg of graphitized charcoal (Carbograph 4). VOCs are trapped by adsorption, recovered by thermal desorption, and analyzed by capillary gas chromatography and MS detection. At 25 °C (298 K), the validated uptake rate was 27.7 mL/min. The recommended exposure time ranged from 8 hours to 7 days. The validation showed that the uptake rate was unaffected by humidity in the range of 15-90% and with a wind speed of 0.1 and 10 m/s. Table 5 outlines some specifications for the Radiello[®].

The Assay Technology 566 OVM offers a 76-hole sampling grid which allows for a sampling rate of around 9.69 mL/min, specifically for benzene. The 566 utilizes a flexible, inert charcoal wafer that allows a sampling time ranging from 15 minutes to 12 hours. The limit of quantification was specified at ≥ 0.40 µg. Table 6 outlines specifications for the OVM.

Table 5: Radiello® Sampler Specifications (18)

Intituti Clinici Scientifici Maugeri , Radiello	
Sampling Medium:	Activated Charcoal, 530 ± 30 mg
Analytes Sampled:	Volatile Organic Compounds
Analytical Method:	Thermal desorption; analysis by gas chromatography with MS detector (GC/MS)
Recommended Sampling Time:	8 hours to 7 days
Sampling Rate (SR) at 25°C:	27.8 mL/min
Limit of Detection	0.05 µg/m ³
Temperature	± 5% for 10 °C variations (upwards or downwards) from 25 °C
Effect of Humidity:	Functions as claimed within 15 - 90% RH

Table 6: Assay Technology OVM Technical Insert Information (8).

Assay Technology Technical Insert for 566 Organic Vapor Monitor	
Sampling Medium:	Activated Carbon, 150 mg, PTFE Binder
Analytes Sampled:	Organic Vapors
Analytical Method:	Desorption in carbon disulfide with appropriate co-solvent; analysis by gas chromatography with flame ionization detector (GC/FID)
Recommended Sampling Time:	STEL=15 min; PEL=8 hrs. or full shift; Functional range: 15 minutes - 12 hours
Sampling Rate (SR):	Typically, 5 - 15 mL/min
Effect of Temperature:	Effect on result ≤ 5% within 0 - 50 °C (32 - 122 °F).
Effect of Humidity:	Functions as claimed within 10 - 80% RH
Accuracy (MTE):	Meets or exceeds OSHA requirements for accuracy: Maximum Total Error (MTE) ≤ 25% at PEL; ≤ 35% at STEL

2.9 THERMAL DESORPTION TECHNIQUES

Woolfeden (2013) compared thermal desorption with solvent extraction for GC analysis as a powerful tool for enhancing the detection and quantification of highly volatile to semi-volatile organic compounds (51). For several reasons, TD was determined to be the preferred method for GC sample preparation and introduction. For instance, TD was observed to provide

much better sensitivity than traditional solvent-based methods, given the higher extraction efficiency of sampled compounds by the TD tube. TD standard methods typically have shown better than 95% extraction efficiency versus the 75-80% liquid extraction methods (best case scenario) (37). As solvent dilution methods are not used with TD, the result is a million-fold enhancement in sensitivity for airborne chemical samples.

One of the biggest concerns with TD early in its infancy was that samples could only be used once before all the analytes in the TD tube were utterly depleted. Over the past 10 years, technology has evolved to allow the recollection of a split portion of TD samples. This has allowed for the analysis of that single sample to be repeated multiple times allowing for the confirmation of results and method validation. Initially, a lot of the drive for early TD development came from occupational hygiene, where scientists wanted to find an alternative to charcoal tubes and carbon disulfide, which would be less toxic from an analyst's perspective and give better detection limits (36; 51).

3.0 FTIR TECHNIQUES

Fourier Transform Infrared (FTIR) spectrometers have been used to identify a wide range of organics and inorganics in the gas phase. The FTIR detects these gas-phase compounds by their absorbance of infrared radiation (IR) and produces a unique spectrum. The sample is exposed to IR light that repeats the exposure over various frequency ranges ten times per second. Multiple spectra are added along with each other according to the selected measuring time, ranging from 1 s, 5 s, 20 s, 60 s, and 5 minutes. Selecting a longer measuring time improves the accuracy by raising the signal-to-noise ratio (25). Once exposed to the broad spectrum, some of the wavelengths are absorbed into the material. The absorption and conversion of IR light into

molecular motion absorbs some of this light energy which causes the molecules to vibrate, rotate and radiate, while some of this light passes right through the sample (52). The detector records this energy that passes through as % transmittance (1/absorbance). The GASMET provides results as actual concentration (ppm) of gases from the sample spectrum using a Classical Least Squares analysis algorithm and its onboard chemical library (25).

Determining how the IR spectrum is used to quantify gases requires understanding the Beer-Lambert Law. Here the amount of light passing through the sample cell decreases exponentially as the thickness of IR absorbing gas increases within the sample cell. The sample cell is filled with the absorbing gas of interest. Absorbance at a given wavelength (λ) is a negative logarithm of transmittance (Equation 2.3) (25). Absorbance is also directly proportional to the gas concentration of interest (c), the path length (b), and the specific gas constant of interest (ϵ) (Equation 2.4) (29). The specific gas constant of interest (ϵ) is calculated from the reference spectra, and the path length (b) is a known quantity of the FTIR (25; 51).

$$A = -\log_{10}(I/I_0) \quad (2.3)$$

A = Absorbance at a given wavelength (λ) of light

I = Transmitted light intensity (light that passes through the sample)

I_0 = Incident light intensity (light that passes to the sample)

$$A = \epsilon * b * c \quad (2.4)$$

A = Absorbance at a given wavelength (λ) of light

ϵ = constant specific to the gas of interest (molar absorptivity)

b = the distance the light passes through the sample (path length)

c = concentration of the gas of interest

Quantifying the actual airborne concentration (ppm) of the chemical of interest is done by building a model spectrum from the reference spectra library over a wide range of wavelengths to determine the concentrations of the gas. The reference spectrum is built from a known concentration of a single gas that is diluted in nitrogen. When a sample is being analyzed, the

absorption peaks are compared with those of the reference spectra. The adsorption strength of a gas measured by the FTIR depends on the molecule's dipole moment (net polarity). When a molecule possesses a strong dipole moment, it absorbs this IR radiation strongly. Molecules with no net charge (no dipole moment) are transparent to IR radiation (25). The molecule must absorb this IR radiation to be measurable. Since nitrogen does not have a dipole moment, it is used for conducting the zero-gas calibration for recording a background spectrum. Gases that the FTIR can measure include inorganic gases and volatile organic compounds. The FTIR does not require periodic recalibration. The daily background spectrum (zero background) measurement with UHP Nitrogen is enough to preserve measurement accuracy. The reference spectra used as a comparison are measured at the Gasmet factory when the instrument is manufactured and are stated not to drift (25; 51).

CHAPTER 3: METHODS AND MATERIALS

3.1 SAMPLING METHOD OVERVIEW

Generation of controlled atmospheres was carried out in a dynamic flow chamber where BTEX target concentrations, mass flow rate, temperature, pressure, relative humidity, and dewpoint were accurately measured. Figures 6 and 7 provide a detailed schematic representation of how the test atmosphere was created, monitored, and controlled. A Miller-Nelson HCS-501 (Miller-Nelson Research, Inc., Livermore, CA) air conditioning system created the desired relative humidity, mass flow rate, and temperature of diluent air entering a Miller-Nelson SV-2000 (Miller-Nelson Research, Inc., Livermore, CA) solvent vapor generator. An airborne vapor stream of BTEX was entrained into the diluent airflow as liquid BTEX was injected into the vaporizer by a Harvard Apparatus (Holliston, MA) syringe pump. A syringe pump injection rate (L/min) was calculated to achieve target BTEX chamber concentrations for each sampling scenario. An HTP.xw sensor (Cousins & Sears Creative Technologies, Brooklyn, NY) verified and monitored relative humidity, pressure, dewpoint, and temperature. A hygrometer and digital thermocouple also helped monitor these parameters.

Thermal desorption in conjunction with GC/MS was used to desorb and analyze the radial samplers. For quantification, liquid calibration standards were created, and TD tubes were spiked with a known volume of benzene and methanol. A nine-point calibration curve was created with an R^2 of 0.99. The GASMET DX4040 portable gas analyzer (Gasmeter, Vantaa, Finland) was used as the reference instrument to independently validate benzene concentrations in the dynamic flow chamber. A Gasmeter factory calibration curve with an R^2 of 1.0 was used.

3.1.1 System for Creating a Controlled Atmosphere of BTEX Vapor

Figures 5 and 6 describe the instruments utilized in creating and conditioning BTEX concentrations as a vapor.

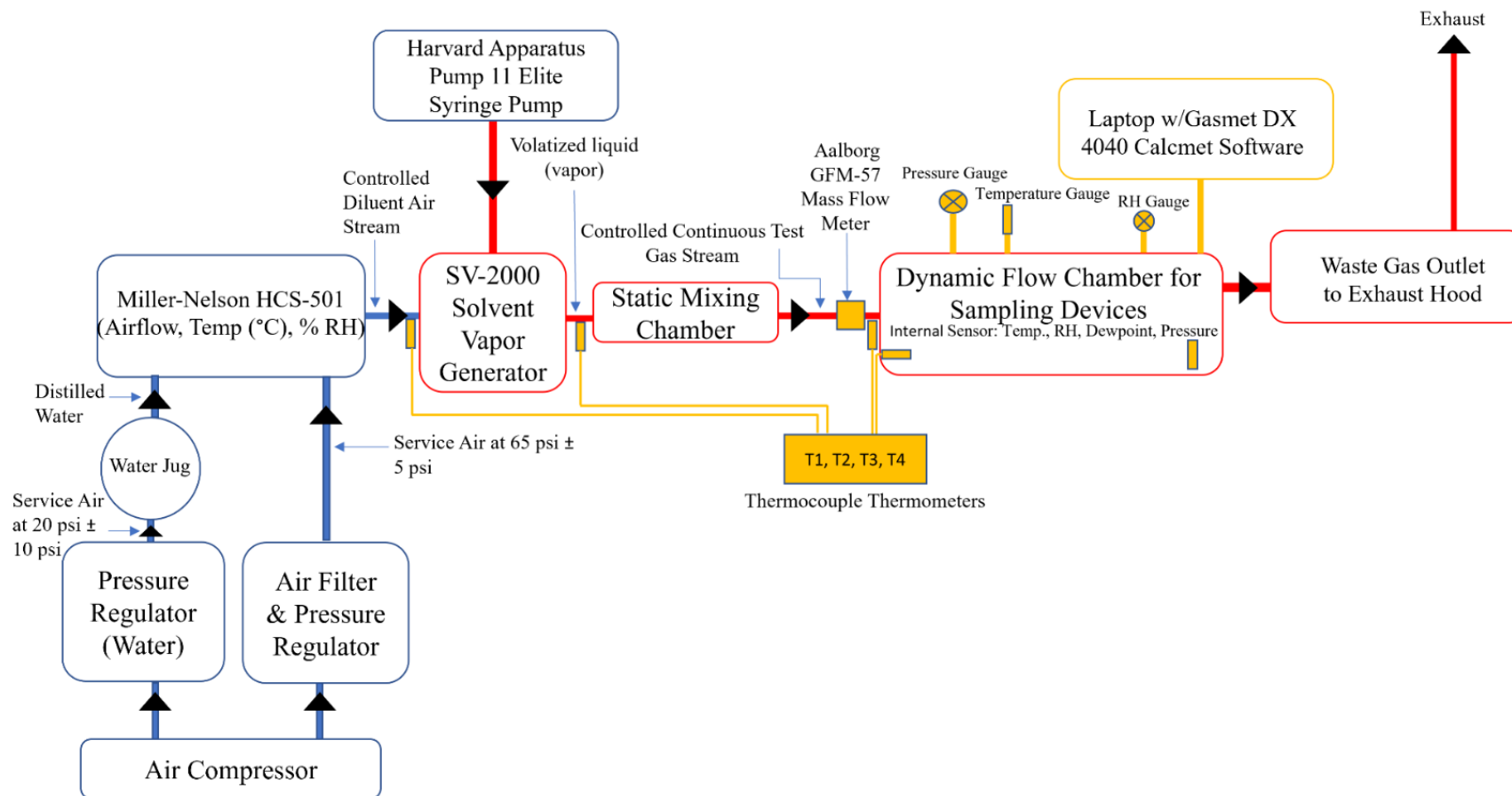


Figure 5: Schematic representation of the system used for creating a controlled atmosphere of BTEX vapor (7; 9).

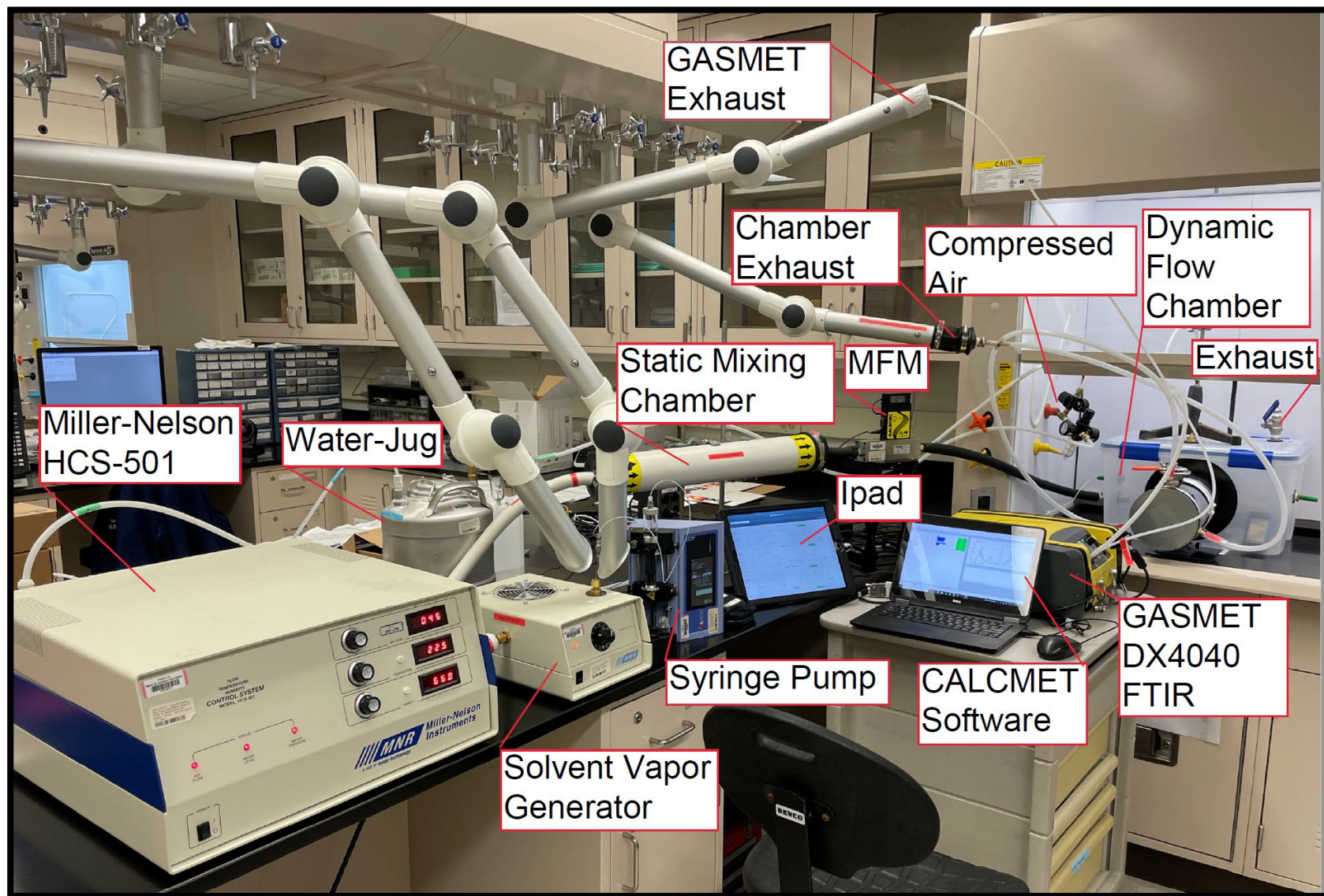


Figure 6: System used for creating a controlled atmosphere of BTEX vapor.

3.1.1.2 Miller-Nelson HCS -501 Instrument (Air Conditioning System)

The Miller Nelson HCS-501 was responsible for conditioning and controlling the airflow before going to the solvent vapor generator. The operator would adjust and monitor a known flow rate (Liters/minute), temperature ($^{\circ}\text{C}$), and relative humidity (%). Compressed service air was supplied through a 3/8 – inch (9.52 mm) PTFE tubing, regulated to approximately 65 ± 5 psi, and connected to a rear bulkhead fitting on the Miller-Nelson. The airflow was controlled with an adjustable internal mass flow rate controller (MFC). Following the MFC, the air passes across the surface of a water reservoir which is heated according to the relative humidity set by the operator. A water jug provides distilled water at a constant pressure of approximately $20 \text{ psi} \pm 10$ psi to a rear bulkhead fitting on the Miller-Nelson HCS-501 through a 1/4 – inch (6.35 mm) PTFE tube. After the air is humidified, it passes over a heater to bring the air to the desired temperature set by the operator. Figures 7 and 8 visually represent the service air connections, water jug, and Miller-Nelson HCS-501 front display and rear connection (10). The parameters used for this study are provided in Table 7.



Figure 7: Miller-Nelson HCS-501 front panel with airflow, temperature, and humidity display.

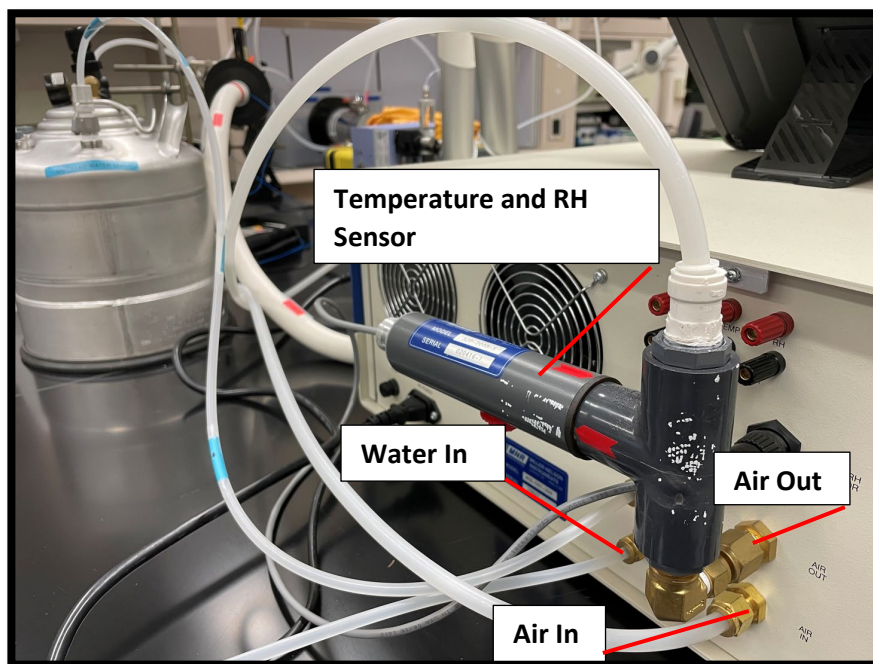


Figure 8: Miller-Nelson HCS-501 rear connections for mass flow air in/out, water inlet for humidity production, and the temperature/RH sensor.

Table 7: Miller-Nelson HCS-501 instrument parameters used for the study.

Miller-Nelson HCS-501 Instrument Parameters			
<i><u>Parameters</u></i>	<i><u>SetPoint</u></i>		<i><u>Accuracy</u></i>
Flow Rate	40	L/min	$\pm 2\%$ of the specified flow rate at all flow rates between 25-100%
Temperature	25	$^{\circ}\text{C}$	$\pm 0.5\text{ }^{\circ}\text{C}$
Relative Humidity	70	%	$\pm 3.0\text{ \% RH}$

3.1.1.3 Miller-Nelson Model SV-2000 Solvent Vapor Generator

The Miller-Nelson Vapor Generator was responsible for the evaporation of BTEX to produce an airborne vapor stream (39). An injector port on the SV-2000 Solvent Vapor Generator allowed a syringe needle to be inserted into the septum fed by a syringe pump. The conditioned air from the Miller-Nelson HCS-501 instrument fed into the SV-2000. The heater setting was adjusted to 60 V to ensure full volatilization of the liquid BTEX into the diluent airflow while ensuring that the liquid benzene did not approach its boiling point. The setting used to create the most effective vapor stream was

60 V. The septum for the injection port was replaced once at the beginning of the study to reduce airflow leakage and provide a tight seal for the syringe. Figure 9 provides a functional schematic of the SV-2000 Vaporization System.

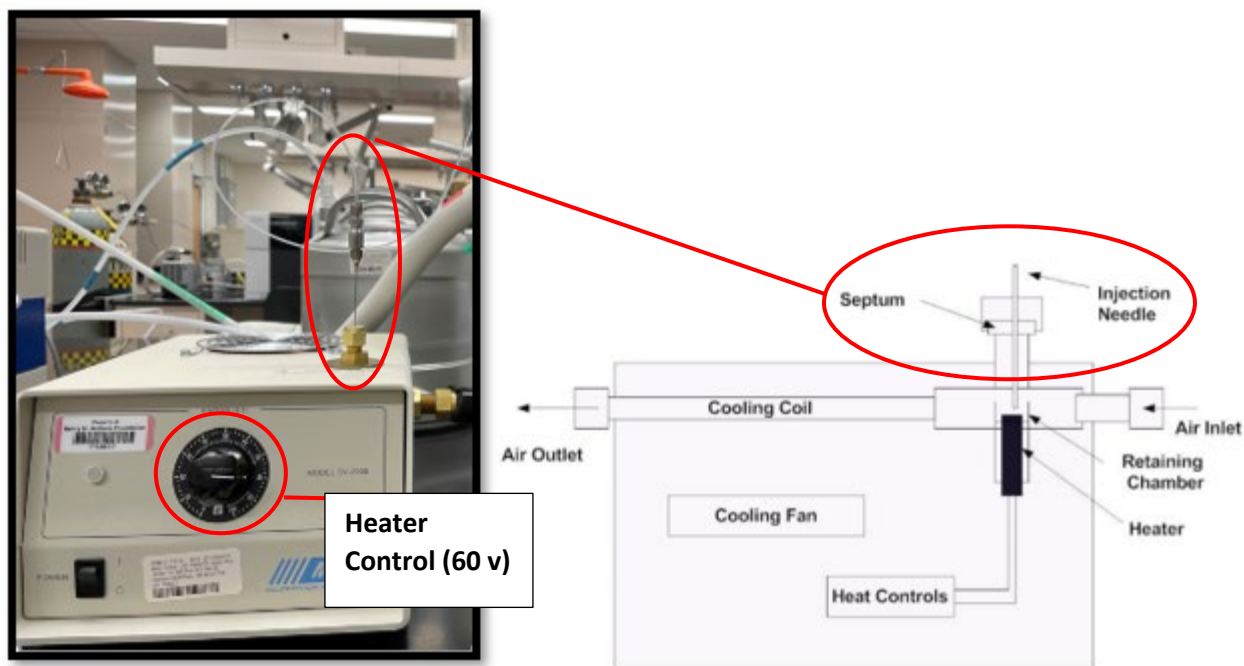


Figure 9: Schematic and Visual Representation of the SV-2000 Vaporization System (39).

3.1.1.4 Harvard Apparatus Pump 11 Elite

The Harvard Apparatus Pump 11 Elite is responsible for delivering accurate and precise measurements of BTEX to the vaporizer (28). A theoretical syringe injection rate (mL/min) was calculated to represent the desired BTEX concentrations produced in the dynamic flow chamber. Variables that served as inputs to this calculation include molecular weight (g/mol), density (g/mL), diluent gas flow rate (L/min), pressure (mmHg), temperature (Kelvin), and weight percent (%). *Equation 3.1* was used to calculate the theoretical injection rate for each of the three exposure scenarios (41). An Excel calculator tool was also created from *Equation 3.1*, and the results were summarized as shown in Appendix A. The dynamic flow chamber's temperature and

pressure values used for the injection rate calculator were updated to the calculator five minutes before BTEX vapor was produced in the chamber to attain the most accurate syringe injection rate according to the actual chamber conditions.

A diluent gas flow rate (q_D) of 40 L/min was chosen to keep the chamber's flow rate as low and stable as possible. Once the individual injection rates were calculated for each chemical, *Equation 3.2* was used to determine the total injection rate. The syringe injection rates used for this study ranged from approximately 8.2 μ L/min (Scenario 1) to 82.1 μ L/min (Scenario 3). A summary of the theoretical injection rates for the three scenarios has been provided in Appendix A.

$$q_L = \frac{(C_{ppm})(q_D)(M)}{(24.45)(10^6)(T_{\text{Chamber}}/298(760 \text{ mmHg}/P_{\text{Chamber}})(\rho)} \quad (3.1)$$

q_L = injection rate (mL/min)
 C_{ppm} = desired analyte concentration (ppm)
 q_D = diluent gas flow rate (L/min)
 M = molecular weight of analyte (g/mol)
 T_{Chamber} = temperature in the chamber (K)
 P_{Chamber} = pressure (mmHg)
 ρ = density of analyte (g/mL)

Equation 3.2 was used to calculate the total injection rate for each of the three exposure scenarios (41):

$$q_{L\text{Total}} = q_{L\text{Benzene}} + q_{L\text{Toluene}} + q_{L\text{Ethylbenzene}} + q_{L\text{mXylene}} \quad (3.2)$$

q_L = injection rate (mL/min)

An Aldrich 24– inch (609.6 mm) long, 20 gauge Teflon (PTFE) hose with a Kel-F Luer Hub (Milwaukee, WI) connected a gastight syringe to a 20 gauge needle. The hose had an outer diameter of 0.059 – inches (1.49 mm) and an inner diameter of 0.035 – inches (0.889 mm). A Component Supply Company (Sparta, TN) stainless steel male Luer lock to a 1/16 – inch (1.58 mm) compression fitting with a 1/16 – inch (1.58 mm) custom drilled ferrule to 0.063 – inch

(1.60 mm) and HTX-22R insert were used as a connection point from the hose to the 20 gauge needle. The needle used was a four-inch needle since the distance from the Miller Nelson SV-2000 internal hot plate to the top of the injection port septum was 2.25 – inches. Compatibility between the hose material (PTFE) and the BTEX chemicals was required to prevent leaks and deterioration of the Luer-lock hose fittings.

A Harvard Apparatus (Holliston, MA) adapter was used to ensure syringe mechanical compatibility with the syringe pump. Maintenance was conducted by lubricating the guide rods and lead screws with 1 cc of SuperLube Lubricant (SYNCO Chemical Corporation, Bohemia, NY). While in operation, it was essential to ensure that no air bubbles formed in the injection hose. If the needle was left in the injection port without starting the pumping sequence, then conditioned air produced by the Miller Nelson HCS-501 would force air bubbles into the injection hose. The needle was introduced into the injection port when the pumping sequence started. The syringe pump was rotated to the vertical position to reduce kinking of the syringe hose (Figure 10).

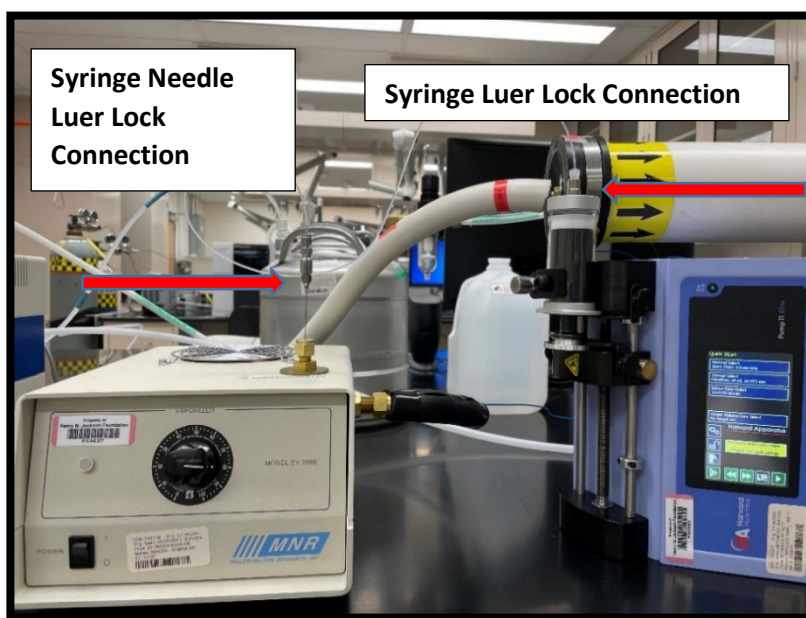


Figure 10: Harvard Apparatus Syringe Pump connection points from syringe pump to SV-2000

3.1.1.5 Static Mixing Chamber

A PVC static mixing chamber comprised of a PVC pipe with dimensions consisting of a 3–inch (76.2 mm) internal diameter and length of 24 –inches (609.6 mm) was installed downstream of the Solvent Vapor Generator SV-2000 in an attempt to further mix the BTEX vapor before entering the MFC (Figure 11). The mixing chamber contained internal baffle plates to help mix the air/BTEX stream. A pilot study was conducted to determine the system's effectiveness with and without the mixing chamber. When the mixing chamber was removed, a pressure sensor placed in the dynamic flow chamber showed erratic fluctuation of the air pressure in the chamber. The sensor data showed steady and consistent chamber pressures when the mixing chamber was reinstalled. As a result, the mixing chamber was left in place for the remainder of the study.

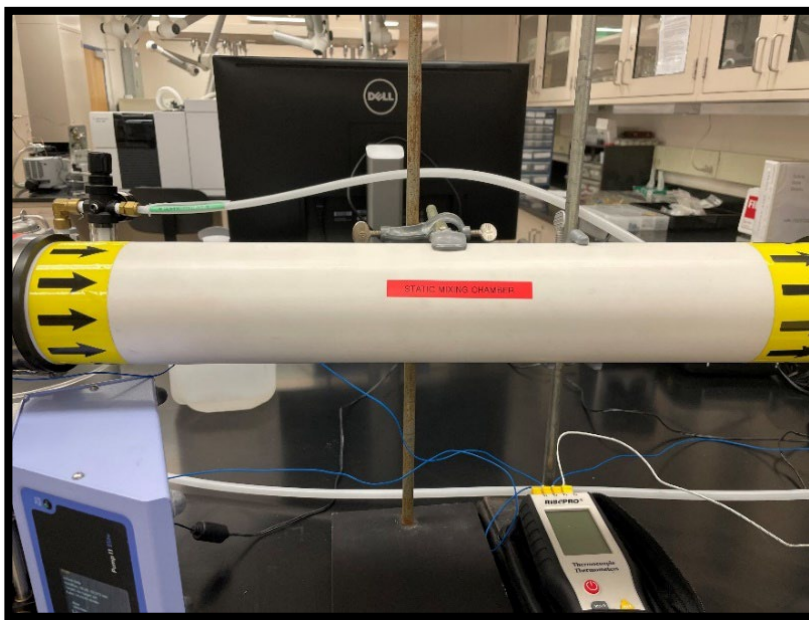


Figure 11: Static Mixing Chamber.

3.1.1.6 Aalborg Mass Flow Meter

The Aalborg GFM-57 Mass Flow Meter (Orangeburg, NY) was located downstream of the static mixing chamber before the inlet port to the dynamic flow chamber. The MFM generated a signal based on the amount of heat carried by the gases to indicate mass-molecular-based flow rates and had an operating range of 0-200 L/min with an accuracy of $\pm 1.5\%$ (1).

Figure 12 provides a visual representation of the MFM used in this study.

This instrument demonstrated a 3-4 liter/min drop in mass flow compared to the mass flow coming from the Miller-Nelson HSC-501. This mass flow drop was attributed to the static mixing chamber. This difference in measured flow rates was reduced to approximately 1 liter/min when operating at 100 liters/minute. The appreciable pressure drop was measurable and controlled for in the dynamic flow chamber.



Figure 12: Aalborg GFM-57 Mass Flow Meter.

3.1.1.7 Development of the Dynamic Flow Chamber

A transparent dynamic flow chamber was fabricated in-house using an IRIS USA, Inc., 44-quart polypropylene weathertight bin. The dimensions of the container include a 19.7– inch (500.3 mm) length, 15.75 – inch (400 mm) width, and 11.20 –inch (284.4 mm) height (Figures 13 and 14). Freshly mixed BTEX vapor was piped to a custom-designed inlet port on the left-hand side of the dynamic flow chamber. A ½ – inch (12.7 mm) ball valve to a steel 3/8 – inch (9.52 mm) barb hose fitting was installed at the chamber's top to maintain the chamber at atmospheric pressure. The valve was kept 50% open during operation to allow the BTEX concentration to build up in the chamber while keeping the internal pressure close to atmospheric pressure (approximately 760 mmHg). Three brass bulkhead fittings of ½ – inch female to ¾ – inch male with a 3/8 – inch (9.52 mm) barb fitting were uniformly distributed on the left-hand side, right-hand side, and top of the chamber to provide a sealed port for the Gasmet probe.

A Roowarmer HVAC 5.90 – inch (150 mm) damper with a manual on/off valve was mated onto an A.C. Infinity 6 – inch (152.4 mm) steel duct flange. The duct flange was laid flat on the side of the chamber, creating an airtight seal. Three ¼ – inch (6.35 mm) brass barbed fittings were evenly distributed around the HVAC damper and piped to an exhaust line to provide additional personal protection in case of a BTEX leak around the silicone seal within the HVAC damper. The HVAC damper and duct flange connection allowed the axial and radial samplers to be inserted into the dynamic flow chamber while minimally affecting the atmospheric conditions and desired target concentration. When daily sampling was complete, the system was secured, the duct flange capped, and the duct valve was opened to allow the lab's exhaust system to remove any residual vapors in the chamber.

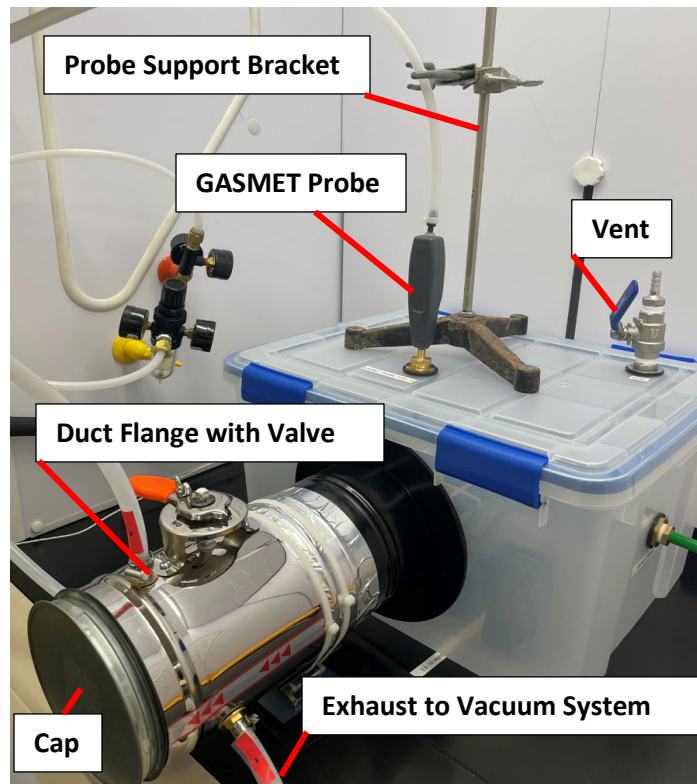


Figure 13: Dynamic flow chamber with various fittings and atmospheric monitoring devices.

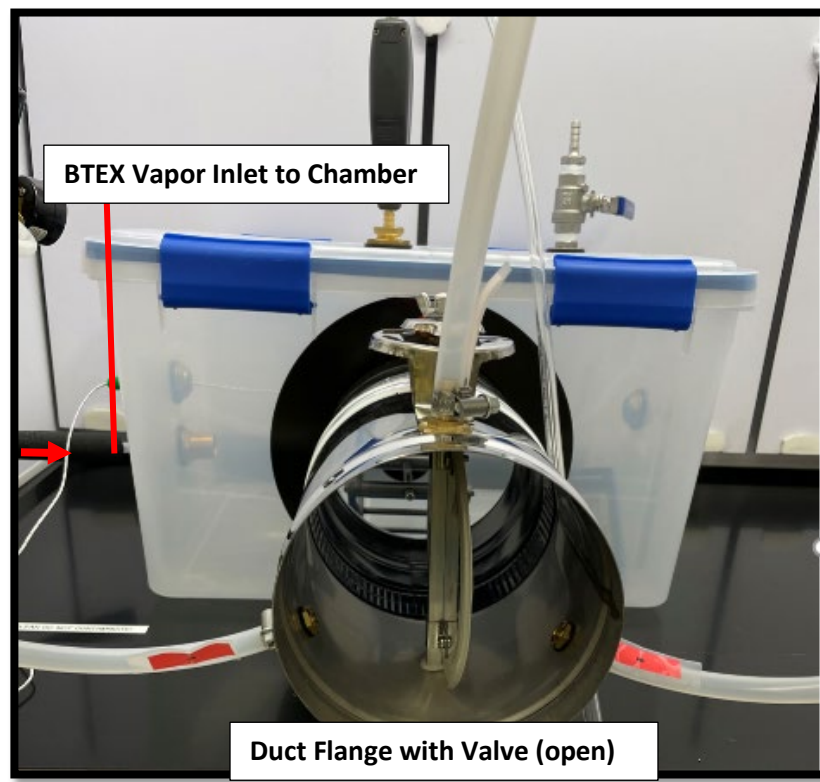


Figure 14: Dynamic flow chamber showing duct flange and valve in the open position.

3.1.1.8 Monitoring Atmospheric Conditions

Monitoring atmospheric conditions were crucial in this study since syringe pump injection rate calculations depended on the temperature and pressure readings within the dynamic flow chamber (*Equation 3.1*). To monitor changes in temperature throughout the system, a Risepro (Rise E-Commerce Nedre Vats, Norway) 4-Channel Digital Thermocouple Thermometer Sensors Model HT-9815 (Figure 15) was installed. The four points measured include inlet to SV-2000 Solvent Vapor Generator (Point 1), inlet to Static Mixing Chamber (Point 2), and the outlet of Aalborg GFM-57 Mass Flow Meter (Point 3), and inside the dynamic flow chamber (Point 4) (Figure 6). The temperature range for the thermocouple thermometer was -200°C to 1372°C with an accuracy of $>100^{\circ}\text{C}$: $\pm 1^{\circ}\text{C}$, $<100^{\circ}\text{C}$: $\pm 2^{\circ}\text{C}$ (46).



Figure 15: Risepro 4-Channel Digital Thermocouple Thermometer with four sensors (46).

An HTP.xw Extreme Accuracy Water-Resistant Temperature, Relative Humidity, Dewpoint, and Pressure Smart Sensor was placed inside the chamber (Figure 16). The sensor was placed approximately three –inches (76.2 mm) from the sampling devices inside the chamber. Figure 17 provides a top view of the sensor's position inside the dynamic flow chamber—this sensor allowed for continuous monitoring of the various parameters and data logging capabilities.

The data logging and export capability allowed for a comma-separated values file (CSV) to be created and exported to Microsoft Excel for future use. The accuracy of the instrument is $\pm 1.5\%$ relative humidity, $\pm 0.1^\circ\text{C}$ temperature, and ± 0.5 millibars (Mb) pressure (20). The temperature ($^\circ\text{C}$) and pressure (mmHg) values provided by the HTP.xw sensor were used for the syringe pump injection rates (*Equation 3.1*).



Figure 16: HTP.xw Extreme Accuracy Water-Resistant Temperature, Relative Humidity, Dewpoint, and Pressure Smart Sensor.

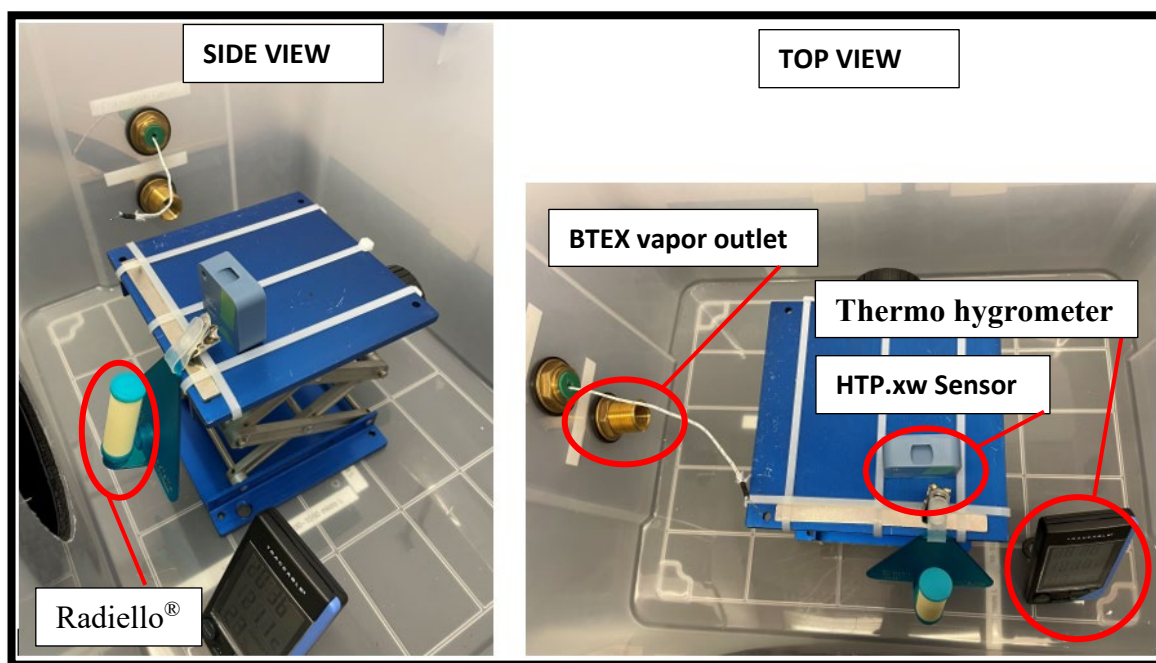


Figure 17: HTP.xw sensor placement inside the chamber relative to the Radiello® sampler.

A Digi-Sense (Innovative Calibration Solutions, Vernon Hills, IL) Thermohygrometer Pre-calibrated Relative Humidity and Temperature Indicator Model 20250-30 (Figure 17;18) was also placed in the dynamic flow chamber to provide another means of visual representation for relative humidity and temperature. The RH range and accuracy are, respectively, 10-90% RH with an accuracy of $\pm 5\%$ RH (40% - 80 % RH); $\pm 8\%$ RH above 80% and below 40% RH. The temperature range and accuracy include 0°C-50°C with an accuracy of $\pm 1.0^\circ\text{C}$. The instrument was calibrated to NIST-traceable standards and included a calibration report with data (23).



Figure 18: A Digi-Sense Thermohygrometer Pre-calibrated Relative Humidity and Temperature Indicator. (23).

3.1.2 Chemicals

Benzene (CAS # 71-43-2) with a purity of $\geq 99.90\%$, Toluene (CAS # 108-88-3) with a purity of $\geq 99.85\%$, and m -Xylene (Cas # 108-38-3) with a purity of $\geq 99\%$ were purchased from Millipore Sigma (St. Louis, MO). Ethylbenzene (CAS # 100-41-4) with a purity of $\geq 99.8\%$ was purchased from Sigma-Aldrich (Atlanta, GA). Methanol (CAS # 67-56-1) with a purity of $\geq 99.8\%$ was purchased from Sigma-Aldrich (Atlanta, GA).

Ultra-high purity helium (99.999%) was purchased from Roberts Oxygen (Rockville,MD) and used as the Agilent carrier gas. High purity nitrogen (99.99%) used as the cryogenic gas and for operating valves on the Markes Unity 2 was purchased from Roberts Oxygen (Rockville, MD) (Figure 19).

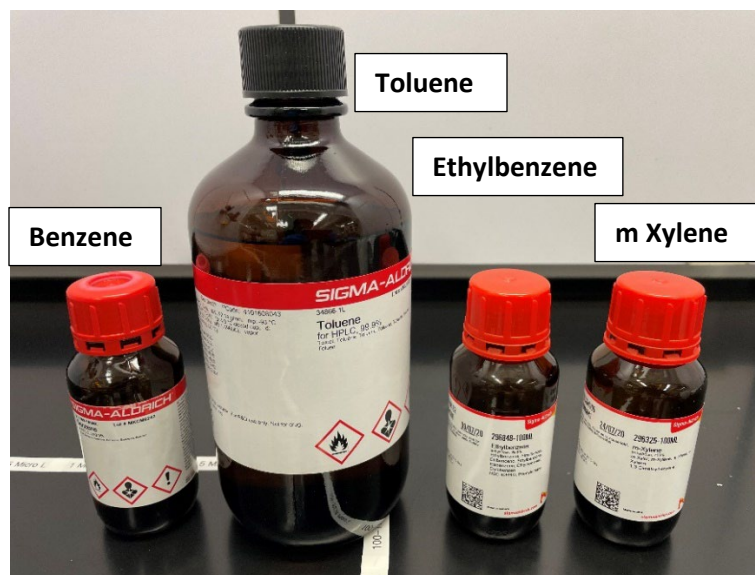


Figure 19: BTEX chemicals used for the study.

3.1.3 Creating BTEX Solution for Vapor Needed in the Dynamic Flow Chamber

In order to produce a high enough syringe pump injection rate for a stable benzene concentration in the dynamic flow chamber, a solution of liquid BTEX was created. Two 100 mL stocks of BTEX solutions consisted of specific volumes, as shown in Table 8. The BTEX chemicals were transferred from the manufacturer's glass storage container to a 5 mL beaker (benzene) and three 50 mL beakers (Toluene, Ethylbenzene, and m -Xylene). Three Eppendorf Pipettes (Hamburg, Germany) with pipette tips were used to measure and transport liquid BTEX to a 100 mL volumetric flask. The pipette size used for the standards were 0.5-10 μ L, 10-100 μ L, and 100-1000 μ L. The BTEX solution was then transferred from the 100 mL volumetric flask to three 40 mL storage vials (six total 40 mL vials) and refrigerated for future use (Figure 20).

The individual weight percent values were calculated using *Equation 3.3* for each BTEX chemical (41). The weight percent calculation was based on a total volume of 100 mL. The numerator was adjusted for each of the BTEX chemicals. The weight percent values were used to determine the individual volumes of the liquid BTEX chemicals needed to make a total volume of 100 mL. This total volume of BTEX would be used as the supply needed to create BTEX vapor in the chamber (*Equation 3.4*). This same BTEX liquid solution was used for all three scenarios.

$$\text{Weight \% Benzene} = \quad (3.3)$$

$$= \frac{(q_L \text{ Benzene}) (\rho \text{ Benzene})}{(q_L \text{ Benzene} * \rho \text{ Benzene}) + (q_L \text{ Toluene} * \rho \text{ Toluene}) + (q_L \text{ Ethylbenzene} * \rho \text{ Ethylbenzene}) + (q_L \text{ m Xylene} * \rho \text{ m Xylene})}$$

q_L = calculated injection rate (mL/min)

weight % = weight Percent (%)

ρ = density of analyte (g/mL)

Equation 3.4 was used to calculate the total weight percent, which should total 100%.

$$\text{Weight \% Benzene} + \text{Weight \% Toluene} + \text{Weight \% Ethylbenzene} + \text{Weight \% m Xylene} = 100\% \quad (3.4)$$

Table 8: Required volumes of liquid BTEX to produce vapor in the dynamic flow chamber.

Scenario # 1		Scenario # 2		Scenario # 3	
Volume (mL) in 100 mL	Volume (μL) in 100000 μL	Volume (mL) in 100 mL	Volume (μL) in 100000 μL	Volume (mL) in 100 mL	Volume (μL) in 100000 μL
Benzene		Benzene		Benzene	
0.900	899.8	0.5	452.0	0.5	452.0
Toluene		Toluene		Toluene	
31.8	31833.8	32.0	31977.7	32.0	31977.7
Ethylbenzene		Ethylbenzene		Ethylbenzene	
30.6	30576.7	30.7	30714.9	30.7	30714.9
m Xylene		m Xylene		m Xylene	
3.1	3053.6	36.9	36855.4	36.9	36855.4
TOTAL		TOTAL		TOTAL	
100	100000	100	100000	100	100000

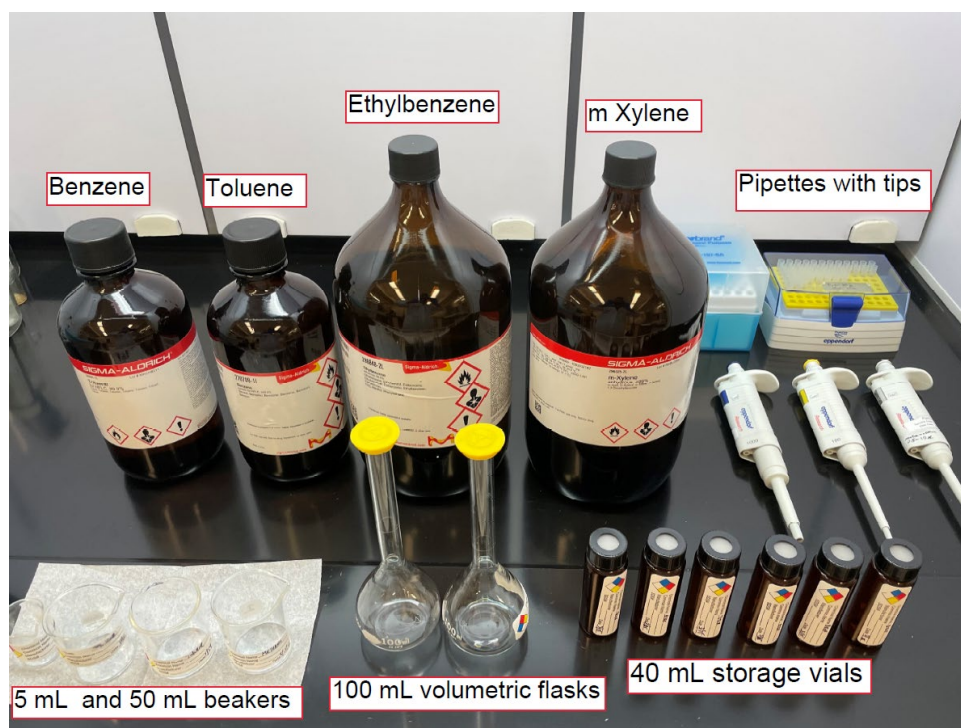


Figure 20: Setup used to create a liquid BTEX solution for the syringe pump.

3.1.4 Analytical Instrumentation

A benchtop laboratory gas chromatograph (Model 7890B, Agilent Technologies, Santa Clara, CA) with a Model 5977 mass selective detector (Figure 14, Agilent Technologies) was used in conjunction with a Markes Unity 2 thermal desorption unit and Series 2 ULTRA autoloader (Figure 5.2, Markes International, Llantrisant, U.K.).

The gas chromatograph contained a Zebron ZB-WAX column with the following column information:

- Column Dimensions: 30 m length x 0.25 mm inner diameter x 0.25 μm film thickness.
- Liquid Phase: 100 % Polyethylene Glycol
- Temperature Limits: 40 to 250/260°C (Isothermal/Program)
- Part Number: 7HG-G007-11-B
- Column Serial Number: 1108786

3.1.4.1 Agilent 7980B Gas Chromatograph Parameters

Analytical parameters were as follows: the column flow rate was 1.2 mL/min, the initial column temperature was 35°C held for 1.5 minutes, and then ramped at 40°C per minute to a maximum temperature of 330°C (held for 3 minutes). The total gas chromatography analysis time was 10.6 minutes. A solvent delay time of 0.25 minutes was used. Peak areas were automatically integrated using Agilent Enhanced Chem Station software (Ver. F.01.03.2357). Ultra-high purity helium (99.999%) purchased from Roberts Oxygen (Rockville, MD) was used as the carrier gas. Appendix B provides a detailed summary of the parameters used for thermal desorption. Appendix C includes screenshots of the MassHunter Data Acquisition Software (Version B.07.04.2260) illustrating the parameters used for the GC/MS operating parameters.

3.1.4.2 Markes Unity 2 Parameters

A Markes International U-T15ATA cold trap designed to analyze VOCs ranging from C₂ to C₃₀ was installed and conditioned before thermal desorption. The thermal desorption system cold trap was programmed to attain –15°C during the desorption phase of the thermal desorption tubes. The cold trap was then flash heated at the highest rate possible (approximately 100°C/sec) to a maximum temperature of 300°C (held for 3 minutes) to ensure complete desorption of the BTEX collected on the cold trap during desorption of the thermal desorption tube. The transfer line temperature to the gas chromatograph was held at 160°C. The desorption flow rate was 12 mL/min, while the desorb split and trap split-flowrates were 200 mL/min, resulting in a total split ratio of 2,690:1. The tube desorption temperature was 315°C with a 10-minute desorption time. Appendix D includes the Markes International Thermal Desorption System Control Program

(Maverick, Version 5.0.0) screenshots illustrating the thermal desorption controlling method parameters.

3.1.5 Thermal Desorption Tube Selection

Empty stainless steel sorbent tubes (Figure 21) compatible with the Markes Unity 2 and Ultra Autoloader were used in this study. The TD tubes measured 89 mm (3.5 in.) x 6.35 mm (1/4 in.) with a 5 mm (0.197 in.) internal diameter. This study used the prescribed procedure and tool use techniques recommended by Markes International. The sorbent-retaining gauzes and gauze retaining springs were removed to install the Carbograph 4 sorbent cartridge. The thermal desorption tube only housed the sorbent cartridge during the Agilent GC/MS calibration curve development and sampling and analysis of the chamber atmospheres. After the Carbograph sorbent was inserted into the tube, an O-ring removal tool was used to help center the sorbent against the top groove. A gauze retaining spring (Figure 22) was then used to secure the sorbent to minimize the risk of slipping out. A TubeMate tool (Figure 23) was used to insert and remove the gauze retaining springs. Markes International (Bridgend, Wales, UK) supplied the stainless-steel tubes, gauze retaining springs, and TubeMate tool.



Figure 21 Empty stainless steel sorbent tube (34).



Figure 22: Gauze retaining spring (35).



Figure 23: Tubemate tool (C-TMBTE) (37).

3.1.6 Sorbent and Diffusive Body Selection

The Carbograph 4 (C-RAD145) radial sampler with the yellow diffusive body (C-RAD1202) is the recommended device when used in conjunction with thermal desorption for passive sampling of BTEX (Figure 24). The yellow diffusive body is a stainless-steel net cylinder with a $3 \times 8 \mu\text{m}$ mesh opening and a 4.8 mm diameter opening. The Carbograph 4 was packed with $350 \pm 10 \text{ mg}$ of graphitized carbon black charcoal. Graphitized carbon black has a lifetime of approximately 200 thermal cycles, including desorption and conditioning cycles, and particle size is 35-50 mesh (3). The sorbent was purchased from Markes International (Wales, UK).

According to the manufacturer's instructions, each tube was preconditioned using a TC-20 sorbent tube conditioner (Markes International) before the initial sample collection (Figure 25). UHP Nitrogen carrier gas was used at a 50-100 mL/min flow rate with an initial conditioning time of 2 hours at 350 °C, followed by 4 hours at 380 °C. Re-conditioning of the tubes after every use required 30 minutes at 380 °C per the instructions provided by the manufacturer. A Bios Defender 510 (Prairieville, LA) was used to ensure a flow of UHP nitrogen of 50 – 100 mL through the tubes during conditioning. The pressure was adjusted using the second stage control valve controller at the UHP Nitrogen tank to approximately 25 psi or 28 psi on the TC-20 instrument pressure gauge (Figure 26). The tube conditioning time was extended by 37 additional minutes to account for the time required for the TC-20 to reach each programmed temperature. The tube manifold block containing the newly conditioned tubes was removed and placed onto the cooling plate upon completing the conditioning process. The UHP Nitrogen flow was adjusted to approximately ten psi on the TC-20 gauge during the cooling process to reduce the risk of sorbent contamination. Once the tubes were cooled, long-term storage caps (brass) fitted with PTFE ferrules were used to store the TD tube.



Figure 24: Carbograph 4 (C-RAD145) with the yellow diffusive body (C-RAD1202) (18).



Figure 25: TC-20 with tube manifold block loaded with TD tubes for conditioning.



Figure 26: TC-20 front side view showing temperature controller (top), UHP nitrogen pressure gauge (middle), and digital timer controller (bottom).

3.1.7 BTEX Concentration/Range of Interest

The target benzene concentrations investigated in this study were 0.20 x STEL, 0.50 x STEL, and 1.0 x STEL, corresponding to a concentration range of 0.50-2.5 ppm.

3.1.8 Creating Liquid Calibration Standards for Agilent

The Agilent 7890/5977 GC/MS was calibrated using nine liquid benzene calibration standards. 5 mL liquid standards were made for each point and based on theoretically calculated benzene volumes in methanol. Methanol was the fully miscible solvent recommended by the Marke's International Radiello® Application Compendium.

The sampling/uptake rate values used in this study were validated and published in 2019 by the Istituti Clinici Scientifici Maugeri (Pavia PV, Italy) (Table 9). Theoretical calculations were made to determine the masses associated with each calibration point based on the concentration of interest, exposure time, and volume sampled. A tolerance of $\pm 30\%$ was factored for Point 1 (lowest standard) and Point 9 (Highest Standard). Each of the masses associated with each calibration point was equally distributed and were to calculate the volume of benzene needed to develop the 5 mL calibration standards. A summary of the benzene masses and volumes used to generate the Agilent GC/MS calibration curves are listed in Table 10.

Table 9: Validated and published uptake rate for benzene (18).

Radiello Uptake Rates for Sampling BTEX (RAD 145 Diffusive Body with RAD 1202 Diffusive Body)						
Compound	Boiling Point (°C)	Uptake Rate (mL/min)	Exposure Time Upper Limit (days)	Linear up to ($\mu\text{g}/\text{m}^3 \cdot \text{min}$)	Uncertainty 2σ (%)	Limit of Detection ($\mu\text{g}/\text{m}^3$)
Benzene	80	27.8	7	410,000	8.3	0.05

Individual 5 mL volumetric flasks were used to combine benzene and methanol. Eppendorf Pipettes with pipette tips were used to measure and transport liquid benzene standards to the 5 mL volumetric flask. The pipette size used for the standards were 0.5-10 μ L and 10-100 μ L (Figure 27). The 5 mL standards were further separated into storage vials (4 mL, 2 mL) and refrigerated for future use (Figure 28). A 2 mL vial was used as the "working" volume using the microsyringe to pull a one μ L standard when spiking TD tubes. A working volume was used to reduce the potential exposure to a large volume of liquid benzene and the possibility of spillage.



Figure 27: Eppendorf micropipettes.

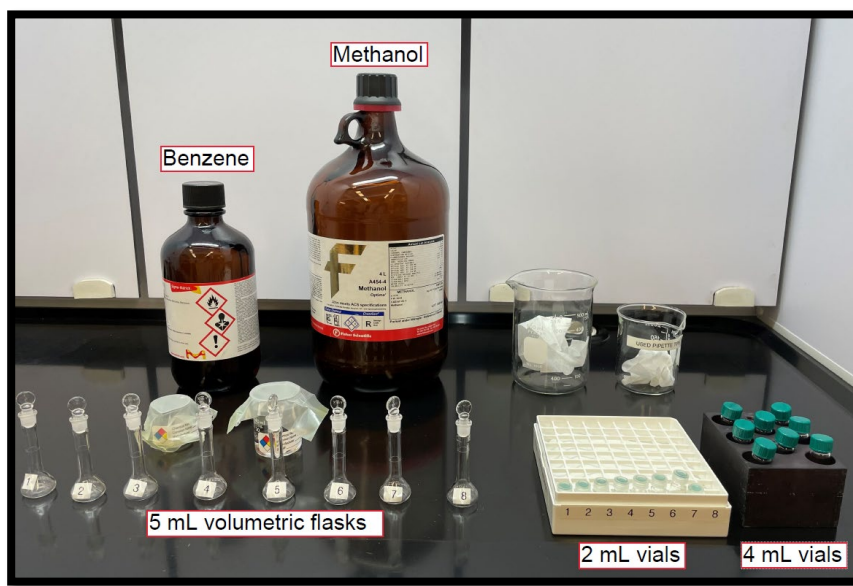


Figure 28: Setup used to make benzene (in methanol) calibration standards.

Table 10: Summary of the Agilent GC/MS 9-point calibration curve for the benzene standards.

Standard #9		
Syringe Volume (μL)	Point 9	
1	Mass (ng)	5,330
	Individual Chemical Volume (μL)	30.32
	Solvent Volume (μL)	4969.68
	Total Volume to prepare (μL)	5,000
Standard #8		
Syringe Volume (μL)	Point 8	
1	Mass (ng)	4,330
	Individual Chemical Volume (μL)	24.63
	Solvent Volume (μL)	4975.37
	Total Volume to prepare (μL)	5,000
Standard #7		
Syringe Volume (μL)	Point 7	
1	Mass (ng)	3,744
	Individual Chemical Volume (μL)	21.30
	Solvent Volume (μL)	4978.70
	Total Volume to prepare (μL)	5,000
Standard #6		
Syringe Volume (μL)	Point 6	
1	Mass (ng)	3,159
	Individual Chemical Volume (μL)	17.97
	Solvent Volume (μL)	4982.03
	Total Volume to prepare (μL)	5,000
Standard #5		
Syringe Volume (μL)	Point 5	
1	Mass (ng)	2,574
	Individual Chemical Volume (μL)	14.64
	Solvent Volume (μL)	4985.36
	Total Volume to prepare (μL)	5,000
Standard #4		
Syringe Volume (μL)	Point 4	
1	Mass (ng)	1,989
	Individual Chemical Volume (μL)	11.31
	Solvent Volume (μL)	4988.69
	Total Volume to prepare (μL)	5,000
Standard #3		
Syringe Volume (μL)	Point 3	
1	Mass (ng)	1,404
	Individual Chemical Volume (μL)	7.98
	Solvent Volume (μL)	4992.02
	Total Volume to prepare (μL)	5,000
Standard #2		
Syringe Volume (μL)	Point 2	
1	Mass (ng)	818
	Individual Chemical Volume (μL)	4.65
	Solvent Volume (μL)	4995.35
	Total Volume to prepare (μL)	5,000
Standard #1 (Lowest Standard)		
Syringe Volume (μL)	Point 1	
1	Mass (ng)	233
	Individual Chemical Volume (μL)	1.33
	Solvent Volume (μL)	4998.67
	Total Volume to prepare (μL)	5,000

3.1.9 Spiking Thermal Desorption Tubes

A nine-point calibration curve was generated by spiking the liquid-phase benzene standards onto thermal desorption tubes filled with a Carbograph 4 sorbent cartridge. A Markes International Calibration Solution Loading Rig (CSLR) (Figure 29) was used to load the sorbent TD Tubes with one μL liquid benzene (Figure 30, 31) standard under ultra-high purity nitrogen flow (40 mL/min) while letting the system purge for 2 minutes. With the 2-minute purge time, the absence of breakthrough of the sorbent was verified by re-analyzing the same TD to ensure no carryover of the analyte of interest. A Hamilton Company (Reno, NV) 88000 Series, 24 gauge, one μL syringe was used to spike each thermal desorption tube. The syringe was cleaned after every use with a three-part cleaning process which included three flushes with methanol (step 1), three flushes with deionized water (step 2), and three flushes with acetone (step 3) (27). A 40 mL vial was used to contain methanol, deionized water, and acetone (Figure 32). After the flush was completed, the syringe was taken to a Hamilton syringe cleaner, where the needle was exposed to a temperature of 370 °C for approximately 30 seconds (Figure 33). Any vapors produced were carried away by the vacuum system connected to the end of the syringe cleaner. Using the Hamilton syringe cleaner allowed the elimination of acetone peaks in the GC/MS analysis. A Bios Defender 510 was used to adjust the ultra-high purity nitrogen flow rate to 40 mL/min (Figure 34). Before the benzene standards were used to spike thermal desorption tubes, they were allowed to acclimate to room temperature for one hour after being taken out of the lab's storage refrigerator.

Once the thermal desorption tubes were spiked with the standard, they were capped with diffusion-locking caps (DiffLok, Markes International, Bridgend, UK). The DiffLock caps prevented sample loss and ingress of contaminants. The thermal desorption tubes were then



Figure 31: Loading one μL of liquid benzene into CSLR (33).

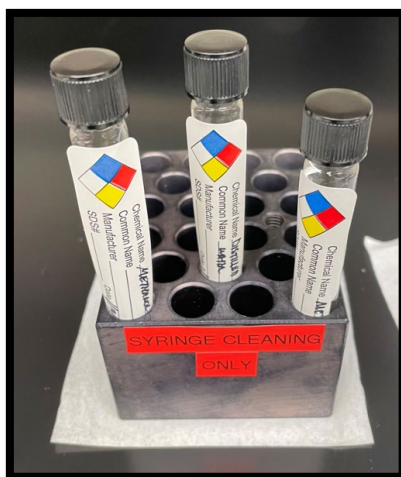


Figure 32: Syringe Cleaning Station with Methanol, De-ionized Water, and Acetone.

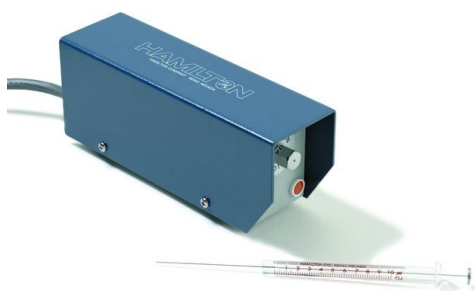


Figure 33: Hamilton syringe cleaner (27).

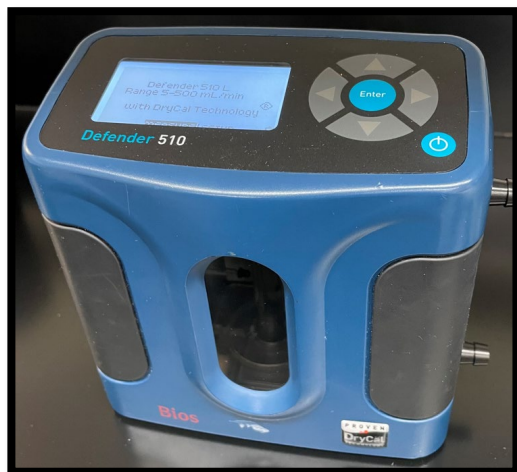


Figure 34: Bios Defender 510 volumetric primary flow standard.

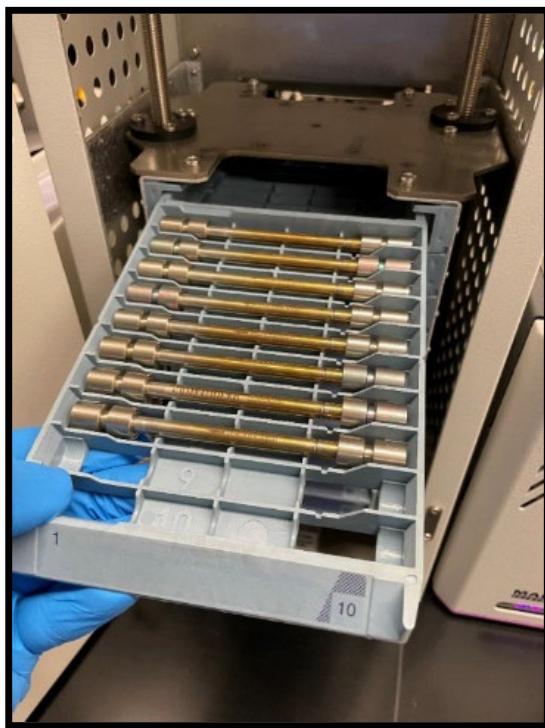


Figure 35: The Markes Series 2 Ultra loaded with spiked TD Tubes.

A benchtop Agilent 7890B Gas Chromatograph with a 5977 Mass Selective Detector was used to analyze the TD Tubes. The Agilent 7890B was coupled to the Markes Unity 2 through an

insulated transfer line (Figure 36, 37) that introduced the sample into the Agilent 7890 B's injection port (Figure 38). The Unity 2 is configured with electronic control of the carrier gas as it leaves the cold trap and enters the fused silica column inside the transfer line.

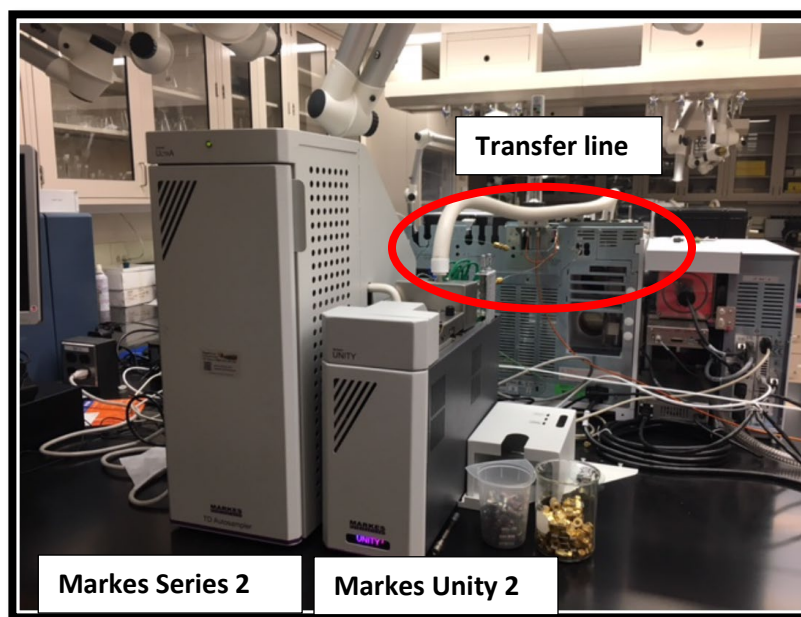


Figure 36: Markes Unity 2 & Series 2 Ultra Thermo Desorption Autosampler with transfer line.

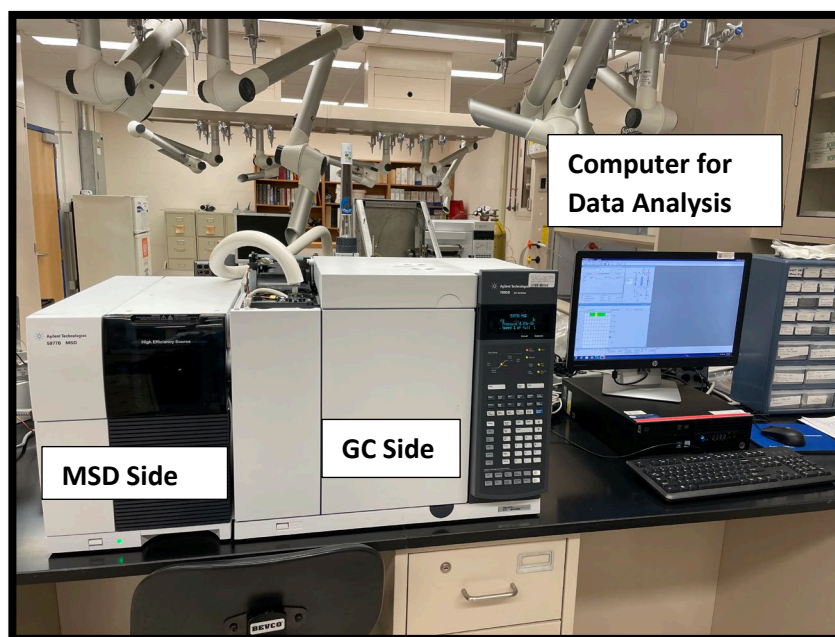


Figure 37: Benchtop Agilent 7890B Gas Chromatograph and 5977 Mass Selective Detector.

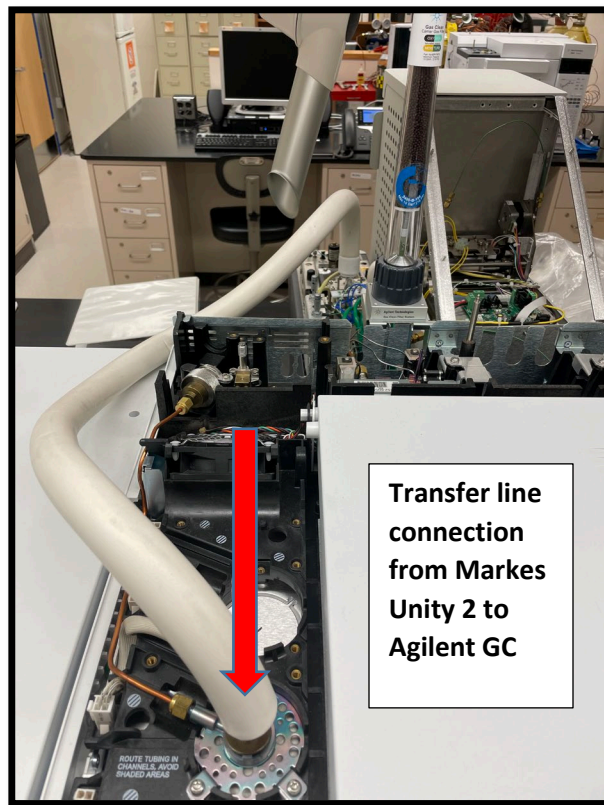


Figure 38: Transfer line from the Markes Unity 2 passing through the Agilent 7890B Gas Chromatograph and connecting to the analytical column.

3.1.10 Gasmeter DX4040 Calibration, Analysis Areas & Settings

An external calibration curve was not conducted for the Gasmeter DX4040 since the target concentration for benzene was within the manufacturer's measuring range. The manufacturer's measuring range for benzene was 0-20 ppm. The theoretical lower limit detection was 0.13 ppm based on 60 seconds of measuring time. There were two reference spectra associated with benzene: a 5 ppm and 20 ppm reference in the analysis library. The Calcmeter Software automatically picked the closest reference to the calculated concentration for the analysis. The 5-ppm reference library was automatically used for this experiment since the target concentrations for benzene ranged from 0.50 to 2.5 ppm. The analysis settings for BTEX were also optimized by

conducting several pilot studies, visual intuition, and Gasmet technician expertise. Selecting or de-selecting wavelength areas to enhance detection and quantification was specific to the Gasmet's Calcmeter software, and thus optimization required input from the Gasmet scientific team. The application library used for the analysis areas was SN19657_BTEX_c12_rev1 (Table 11). Gasmet recommended that when measuring lower concentrations then, a longer sampling time should be used. The measuring time for the sample measurement was set to 60 seconds.

Table 11: Analysis area settings for BTEX chemicals used in the application library.

Analysis Information - SN19657_BTEX_c12_Rev1.LIB							
Ch	Component	Referenc...	Interfere...	Measuring r...	Analysis area 1	Analysis area 2	Analysis area 3
1	Benzene	2	6	0 - 50	-	-	2550 - 3150 (1.0)
2	Toluene	4	6	0 - 200	-	-	2550 - 3150 (1.0)
3	Ethyl benzene	4	6	0 - 100	-	-	2550 - 3150 (1.0)
4	M-Xylene	4	6	0 - 200	-	2550 - 3150 (1.0)	-
5	Methane	3	6	0 - 100	-	2550 - 3200 (1.0)	-
6	Water vapor	7	1	0 - 3	-	-	3200 - 3400 (1.0)
7	Carbon dioxide	4	7	0 - 2000	-	1900 - 2267 (1.0)	2500 - 2600 (1.0)
8	Nitrous oxide	3	7	0 - 100	-	1900 - 2233 (1.0)	2500 - 2600 (1.0)
9	Carbon monoxide	4	7	0 - 200	-	1900 - 2223 (1.0)	2500 - 2600 (1.0)

3.1.11 Prepping the System Before Sampling

Gasmet DX4040 Zero Background

A zero background was conducted for the Gasmet DX4040 before sampling for the day per the manufacturer's instructions (120-second flush time, 60-second measuring time, and pump in off the position). UHP Nitrogen from a cylinder to a two-stage regulator was used to bring down the cylinder pressure before being introduced to the CSLR setup. The CSLR was used to introduce UHP Nitrogen to the Gasmet “Zero Gas Port” at a flow rate of 2 L/min. A Bios Defender 520 primary flow meter adjusted the CSLR flow rate to 2 L/min. An exhaust connection led from the Gasmet “Sample Out” port to the lab’s exhaust system (Figure 39). Once

the flow rate was adjusted, a four-foot Tygon hose was connected to the end of the empty TD tube within the CSLR (Figure 40). Figure 41 shows an image of the complete setup used for the Zero Calibration.

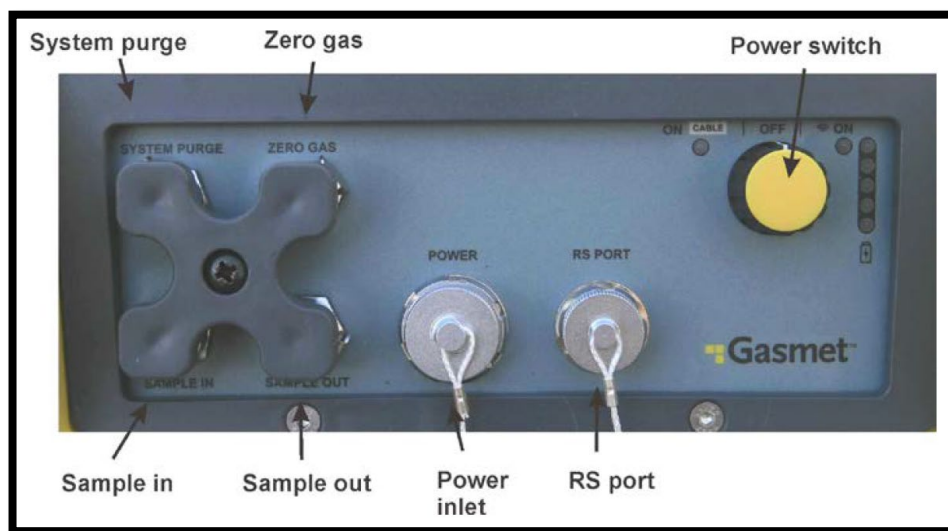


Figure 39: Gasmet DX4040 front panel showing sample gas fittings (25).

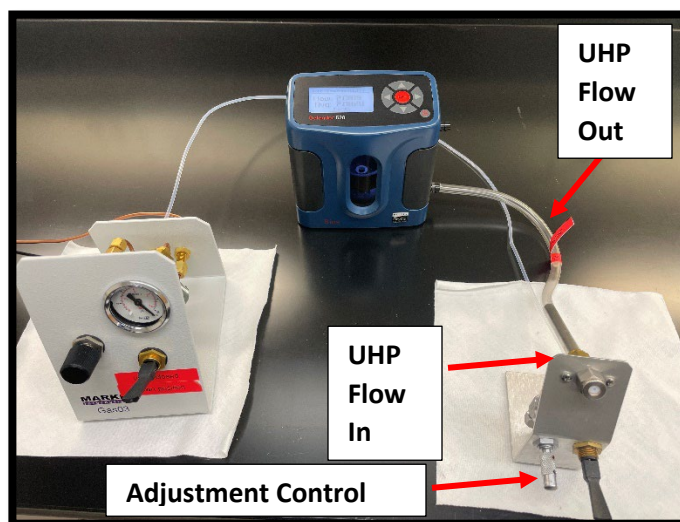


Figure 40: Bios Defender 520 was used to adjust the CSLR flowrate to 2 L/min.

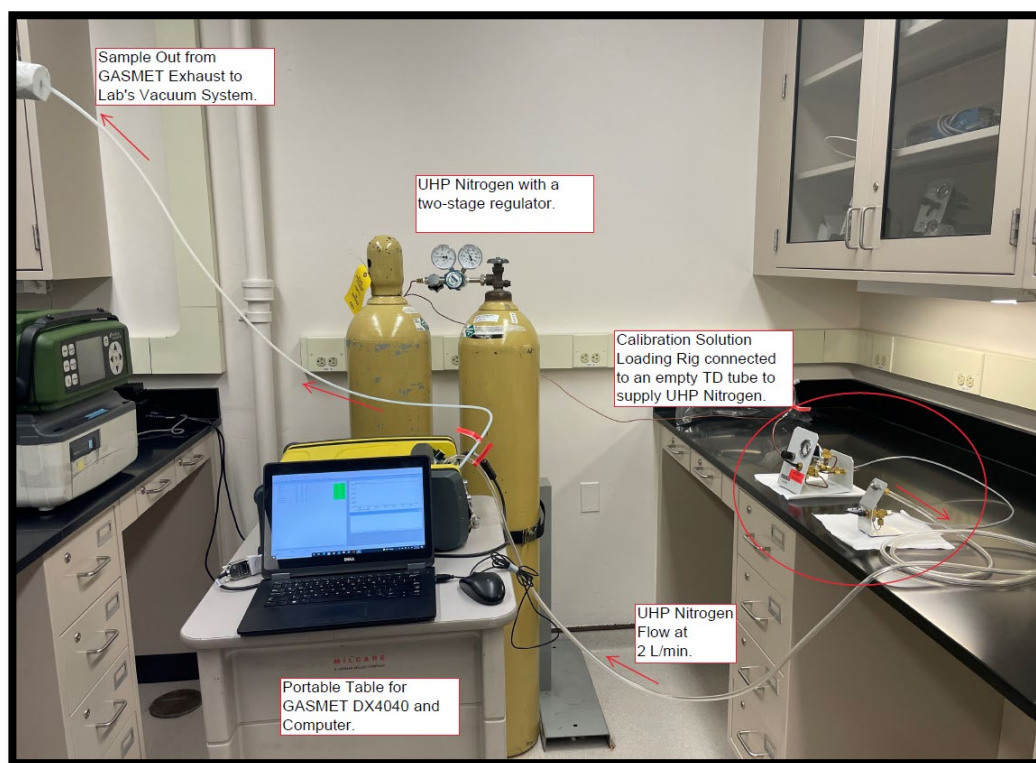


Figure 41: Gasmet DX4040 with the setup used for the Zero Calibration.

Purging the System Before Sampling

Servel pilot studies for this experiment demonstrated that BTEX was adsorbed to various materials in the dynamic flow chamber and Gasmet DX4040. Several steps were taken to remove any BTEX residues from the Gasmet DX4040's pump, hoses, and sample probe. The dynamic flow chamber was also purged to remove any BTEX residues.

The Gasmet DX4040 probe was used to pull continuous samples from the dynamic flow chamber into the Gasmet DX4040's sample inlet port. The pilot studies conducted during this project showed residues of BTEX being measured by the Gasmet before running the syringe pump. The Gasmet probe's internal (PVC) filter was removed to correct these readings, and the inlet hose was changed to a Teflon (PTFE) material. Before sampling, the probe and Teflon hose

were flushed with UHP nitrogen for approximately 15 minutes (Figure 42). This technique was based on the Gasmet's technician troubleshooting and recommendations.

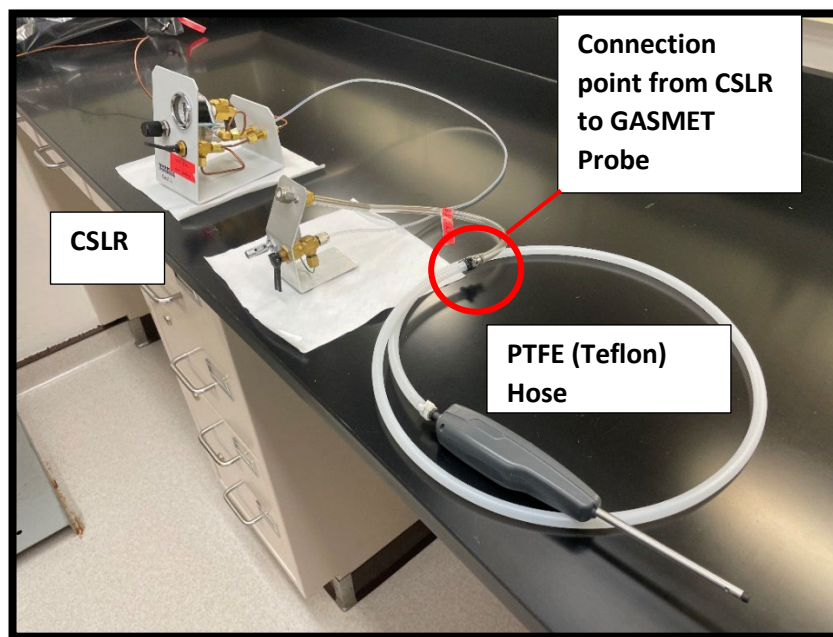


Figure 42: Flushing Gasmet Probe with UHP Nitrogen.

After the Gasmet Zero Calibration was conducted, the Calcmnet software was set up on continuous sampling with a 60-second measurement. A 5-liter SKC bag was filled with UHP Nitrogen to flush out any BTEX leftover in the Gasmet internal pump from the previous sampling period (Figures 43;44). An SKC bag is preferred over a direct connection from the CSLR. Over pressurizing the sample cell and pump could damage the Gasmet internal system, so a direct connection from the CSLR was not made. Once the BTEX readings showed 0 ppm in the Calcmnet software, the SKC bag was disconnected. The Gasmet probe was then connected to sample the chamber concentrations while the syringe pump was in the off position. If the Gasmet detected residual levels of BTEX, then UHP Nitrogen was connected directly to the chamber to help further reduce any residual BTEX (Figure 45). The UHP Nitrogen connections were removed once the residual BTEX concentrations were zero.



Figure 43: CSLR connection to fill the 5 Liter SKC bag with UHP Nitrogen.

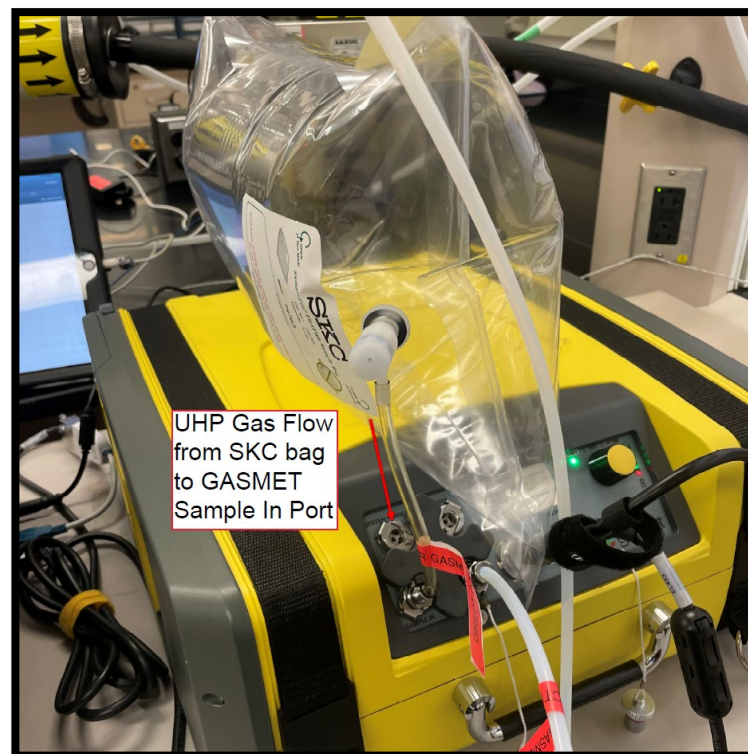


Figure 44: SKC Bag connection to the Gasmet sample in port.

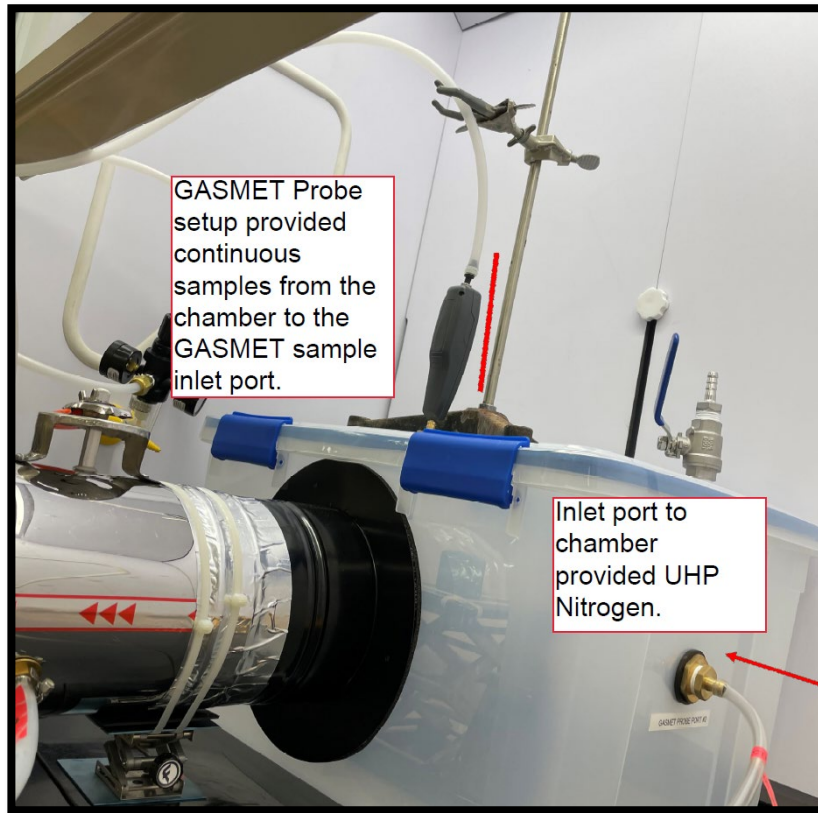


Figure 45: CSLR to chamber connection providing UHP nitrogen.

3.1.12 Placing & Removing Samplers Into/From the Dynamic Flow Chamber

A workstation was created to help organize the Radiellos[®] and TD tubes so that they would be efficient when sampling continuously. Seventeen of the Carbograph 4 sorbents were conditioned and placed inside the Radiello[®] diffusive bodies in preparation for sampling. Three of the Carbograph 4 sorbents were placed in stainless steel TD tubes which served as the blanks needed for each scenario. Seventeen empty TD tubes were prepared with one DiffLock cap on one end (Figure 46).

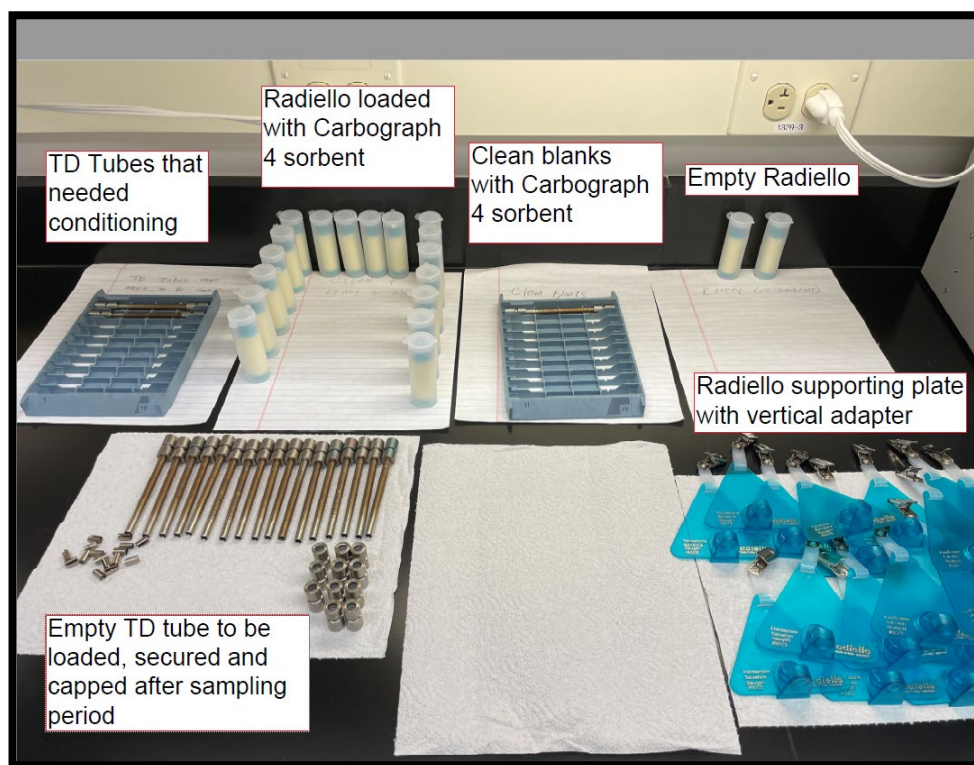


Figure 46: Radiello[®] workstation where clean and used samplers were processed.

Once the dynamic flow chamber was at the proper concentration, each sampler was introduced one at a time. As recommended by Gasmeter, the scenario with the highest concentration (Scenario 3) was completed first. A magnetic bar inside the chamber attracted the metal clip to the sampler (Figure 47). The Radiello[®] was inserted first and placed on the magnetic bar's right side, while the OVM was inserted second and placed on the left-hand side of the magnetic bar. Once placed in the proper position, the chamber's duct flange valve was closed, and a timer was started. During the 15 minutes, parameters such as mass flow and relative humidity were adjusted on the Miller-Nelson to achieve the desired target concentration and relative humidity. A workstation computer was used for logging the multiple parameters such as pressure, dewpoint, temperature, syringe injection rate, and the serial numbers for the OVMs (Figure 48).

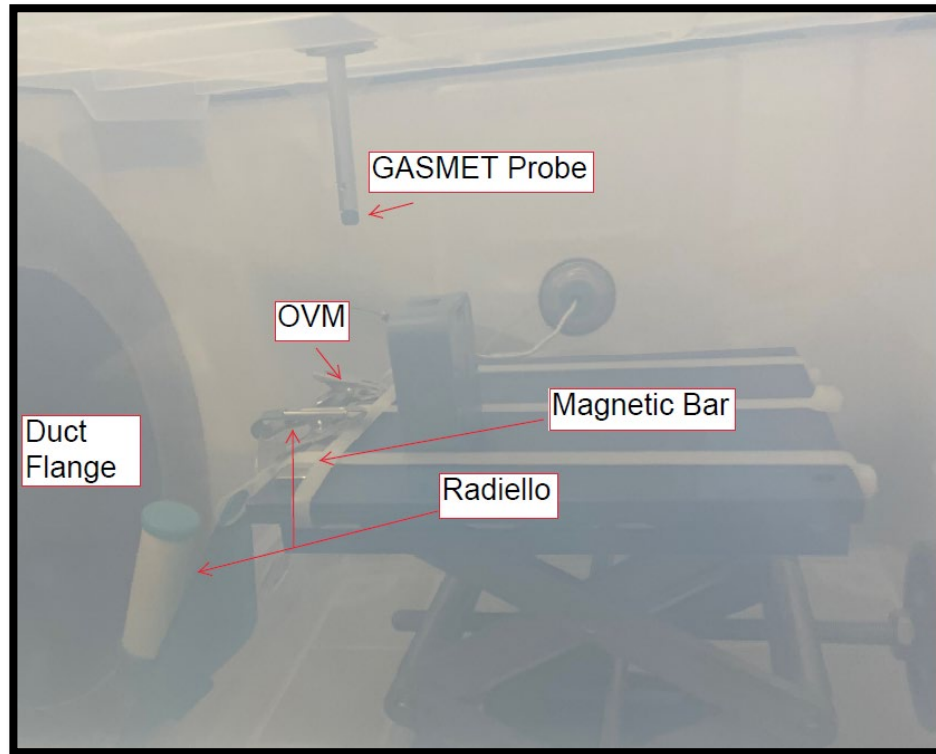


Figure 47: The transparent chamber's right-side view (look through from outside the container) shows the Radiello® and OVM placement.

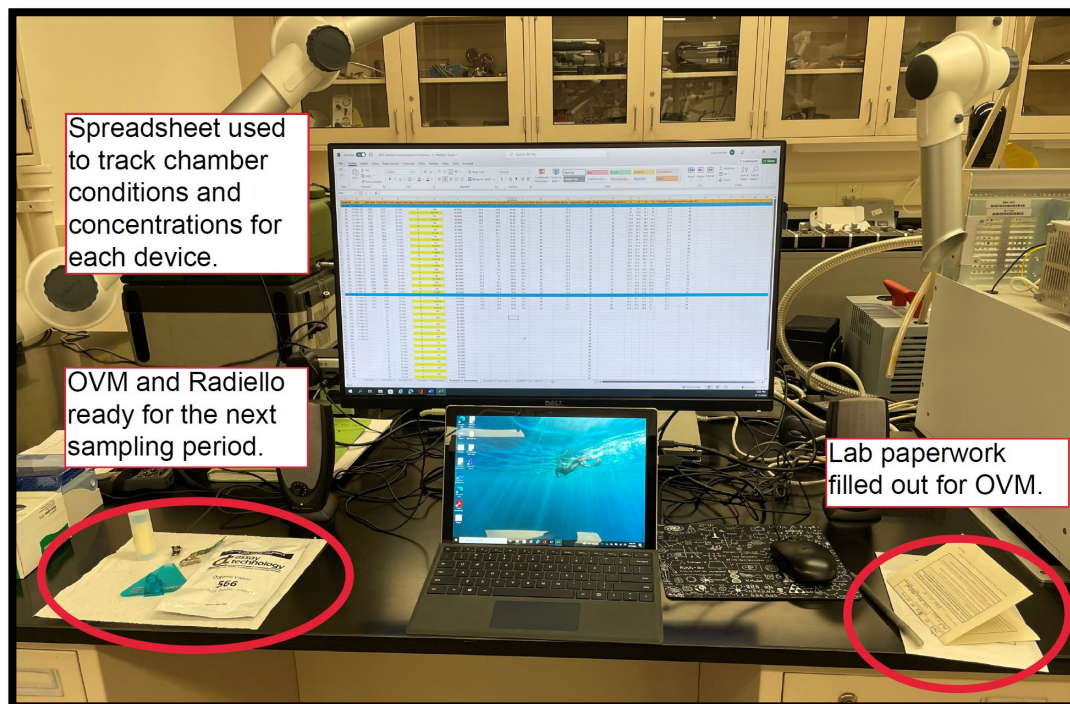


Figure 48: Workstation next to the dynamic flow chamber used to track chamber conditions.

After 15 minutes of sampling, the Radiello and OVM samplers were removed and shifted to a workstation to be processed. The OVMs were packaged, and lab documents were filled out for shipment. The Carbograph 4 sorbent was removed from the Radiello[®] diffusive body and placed into an empty TD tube. A spring was inserted to hold the sorbent in place, and a second DiffLok Cap was added. The TD tube was then placed into the Markes Series 2 Ultra Thermal Desorption Autosampler for thermal desorption and analysis.

3.1.13 Field Blanks and Media Blanks

According to NIOSH sampling methods, the Industrial Hygiene Field Operations Manual (Chapter 3) was used to determine the required Field and Media blanks. Field blanks were used to check for contamination from the sampling process and the background contamination from the lab site (40). Since the number of Radiello[®] and OVMs used for this study was greater than 20, the number of blanks required by NIOSH was 10% of the total number of samplers, which equated to three blanks. Field blanks for the OVMs were collected per the method requirements/manufacture recommendations. In the sequence of analyzing these blanks, they were placed first, 14th, and last. One media blank per lot number was also analyzed for the OVMs. This study had three OVM lots, equating to three total media blanks. Media blanks were used to check the media and analyte background levels and for laboratory reagents and methodology (40). These media blanks were unopened, labeled as media blanks, and sent to the laboratory with the field blanks and samples. All samples were sealed with the required lab documentation and mailed by FedEx to the Assay Technology Laboratory in Boardman, OH.

3.1.14 Prepping up the Agilent GC/MS

The MassHunter Data Acquisition Software controlled the Agilent 5977 MSD and the 7890 GC from the instrument control view. This screen allowed for controlling 5977 instrument settings, setting up sequences, tuning (calibrating) the 5977 MSD, setting up GC/MS acquisition parameters, and monitoring the chromatogram and mass spectra for the samples.

Air and water checks were conducted before operating the Agilent GC/MS. The presence of water or air in the system could contaminate the ion source. This could result in reduced sensitivity and will have a negative effect on the chromatography. Air leaks in the system could contribute to loud gurgling noise from the foreline pump, the inability of the turbopump to reach 95% or high-pressure readings on the high vacuum gauge controller (3). Some air components, such as oxygen, can also deleteriously affect parts of the detector. For example, oxygen can result in a burned-out ionizer filament (as oxygen in an incandescent light bulb will result in a burned-out filament). An Agilent G3388B leak detector was used to identify any helium leaks for the GC/MS if a leak was suspected. Therefore, air and water checks were done to ensure contaminants were at acceptable levels before proceeding with the analysis of the TD tubes. As an example, a copy of this report has been provided in Appendix C.

A HES autotune was also performed before analyzing TD tubes. This allowed the MSD to achieve the maximum mass spectral sensitivity and proper resolution (2). A tune evaluation report was then produced and reviewed to ensure all the parameters were within range. All data results are affected by how the instrument is tuned. A copy of an air/water report, tune report, and evaluation report has been provided in Appendix E.

3.1.15 Setting up a Software Sequence and Analyzing the Data for the Radiello®

The Markes Maverick Software (Version 5.2.0) was used to create a controlling method for thermal desorption (Appendix D). Once the method was developed, a new sequence was linked to the method based on how many TD tubes were to be analyzed. Once the sequence was set, a shift to the MassHunter Data Analysis software package was made. A method, a sampling sequence table, and a start sequence were also created within the MassHunter software (Appendix F). The sequence typically took between 19 and 20 minutes. Once this sequence was completed, the MassHunter software would start initiating its sequence associated with the GC/MS, which would take approximately 21: 92. The data file was accessed using Agilent MSD ChemStation (Ver. F.01.03.2357). This software allowed automatic or manual integration to determine the areas associated with the benzene peaks.

Peak areas were then converted to a mass using the linear equation determined when a calibration curve was created (*Equation 3.5*). The update rate was adjusted for temperature variations in the chamber (*Equation 3.6*). The total volume sampled was determined using the Radiello®'s adjusted uptake rate and multiplying it by the total sampling time (*Equation 3.7*). Next, the concentration was ng/mL and converted to mg/m³ (*Equation 3.8*). Finally, the concentration was converted to ppm (*Equation 3.9*). Values recorded by the HTP.xw were extracted to a CSV file for the chamber's pressure and temperature during each sampling period. These values were averaged for each sampling period and used for the temperature (Kelvin) and pressure values (mm Hg).

Determining Radiello® Mass from Integrated Areas:

$$\text{Mass}_{\text{ng}} = \text{Integrated area} / 66883 \quad (3.5)$$

Mass_{ng} = mass in nanograms

Integrated area = areas determined by using the Agilent Enhanced Chem Station software.

Note: 66883 was determined from calibration curve linear equation (no y-intercept)

Adjusted Uptake (Sampling) Rate (18)

$$Q_k = Q_{298} (K/298)^{1.5} \quad (3.6)$$

Q_k = Radiello[®] validated uptake value in mL/min at 298 Kelvin (25°C)

Determining Total Volume Sampled in 15 minutes

$$\text{Total Volume Sampled}_{\text{mL}} = (\text{Adjusted Uptake Rate}) \times (\text{Sampling Time}) \quad (3.7)$$

Benzene Adjusted Uptake Rate = mL/min

Sampling Time = 15 minutes

Determining Concentration in ng/mL:

$$C_{\text{ng/mL}} = \text{Mass}_{\text{ng}} / \text{Total Volume Sampled}_{\text{mL}} \quad (3.8)$$

$C_{\text{ng/mL}}$ = concentration in ng/mL

Note: 1 ng/mL = 1 mg/m³

Determining Concentration in ppm:

$$C_{\text{ppm}} = \frac{62.4 \times (273.2 + ^\circ\text{C}) \times (C_{\text{mg/m}^3})}{P \times \text{MW}} \quad (3.9)$$

Temperature= Average temperature in the dynamic flow chamber

Conversion from °C to Kelvin

$C_{\text{mg/m}^3}$ = Concentration in mg/m³

P = Average pressure in the dynamic flow chamber in mm Hg

MW = Molecular weight of benzene = 78.11 g/mol

R = Ideal gas constant = $62.4 \text{ L} \cdot \text{Torr/mol} \cdot \text{K} = 62.4 \text{ mmHg/mol} \cdot \text{K}$

Note: $1 \text{ ng/mL} = 1 \text{ mg/m}^3$

3.1.16 Determining Percent Recovery for the Radiello® Carbograph 4

The ability to recover the analyte from the Radiello® was determined by running a duplicate analysis of the same TD tube spiked with a calibration standard. These were the same standards used when making the calibration curve for the Agilent 7890B/5977B. A one μL sample of liquid benzene in methanol was injected into a TD tube and analyzed using the same analytical parameters in the Markes International Maverick and MassHunter Data Acquisition Software. Standard # 1, 3, 6, 7, 9, and 10 with a mass range of 232 – 5,793 ng (0.18-4.33 ppm) were used when determining the percent recovery. Peak areas were integrated using Agilent MSD ChemStation. The areas were then converted to a mass using *Equation 3.5*. Following the conversion *Equation, 3.10* was used to calculate the percent recovery.

Determining Percent Recovery (6):

$$\% \text{ Recovery} = \frac{\text{Amount of analyte found on the sampler in ng}}{\text{Amount of analyte fortified on the sampler in ng}} \times 100 \quad (3.10)$$

3.1.17 Statistical methods

Appropriate sample size calculation and power analysis were conducted using the latest G*Power Software (Version 3.1.9.7). It was determined that the minimum sample size for each scenario would consist of 26 OVM and 26 Radiello® samplers. The parameters for the statistical analysis were a two-tailed test, 80% effect size, 5% error probability, and 80% power.

Data were analyzed using Microsoft Excel (Office 365) and IBM® SPSS® Statistics Software (Version 28.0.1.0) (142) to obtain descriptive statistics (mean standard deviation, coefficients of variation) and linear least squares regression analysis.

Comparisons between the groups (Gasmet vs. Radiello[®], Gasmet vs. OVM, and Radiello[®] vs. OVM) were made within every target concentration. A one-way ANOVA was used to determine if the devices had different average concentrations for each target concentration. If a p-value were statistically significant, meaning that the p-value was less than 0.05, then a Post-Hoc test would be needed to determine which groups differed. The Post-Hoc (pair-wise comparison) test was made to explore the difference between multiple groups means utilizing the LSD method (un-adjusted p-values) and a Sidak method (adjusted for multiple comparisons). Bland Altman plots were made in excel to show by concentration which device was under or overestimating the direct reading reference standard (Gasmet).

CHAPTER 4: RESULTS

4.1 CALIBRATION DATA: AGILENT 7980B/5977B GC/MS

Calibration was performed using a 9-point curve. The curve had excellent linearity, with an R^2 value = 0.994 (Figure 49). The range of masses covered by the curve was 233-5,330 ng (0.223 – 5.33 μ g). Analysis of each expected (theoretical) mass was performed in triplicate. The accuracy of the actual benzene mass was also good, with an average relative error across the calibration range of 12% (Table 12).

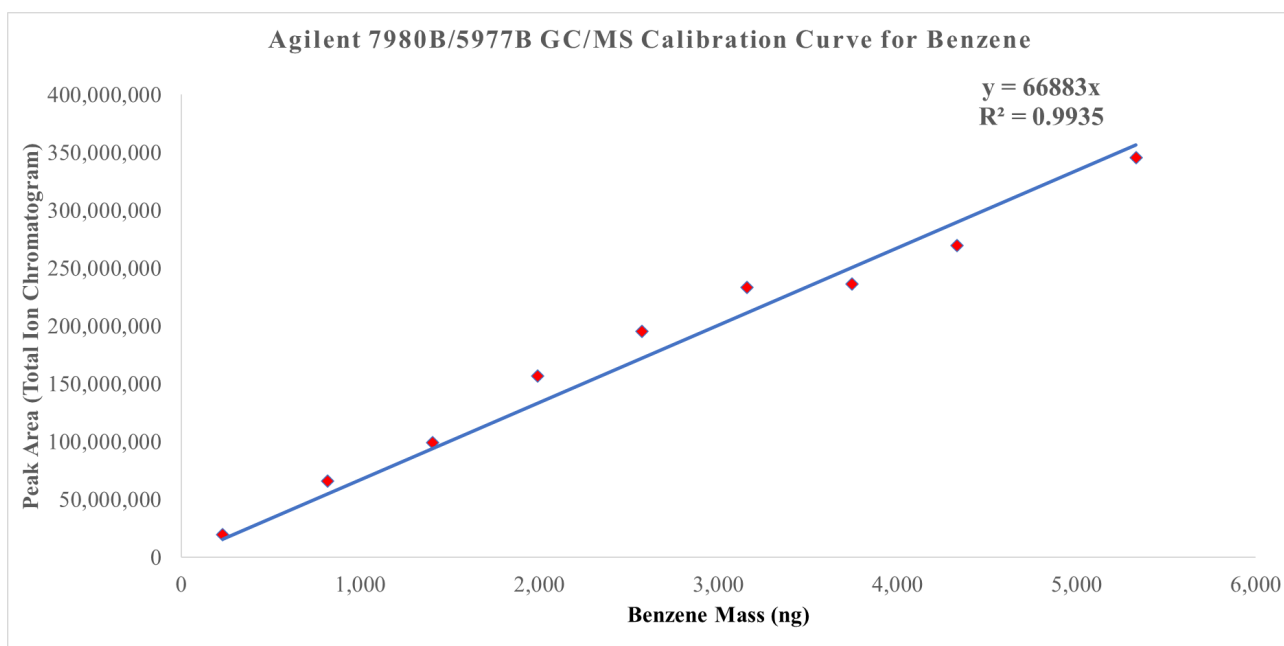


Figure 49: Nine-point calibration curve for the Agilent 7890B/5977B GC/MS.

Table 12: Summary of the percent error for standards 1-9.

Standard No.	True Value of Benzene Mass (ng)	Peak Area (Total Ion Chromatogram)	Observed Benzene Mass (ng)	Relative Error (%)
1	233	19,464,567	293	26
2	818	65,892,539	993	21
3	1,404	99,444,861	1,499	7
4	1,989	156,883,547	2,364	19
5	2,574	195,507,118	2,946	14
6	3,159	233,401,344	3,517	11
7	3,744	236,307,411	3,561	5
8	4,330	269,836,695	4,066	6
9	5,330	345,814,277	5,211	2
Average Error:				12

4.2 CALIBRATION DATA: GASMET DX4040

The three-point factory calibration curve had linearity with an R^2 value = 0.99 (Figure 50). The concentration range covered was from 0-20 ppm for benzene. The absorbances were described in absorbance units (a.u.).

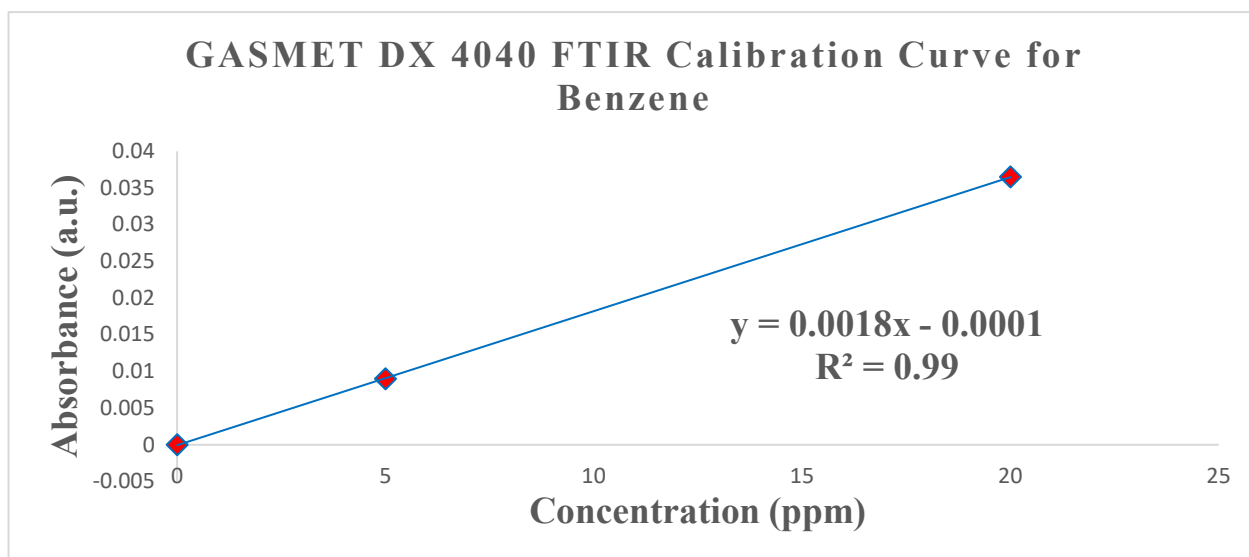


Figure 50: Three-point factory calibration curve for the Gasmet DX4040 FTIR.

4.3 RECOVERY RATE OF SPIKED BENZENE ON THE RADIELLO® CARBOGRAPH 4 SORBENT

The recovery rate is the ratio between the values measured and expected values. As displayed in Figure 51, a linear recovery rate with an average recovery rate of 99% was obtained. Table 13 includes benzene's recovery rate values with an approximate concentration value associated with the spiked mass (after a conversion). Table 14 includes the % relative error associated standards used to determine the recovery rate.

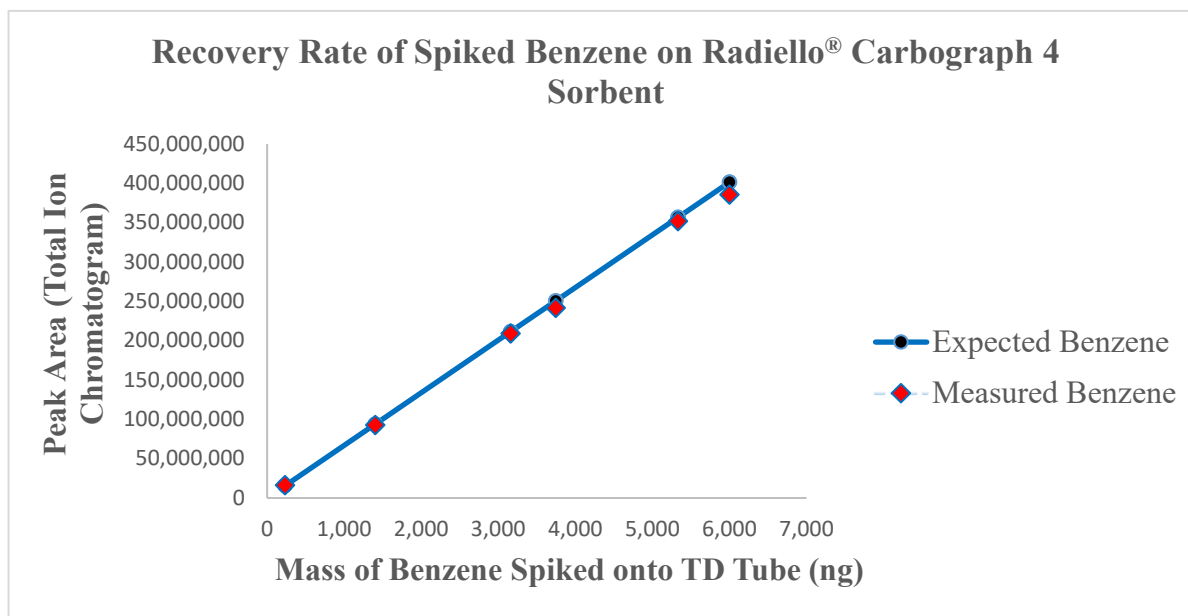


Figure 51: Recovery rate of spiked benzene on Radiello® CarboGraph 4 Sorbent.

Table 13: Benzene recovery rates (%) on CarboGraph 4 Sorbent.

Standards No.	Spiked Mass (ng)	≈ Concentration (ppm)	Recovery Rate % (mean ±SD)
1	233	0.18	105 ± 7
3	1,404	1.04	99 ± 3
6	3,159	2.35	99 ± 1
7	3,744	2.71	96 ± 2
9	5,330	3.95	99 ± 0
10	6,000	4.33	96 ± 1
Average Recovery Rate			99 %

Table 14: Summary of the percent relative error for standards used to determine recovery rate.

Standard No.	True Value of Benzene Mass (ng)	Peak Area (Total Ion Chromatogram)	Observed Benzene Mass (ng)	Relative Error (%)
1	233	19,464,567	293	26
3	1,404	99,444,861	1,499	7
6	3,159	233,401,344	3,517	11
7	3,744	236,307,411	3,561	5
9	5,330	345,814,277	5,211	2
10	6,000	385,150,079	5,804	3
Average Error:				9 %

4.4 NORMALITY OF DATA

4.4.1 Kolmogorov-Simmons & Shapiro-Wilk Tests of Normality

A Kolmogorov-Simmons and a Shapiro-Wilk normality test were conducted to determine the data's normality. A Shapiro-Wilk test serves the same purpose as a Kolmogorov-Simmons test, but the Shapiro-Wilk provides higher statistical power and more sensitivity for smaller sample populations. The null hypothesis states that the variable is normally distributed in some populations for both tests. So, the null hypothesis would be rejected if the p-value is below 0.05 ($p < 0.05$), which would mean that the data was not normally distributed. Table 15 provides the significance values for both the Kolmogorov-Smirnov and the Shapiro-Wilk. At the three target concentrations, the significance values of all the data have a p-value > 0.05 .

Table 15: Tests of Normality: Kolmogorov-Smirnov & Shapiro-Wilk.

Tests of Normality							
Target Concentration (ppm)	Device	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
0.50	Gasmet	0.151	30	0.08	0.964	30	0.4
	Radiello	0.072	29	.200*	0.992	29	0.997
1.25	Gasmet	0.082	29	.200*	0.98	29	0.836
	Radiello	0.084	28	.200*	0.978	28	0.811
	OVM	0.129	29	.200*	0.928	29	0.049
	Gasmet	0.145	26	0.168	0.963	26	0.457
2.5	Radiello	0.068	26	.200*	0.976	26	0.783
	OVM	0.126	26	.200*	0.95	26	0.229

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

4.4.2 Histograms

Histograms were created to demonstrate the degree to which the device data show a central tendency and a symmetrical distribution relative to the data's mean. An overlay was added over the data to show the Gaussian distribution through a bell-shaped curve. Figures 52-54 demonstrate normality for each scenario while comparing each device to another. Figures 55-62 evaluate normality independently and have been re-scaled on the x-axes (actual device concentrations) to show more defined bell-shaped curves. The individual histograms have included the mean, standard deviation, and sample size.

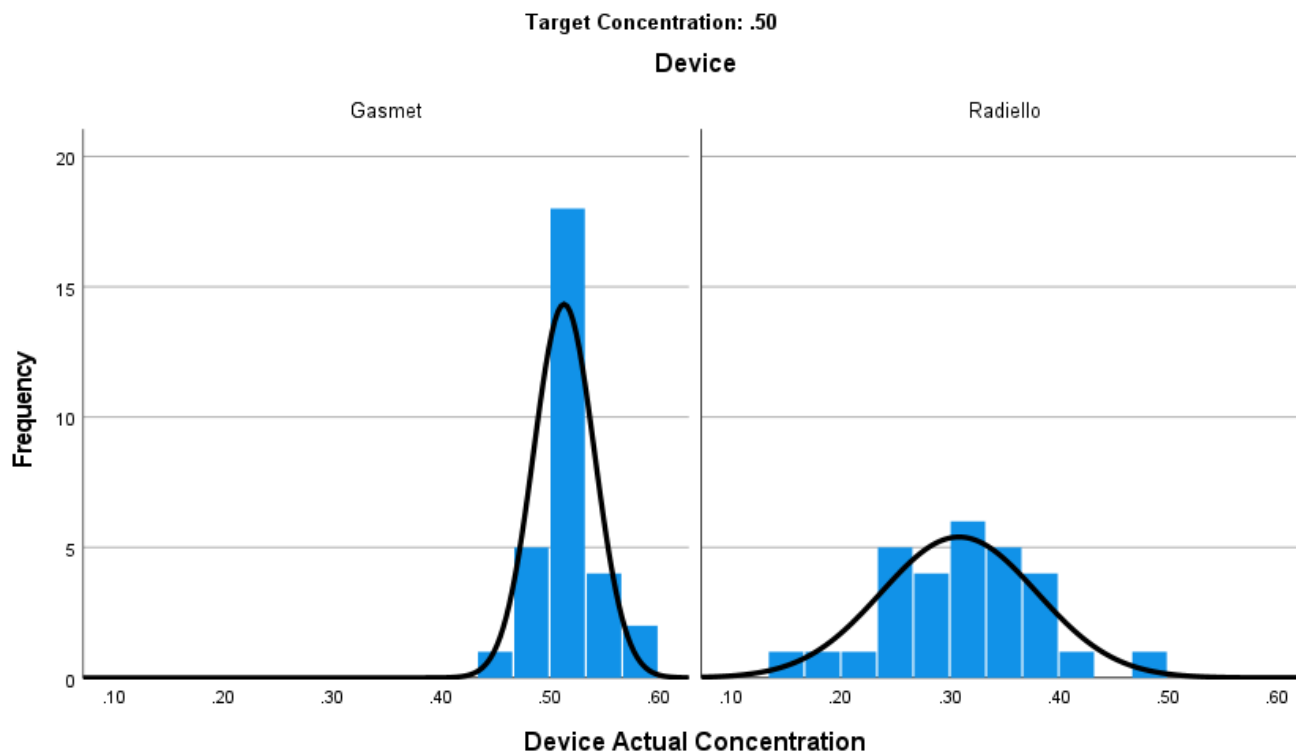


Figure 52: Scenario 1: Histogram for the Gasmet and Radiello® data.

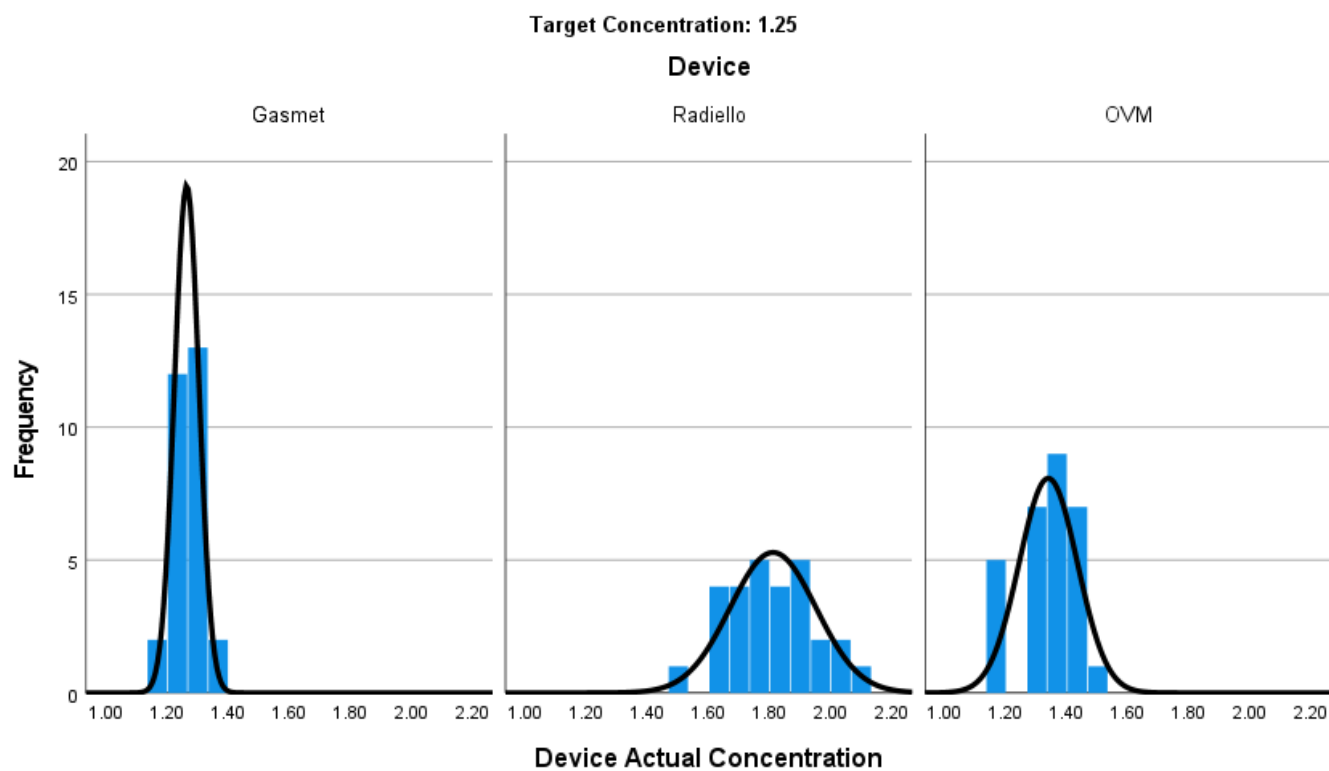


Figure 53: Scenario 2: Histogram for the Gasmet, Radiello®, and OVM data.

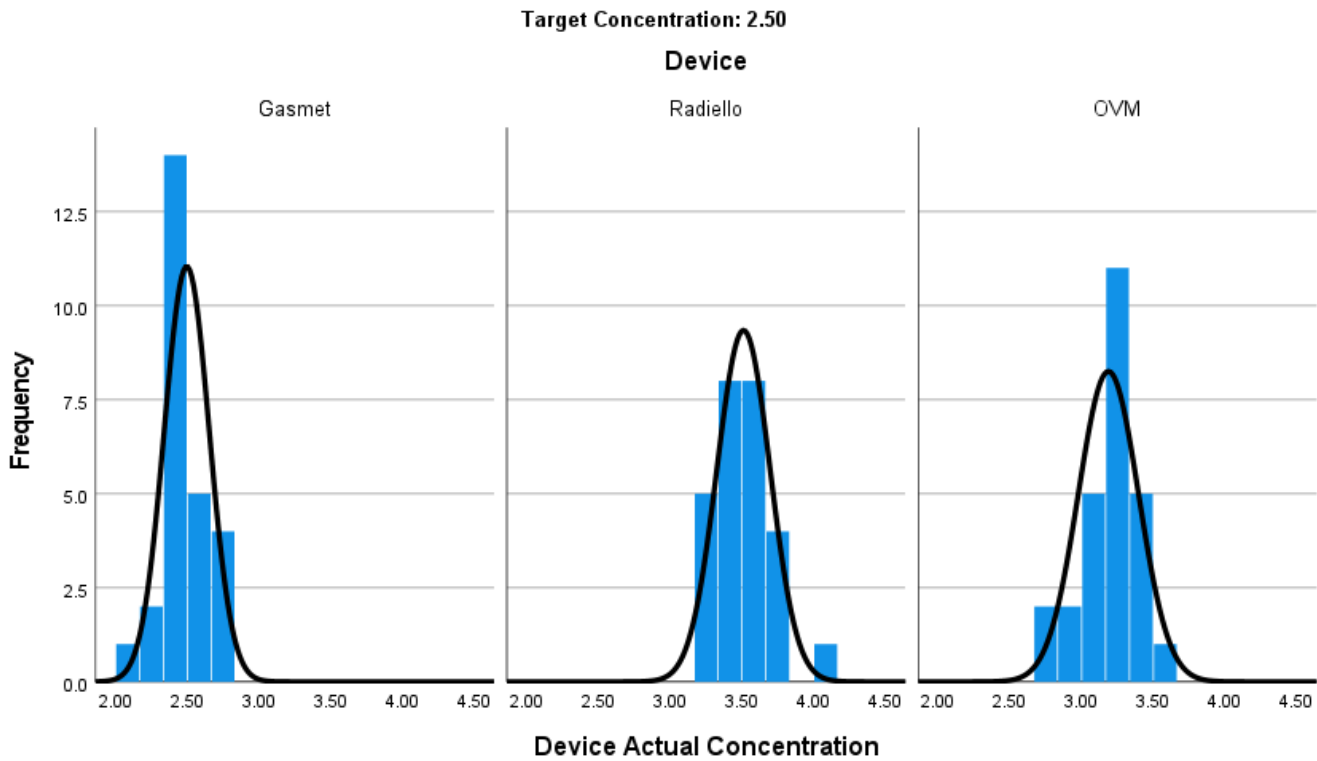


Figure 54: Scenario 3: Histogram for the Gasmet, Radiello® and OVM data.

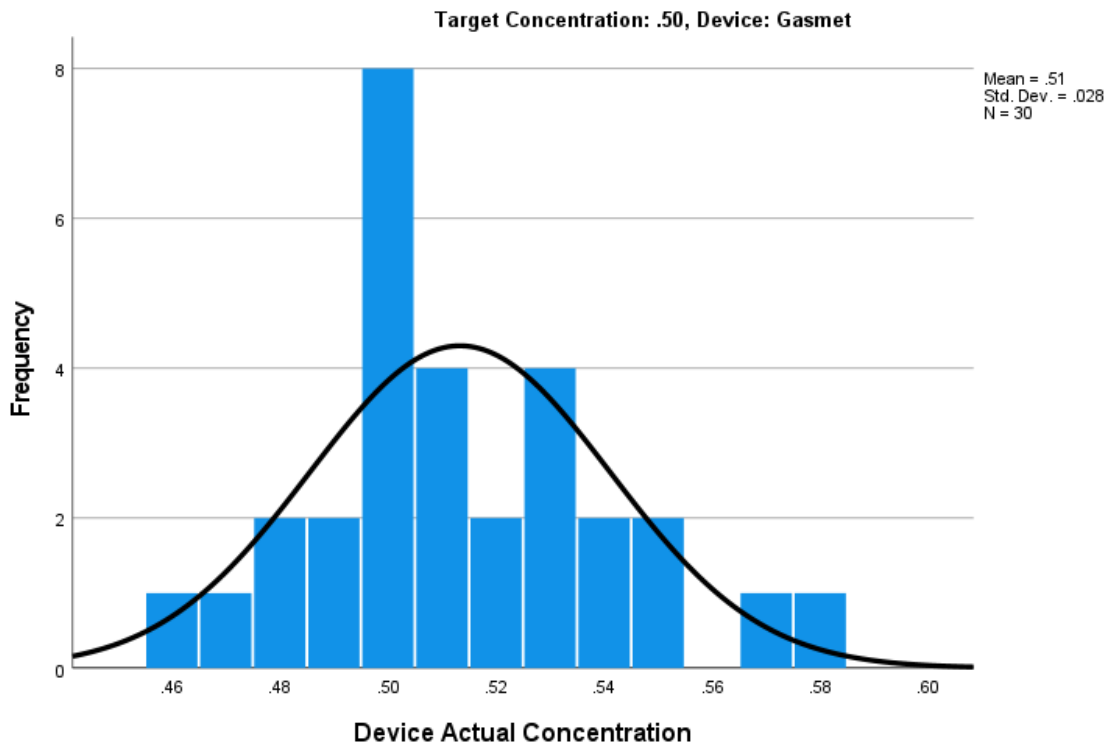


Figure 55: Scenario 1: Gasmet histogram showing a more defined bell curve.

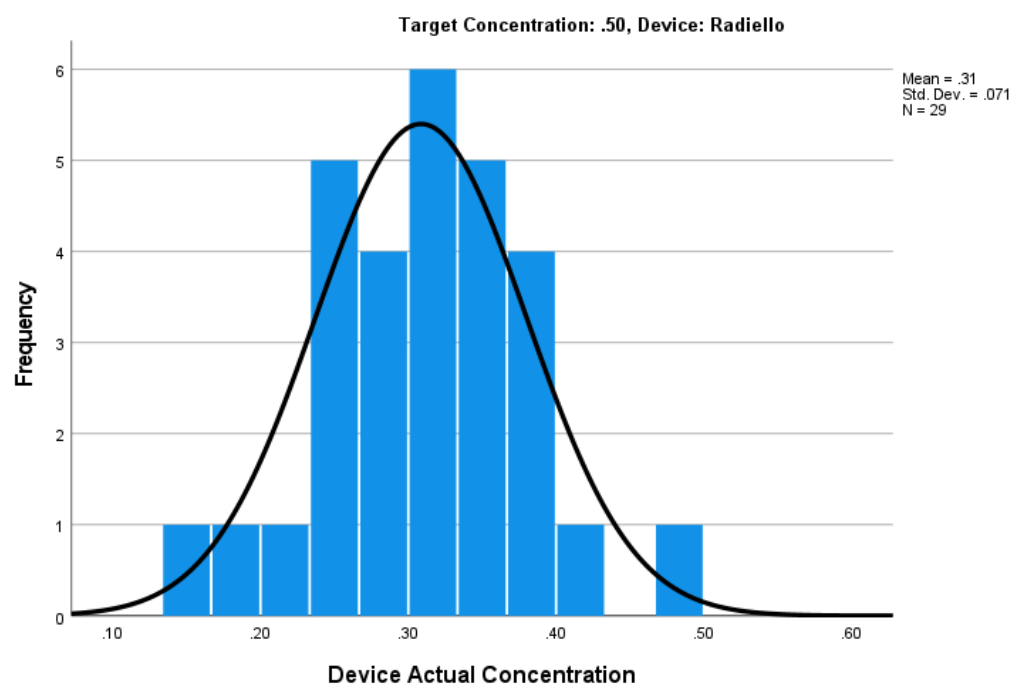


Figure 56: Scenario 1: Radiello® histogram showing a more defined bell curve.

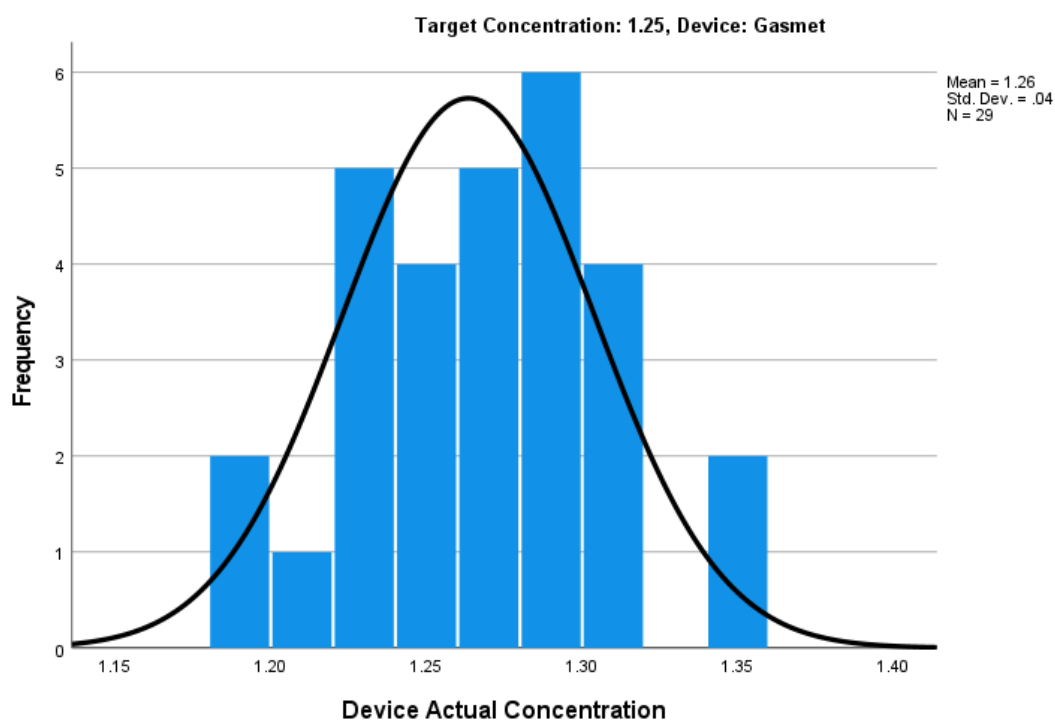


Figure 57: Scenario 2: Gasmeter histogram showing a more defined bell curve.

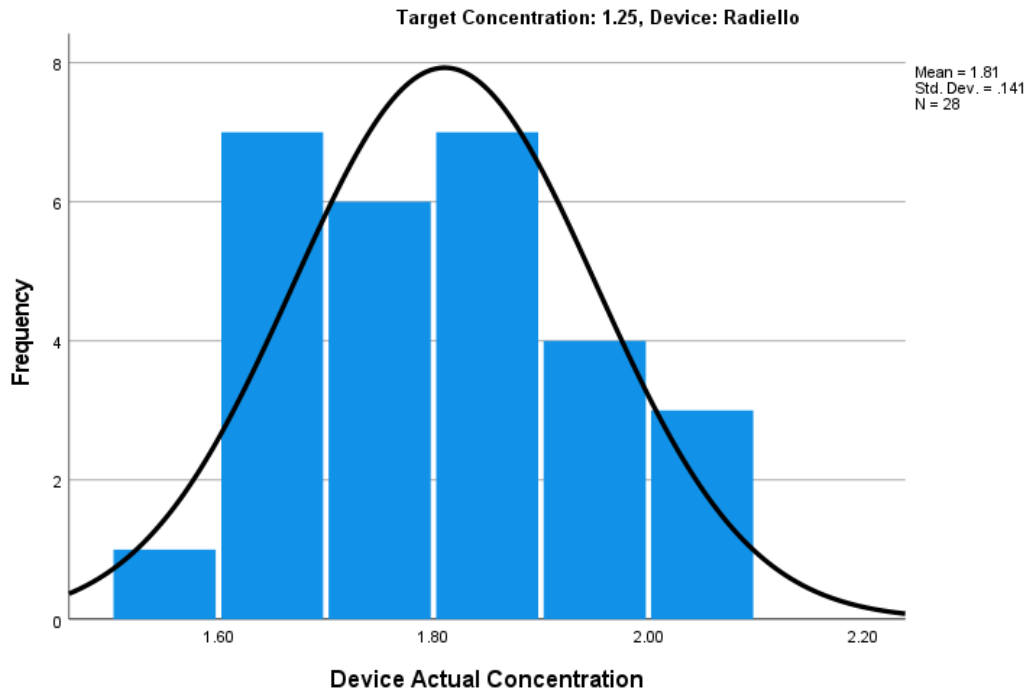


Figure 58: Scenario 2: Radiello® histogram showing a more defined bell curve.

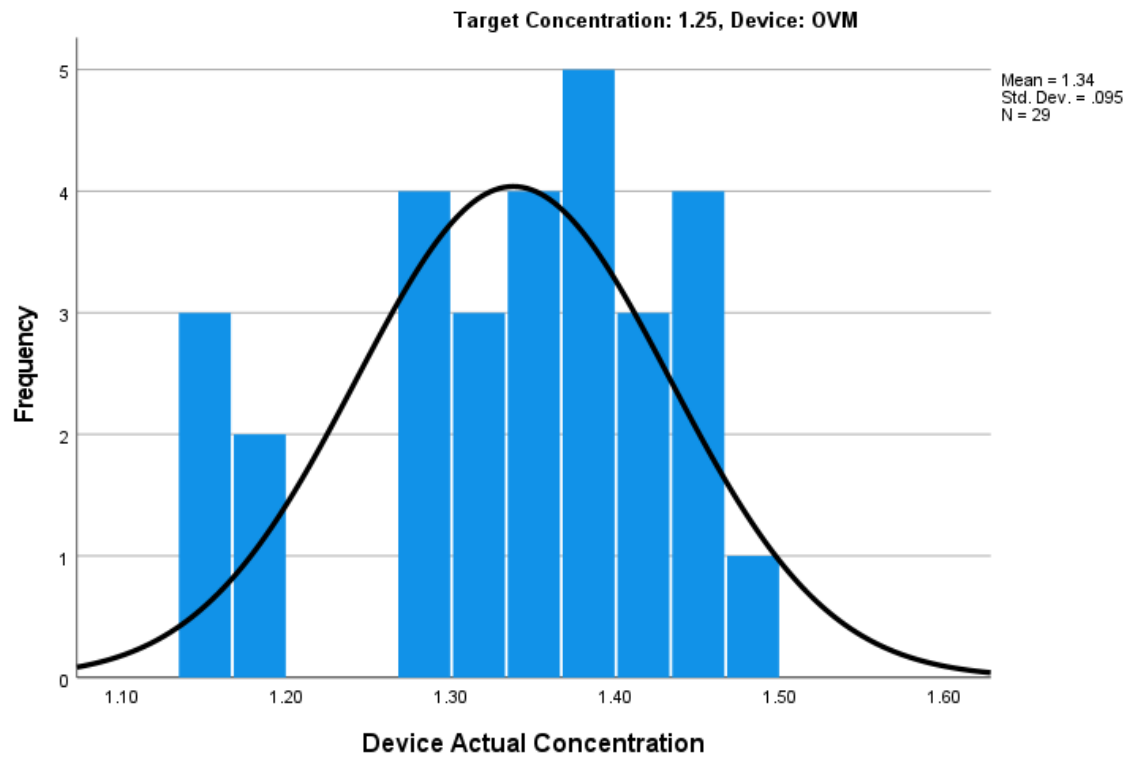


Figure 59: Scenario 2: OVM histogram showing a more defined bell curve.

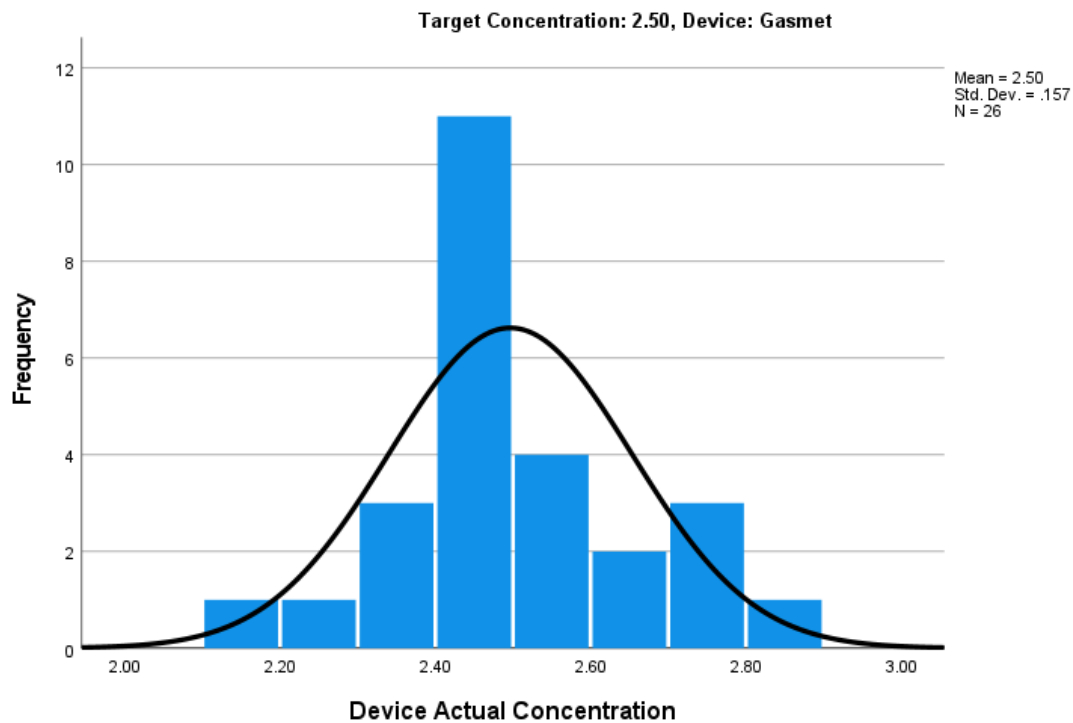


Figure 60: Scenario 3: Gasmet histogram showing a more defined bell curve.

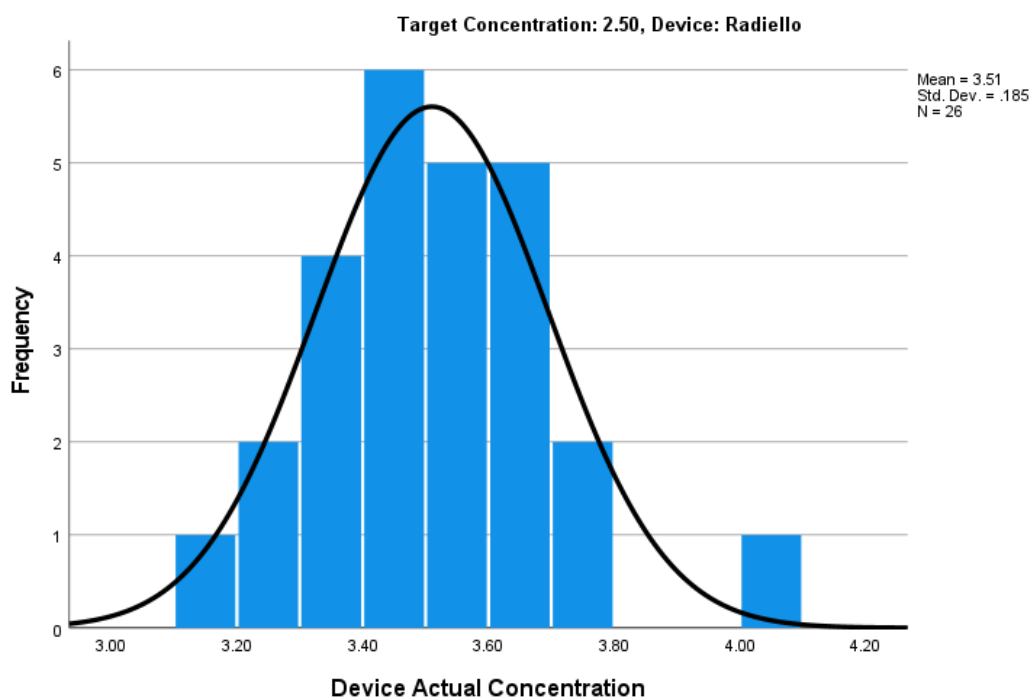


Figure 61: Scenario 3: Radiello[®] histogram showing a more defined bell curve.

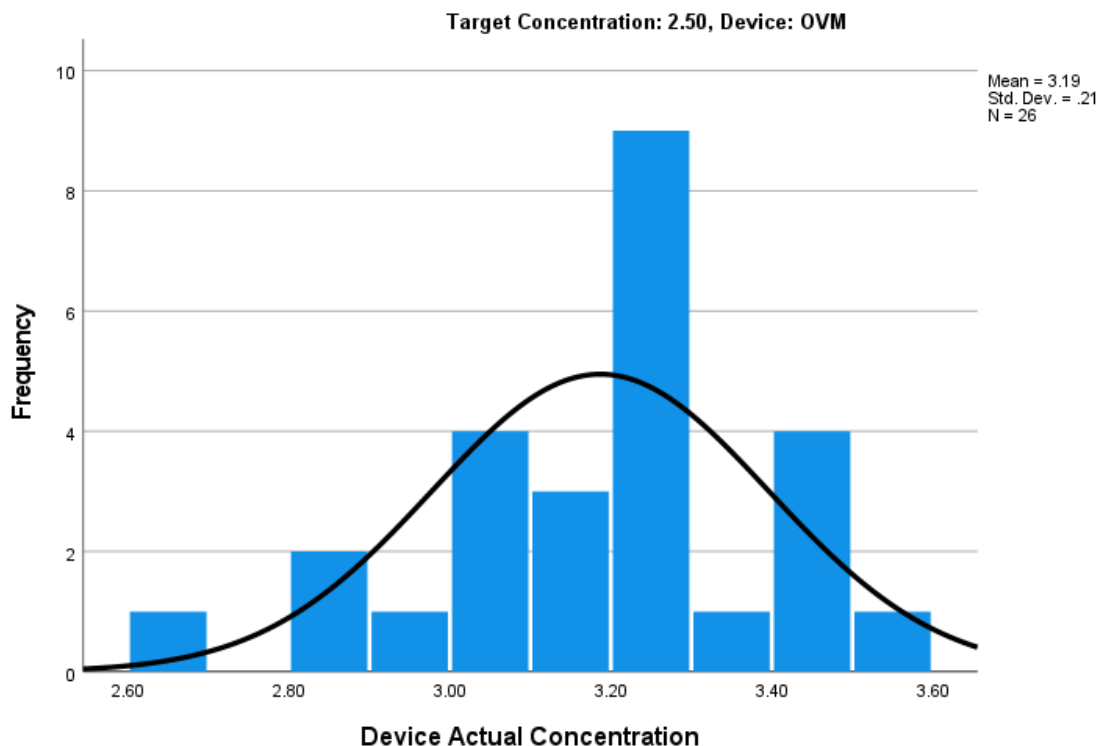


Figure 62: Scenario 3: OVM histogram showing a more defined bell curve.

4.5 DEVICE MEANS AND BOX PLOTS COMPARED TO THE REFERENCE INSTRUMENT

Appendix G gathers the mean values for each device and is compared to the reference instrument (Gasmeter DX4040) target concentration for each scenario. The box plots display each device's mean, max, min, median, first quartile, and third quartile. Lines extend out from each box to capture the range of the remaining data. Outliers were also shown as tiny circles.

At a benzene chamber concentration of 0.50 ppm (Scenario 1), the Radiello®, at a mean of 0.31 ppm, underestimated the Gasmeter's measured average concentration of 0.51 ppm (Figure 63). The relative error for the Radiello® when compared to the reference instrument at Scenario 1 was 40% (Table 16). No data was provided for the OVM for Scenario 1 because the data were censored. The limit of quantification, 0.40 µg, was not achieved due to the inability of

the OVM method to capture enough benzene mass for quantification by the analytical instrument. At a benzene chamber target concentration of 1.25 ppm (Scenario 2), the Radiello[®], at a mean of 1.81 ppm, and OVM, at a mean of 1.34 ppm, both overestimated the Gasmet's average measured concentration of 1.26 ppm (Figure 64). The OVM's average measured concentration was closer to the Gasmet's average measured concentration with a relative error of 8%, while the Radiello[®] had a relative error of 43% (Table 16). At a benzene chamber target concentration of 2.50 ppm (Scenario 3), the Radiello[®] produced a mean of 3.51 ppm, and the OVM produced a mean of 3.20 ppm, which represented overestimations of the reference instrument (Gasmet)'s average measured concentration of 2.50 ppm (Figure 65). The OVM's average measured concentration was closer to the Gasmet's average measured concentration with a relative error of 28%, while the Radiello[®] had a relative error of 41%.

The box plots also did a better job showing the slight skewness of the OVM and Gasmet data. If a distribution was skewed, the median would not lie in the middle of the box but will deviate more to one side. For scenario one, the median concentration is highest for the Gasmet and lowest for the Radiello[®]. The variation in concentration was also highest with the Radiello[®], which can be seen by how long its box plot is compared to the Gasmet. The Gasmet slightly differed in concentration at the 0.50 ppm target concentration but had a smaller skewness in its data distribution. For scenario 2, the median concentration was highest with the Radiello[®] along with a higher variation of concentrations. The OVM showed a closer median concentration relative to the Gasmet with a minor variation in its data distribution. There was slight skewness with the OVM and Gasmet concentrations at the 1.25 ppm target concentration. For scenario 3, the Radiello[®] and OVM demonstrated high median concentrations relative to the Gasmet. They also had a similar variation in the distribution of their data. There was slight skewness with the OVM and Gasmet concentrations at the 2.50 ppm target concentration.

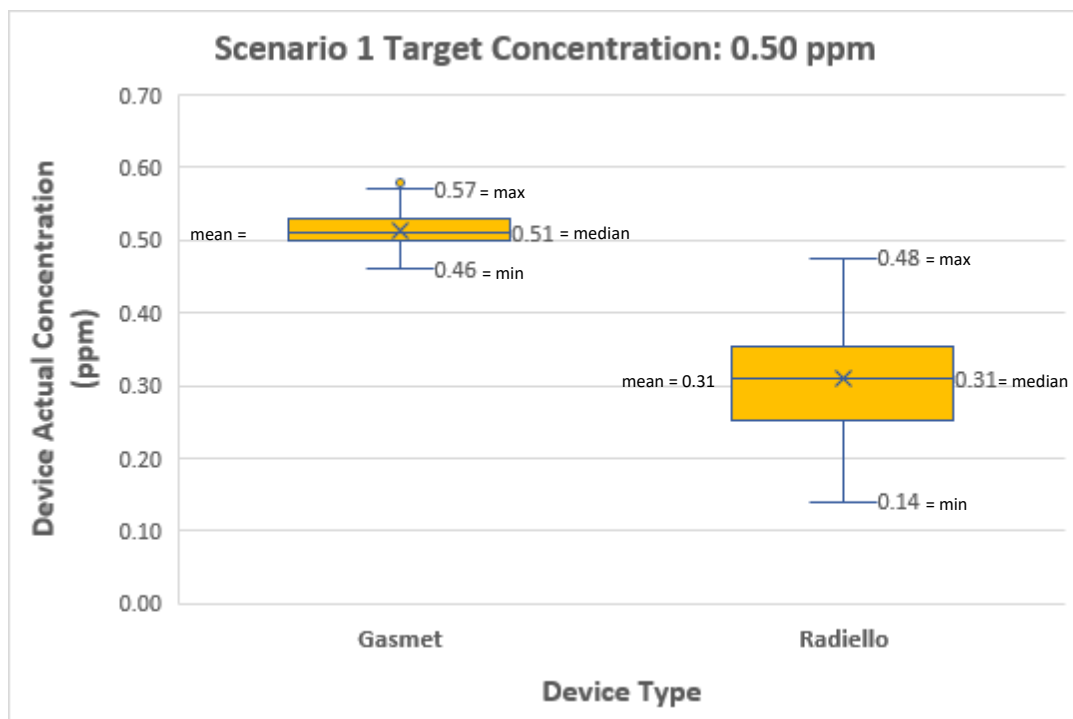


Figure 63: Scenario 1: Boxplot of the Radiello[®], compared to the reference standard (Gasmet).

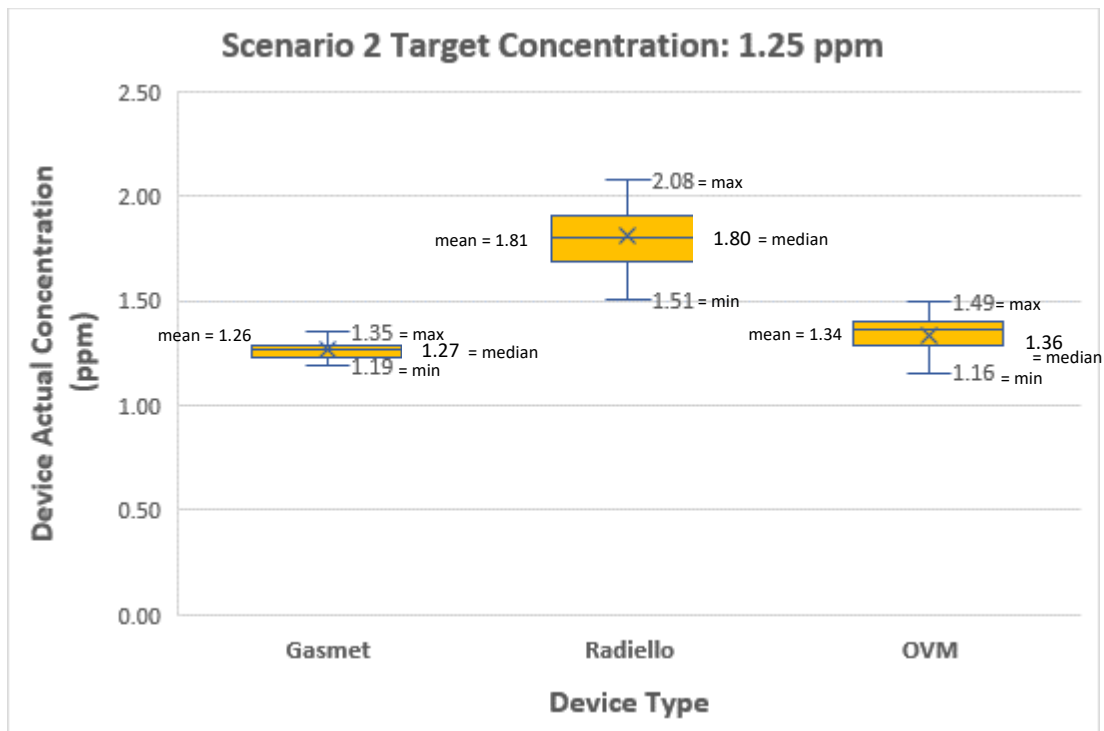


Figure 64: Scenario 2: Boxplot for each device compared to the reference standard (Gasmet).

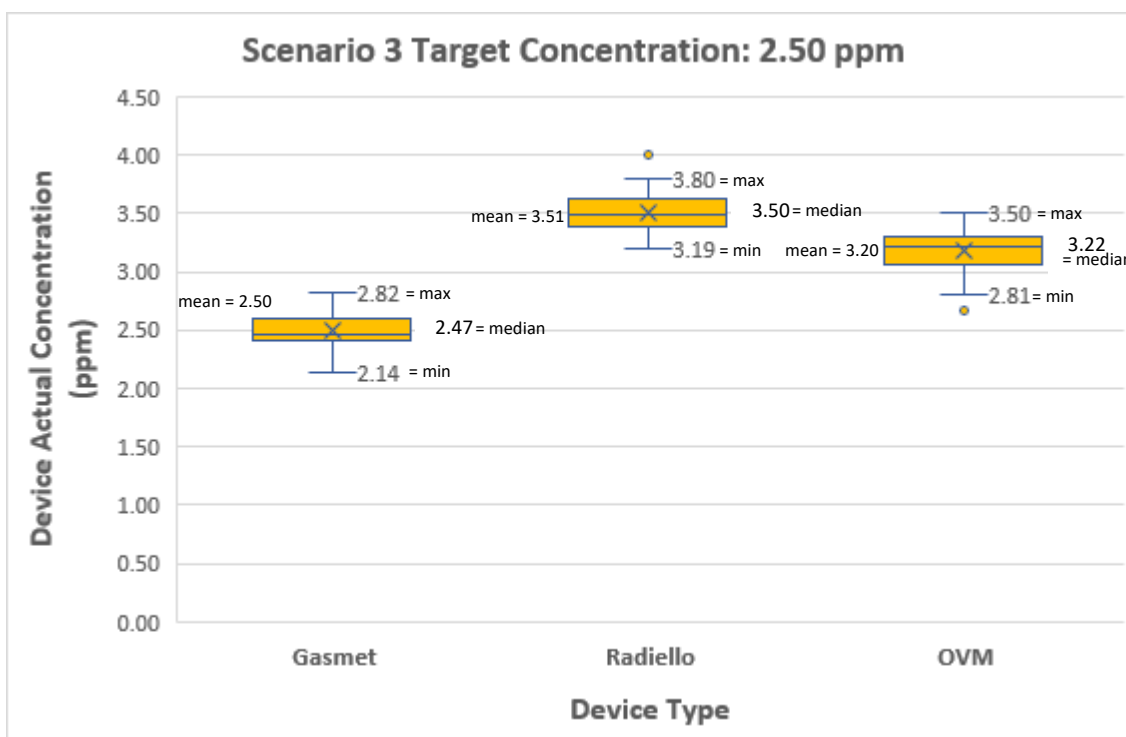


Figure 65: Scenario 3: Boxplot for each device compared to the reference standard (Gasmet).

4.6 PERCENT RELATIVE ERROR

Percent error (%) for each of the devices was calculated. An average relative error was determined by averaging all the samples for the scenario and summarized in Table 16. Appendix H includes the individually calculated relative errors for each sample.

Table 16: Summary of the percent relative error.

Gasmet - Radiello®		
Scenario	Target Concentration (ppm)	Relative Percent Error (%)
1	0.5	40
2	1.25	43
3	2.5	41
Gasmet - OVM		
Scenario	Target Concentration (ppm)	Relative Percent Error (%)
1	0.5	Not Detected
2	1.25	8
3	2.5	28

4.7 ONE-WAY ANALYSIS OF VARIANCE (ANOVA)

Before an ANOVA was conducted, several assumptions were made, including normality, sample independence, and variance equality. A Levene test was used to test the null hypothesis that the variances are equal across the three devices (Table 17). A p-value < 0.05 indicates that the assumption has been violated and variances are not equal. Results of Levene's test for Scenario 1 (0.50 ppm) and Scenario 2 (1.25 ppm) showed a p-value < 0.05 , meaning that the variances were not equal. A Welch's t-test was conducted to determine the adjusted p-value. A Welch's test assumes that the data follows a normal distribution but does not assume that the samples have the same variance. Results of Levene's test for Scenario 3 showed a p-value < 0.05 , meaning that the variances were equal across the three devices.

A one-way ANOVA was then conducted to determine significance in the overall model between the devices at the 2.50 ppm target concentration. Overall, the Welch test and Levene tests demonstrated homogeneity of variances. The associated p-values also demonstrated a statistically significant difference in the measured benzene concentrations between the three devices. A follow-up analysis was conducted with a post hoc (pairwise comparison) test to compare two means. Appendix I illustrates a flowchart to describe the Levene and Welch tests used for this study.

Table 17: Descriptive statistics at each target concentration.

Descriptive Statistics						
Target Concentration (ppm)	N	Mean (ppm)	Std. Deviation	95% Confidence Interval for Mean (ppm)		ANOVA p-value
				Lower Bound	Upper Bound	
0.5	Gasmet	30	0.51	0.03	0.50	< 0.001*
	Radiello	29	0.31	0.07	0.28	
	Total	59	0.41	0.12	0.38	
1.3	Gasmet	29	1.26	0.04	1.25	< 0.001*
	Radiello	28	1.81	0.14	1.76	
	OVM	29	1.34	0.10	1.30	
	Total	86	1.47	0.26	1.41	
2.5	Gasmet	26	2.50	0.16	2.43	< 0.001
	Radiello	26	3.51	0.19	3.44	
	OVM	26	3.19	0.21	3.10	
	Total	78	3.06	0.46	2.96	

*The mean difference is significant at the 0.05 level.

*Welch's correction applied for ANOVA

4.8 POST HOC PAIRWISE COMPARISON TEST BASED ON T STATISTIC

To compare the group means, a Sidak pairwise (post hoc) multiple comparison tests was used since it adjusted the significance level (adjusted p values) for multiple comparisons and provided tighter (more conservative) bounds than other tests. The output of this test is presented in Tables 18 and 19 and was arranged by target concentrations.

A pairwise (post hoc) comparison test was not conducted for Scenario 1 (0.50 ppm target) because at least three groups were needed for multiple comparisons. No OVM data was available for Scenario 1 because the OVM samplers failed to collect sufficient mass to achieve the analyzing laboratory instrument's limit of quantification. Results for the 1.25 and 2.50 ppm target concentrations show significance ($p < 0.05$). The p -value was below 0.05, which indicated that the two measurements were significantly different from one another.

Table 18: Post Hoc Pairwise Comparison for Scenario 2 (1.25 ppm target).

Multiple Comparisons ^a (ppm)					
Sidak					
(I) Device		Mean Difference (I-J)	p-value	95% Confidence Interval	
				Lower Bound	Upper Bound
Gasmet	Radiello	-.55 [*]	0.00	-0.61	-0.48
	OVM	-.074 [*]	0.019	-0.14	-0.01
Radiello	Gasmet	.55 [*]	0.00	0.48	0.61
	OVM	.47 [*]	0.00	0.41	0.54
OVM	Gasmet	.074 [*]	0.019	0.01	0.14
	Radiello	-.47 [*]	0.00	-0.54	-0.41

*. The mean difference is significant at the 0.05 level.

Table 19: Post Hoc Pairwise Comparison for Scenario 3 (2.50 ppm target).

Multiple Comparisons ^a (ppm)					
Sidak					
(I) Device		Mean Difference (I-J)	p-value	95% Confidence Interval	
				Lower Bound	Upper Bound
Gasmet	Radiello	-1.01 [*]	0.00	-1.14	-0.89
	OVM	-.69 [*]	0.00	-0.82	-0.57
Radiello	Gasmet	1.01 [*]	0.00	0.89	1.14
	OVM	.32 [*]	0.00	0.20	0.45
OVM	Gasmet	.69 [*]	0.00	0.57	0.82
	Radiello	-.32 [*]	0.00	-0.45	-0.20

*. The mean difference is significant at the 0.05 level.

a. Target Concentration = 2.50

4.9 BLAND-ALTMAN ANALYSIS

A Bland-Altman (B-A) analysis was used to investigate the agreement between devices for each target benzene concentration. The B-A scatter plots show the difference between the paired measurements on the Y-axis (A-B), while the X-axis represents the average of those paired measurements. Statistical limits were determined by calculating the mean and standard deviation of the differences between the two measurements. $A \pm 1.96$ standard deviation marks the limits of agreement where it is expected that 95% of the differences between the two measurement methods lie (red dashes). Points that lie above or below the mean difference line indicate a trend that the level of agreement is deviating from a perfect agreement where the average difference equals zero. Linear regression was added to show how the data overestimated or underestimated the measured benzene concentration with increasing magnitude based on the slope. A correlation coefficient was added to show the strength of the relationship between the two variables. A positive correlation indicates that the two variables move in the same direction, while a negative correlation indicates that the two variables move in opposite directions.

4.9.1 Scenario 1: Gasmet vs. Radiello® B-A Plot

Figure 66 shows the B-A plot for the performance of the Radiello® (Scenario 1) relative to the Gasmet at the lowest concentration of 0.50 ppm. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmet and the Radiello® was 0.20 ppm. Linear regression was added to show how the Radiello® underestimated the measured benzene concentrations with increasing magnitude ($y = -1.2929x + 0.7351$). A moderate negative ($R^2 = -0.54$), downhill sloping relationship exists between the two variables indicating that they tend to move in opposite directions. Data values for individual samples have been included in Appendix J.

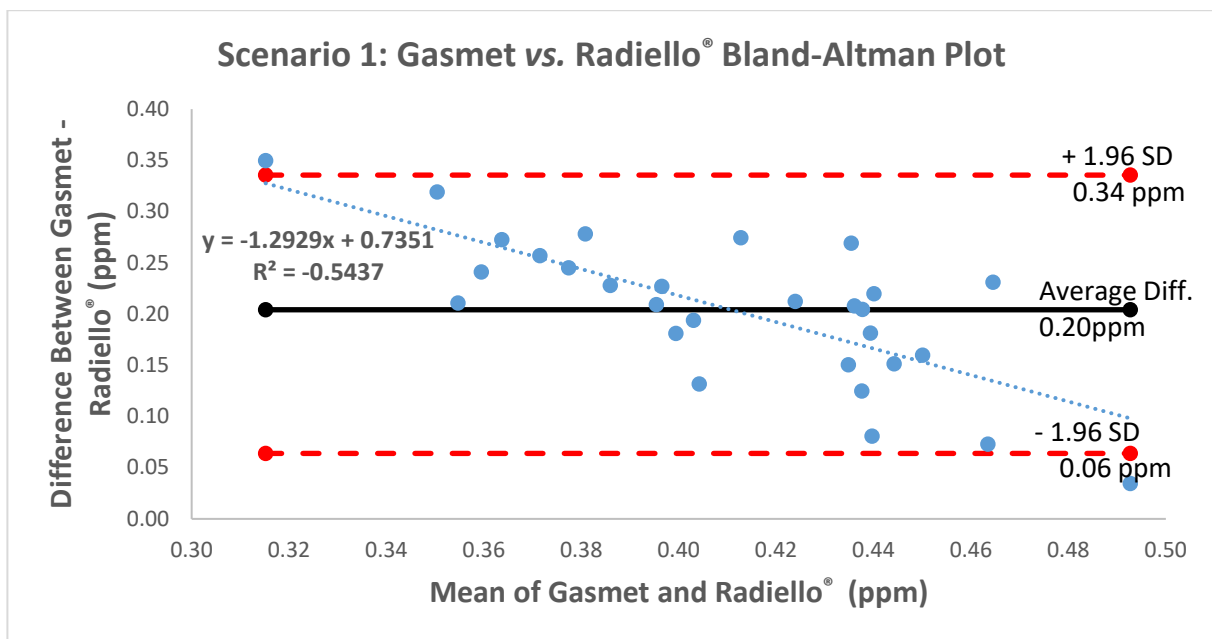


Figure 66: Scenario 1 plot of the average difference between Gasmet and Radiello®.

4.9.2 Scenario 2: Gasmeter vs. Radiello® B-A Plot

Figure 67 shows the B-A plot for the performance of the Radiello® (Scenario 2) relative to the Gasmeter at a 1.25 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmeter and the Radiello® was -0.55. Linear regression was added to show how the data overestimated the measured benzene concentrations with increasing magnitude ($y = -1.4638x + 1.706$). A strong negative ($R^2 = -0.75$) downhill sloping relationship exists between the two variables indicating that they tend to move in opposite directions. Data values for individual samples have been included in Appendix J.

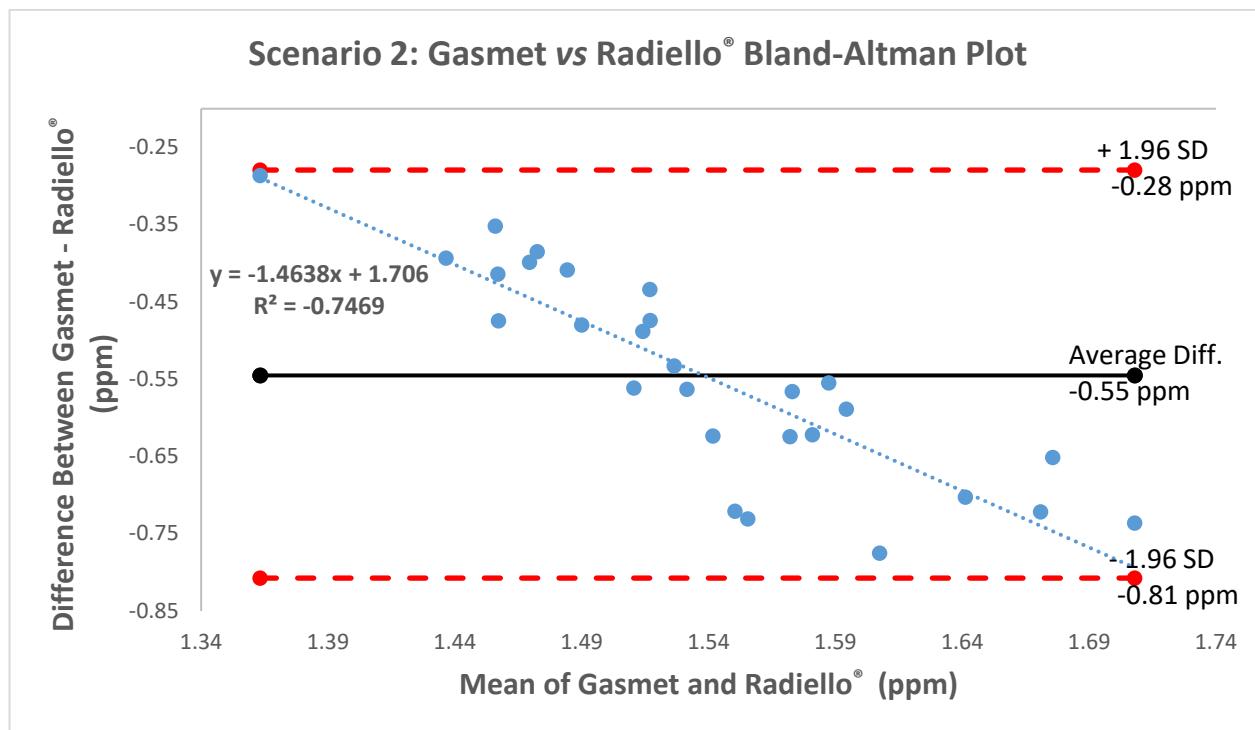


Figure 67: Scenario 2 plot of the average difference between Gasmeter and Radiello®.

4.9.3 Scenario 2: Gasmet vs. OVM B-A Plot

Figure 68 shows the B-A plot for the performance of the OVM (Scenario 2) relative to the Gasmet at a 1.25 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmet and the OVM was -0.07 ppm. Linear regression was added to show how the data slightly overestimated the measured benzene concentrations with increasing magnitude ($y = -1.2681x + 1.5751$). A moderately negative ($R^2 = -0.49$) downhill sloping relationship exists between the two variables indicating that they tend to move in opposite directions. Data values for individual samples have been included in Appendix J.

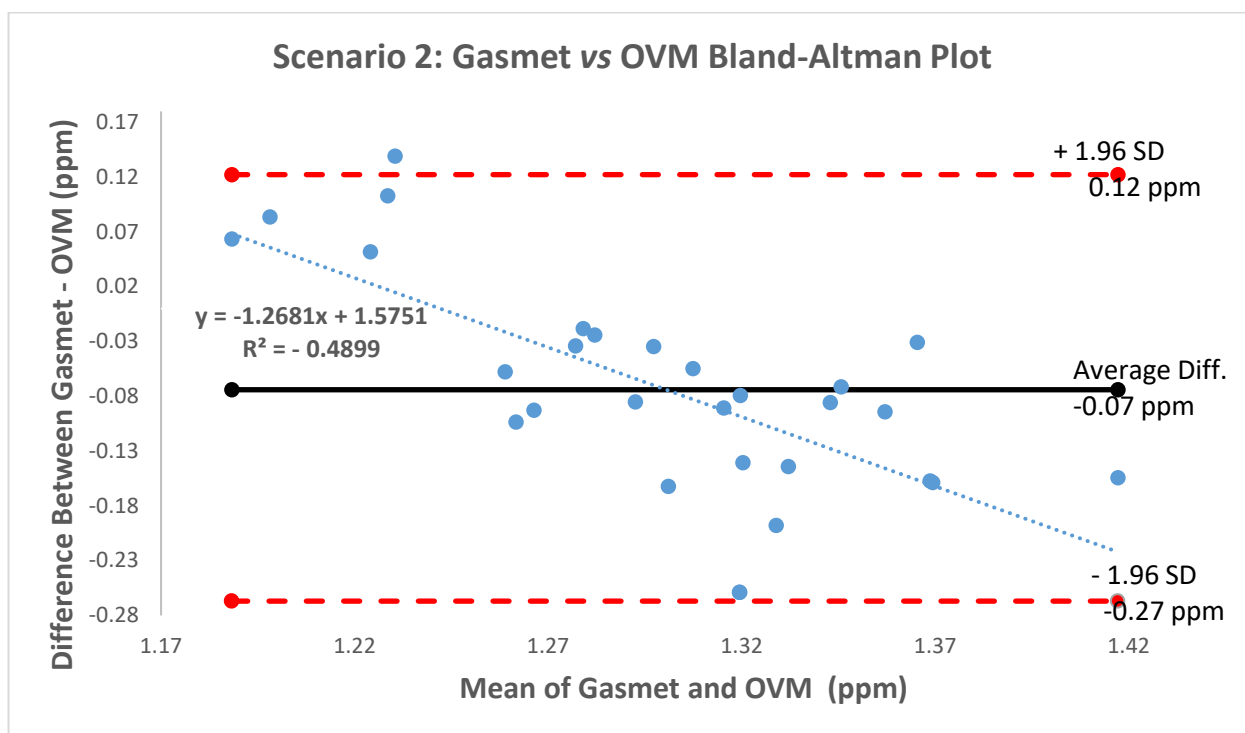


Figure 68: Scenario 2 plot of the average difference between Gasmet and OVM.

4.9.4 Scenario 2: Radiello® vs. OVM B-A Plot

Figure 69 shows the B-A plot for the performance of the Radiello® (Scenario 2) relative to the OVM at a 2.50 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmeter and the Radiello® was 0.47 ppm. Linear regression was added to show how the data overestimated the measured benzene concentrations with increasing magnitude ($y = 0.4415x - 0.2197$). A moderate positive ($R^2 = 0.44$) upward sloping relationship exists between the two variables indicating that they tend to move in the same direction. Data values for individual samples have been included in Appendix J.

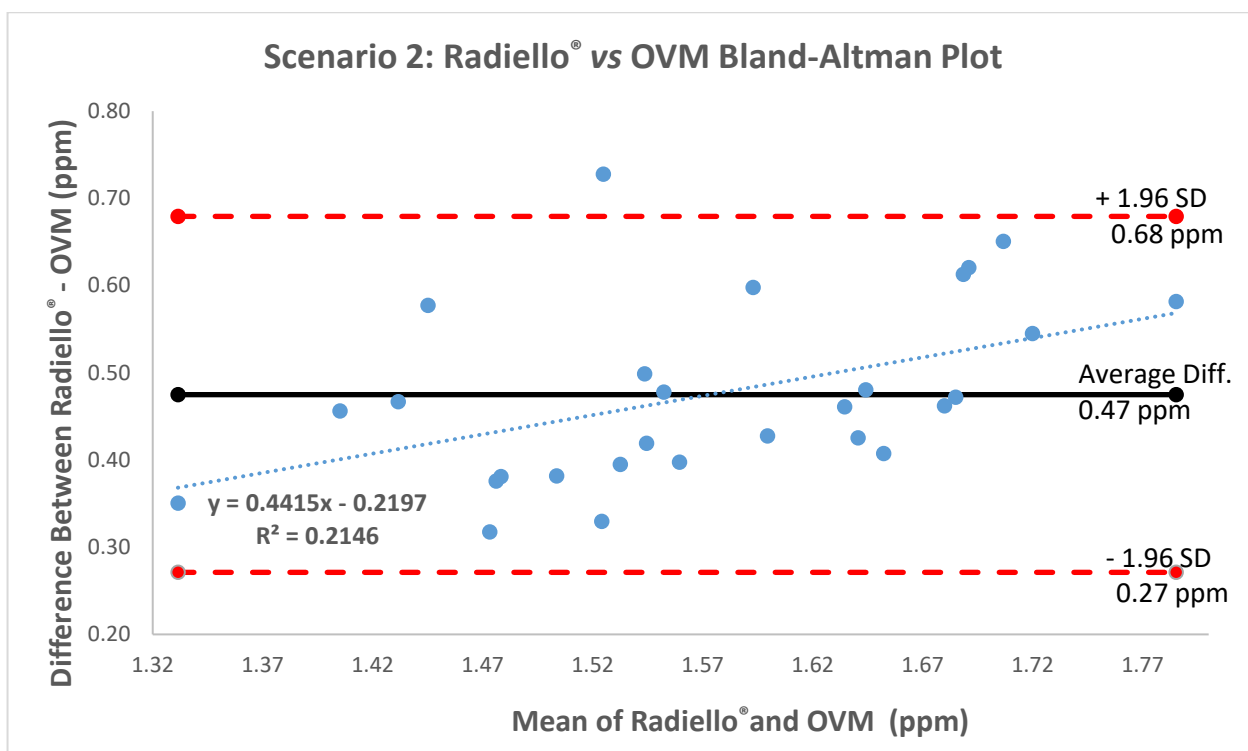


Figure 69: Scenario 2 plot of the average difference between Radiello® and OVM.

4.9.5 Scenario 3: Gasmeter vs. Radiello® B-A Plot

Figure 70 shows the B-A plot for the performance of the Radiello® (Scenario 3) relative to the Gasmeter at a 2.50 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmeter and the OVM was -1.01 ppm. Linear regression was added to show how the data overestimated the measured benzene concentrations with increasing magnitude ($y = -0.3534x + 0.0476$). A minimal linear relationship ($R^2 = -0.02$) exists, downhill sloping, between the two variables indicating that they tend to move in opposite directions very slightly. Data values for individual samples have been included in Appendix J.

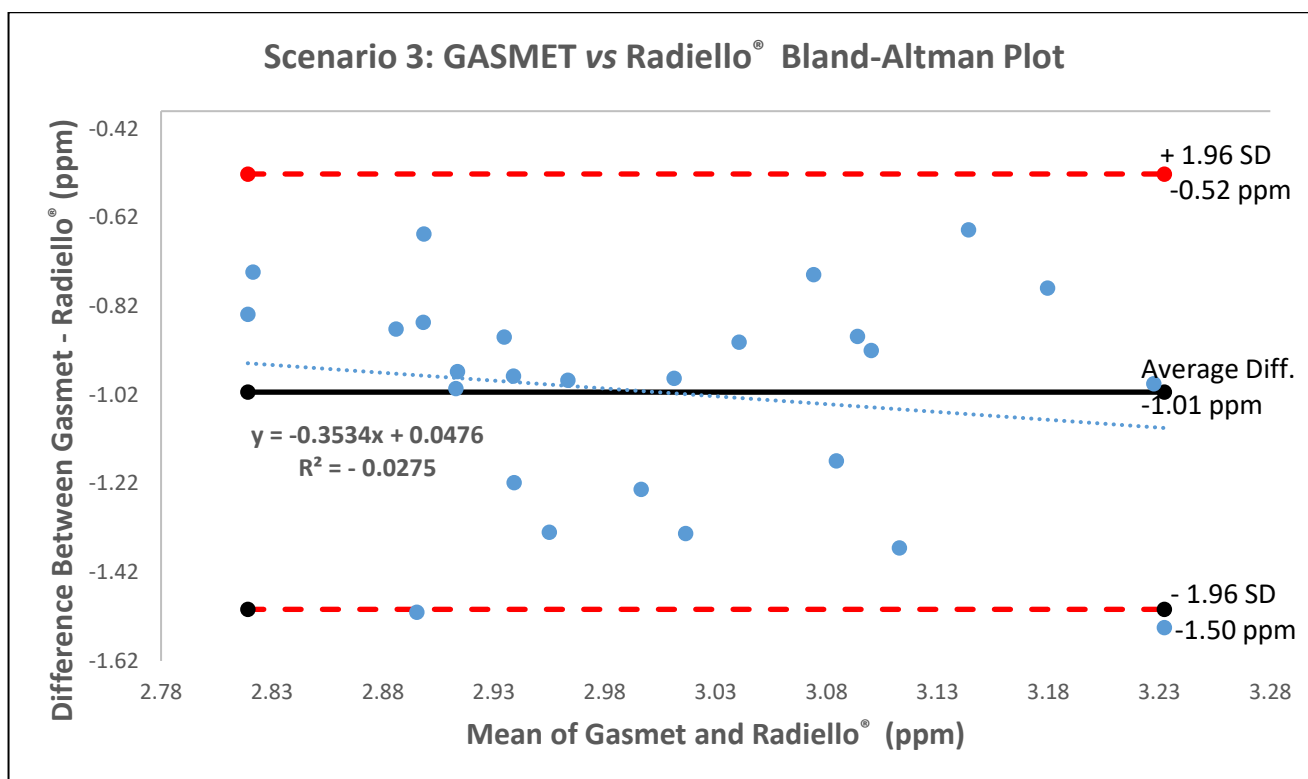


Figure 70: Scenario 3 plot of the average difference between Gasmeter and Radiello®.

4.9.6 Scenario 3: Gasmeter vs. OVM B-A Plot

Figure 71 shows the B-A plot for the performance of the OVM (Scenario 3) relative to the Gasmeter at a 2.50 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmeter and the OVM was -0.69 ppm. Linear regression was added to show how the data overestimated the measured benzene concentrations with increasing magnitude ($y = -0.5608x + 0.9033$). A minimal linear relationship ($R^2 = -0.08$) exists, downhill sloping, between the two variables indicating that they tend to move in opposite directions very slightly. Data values for individual samples have been included in Appendix J.

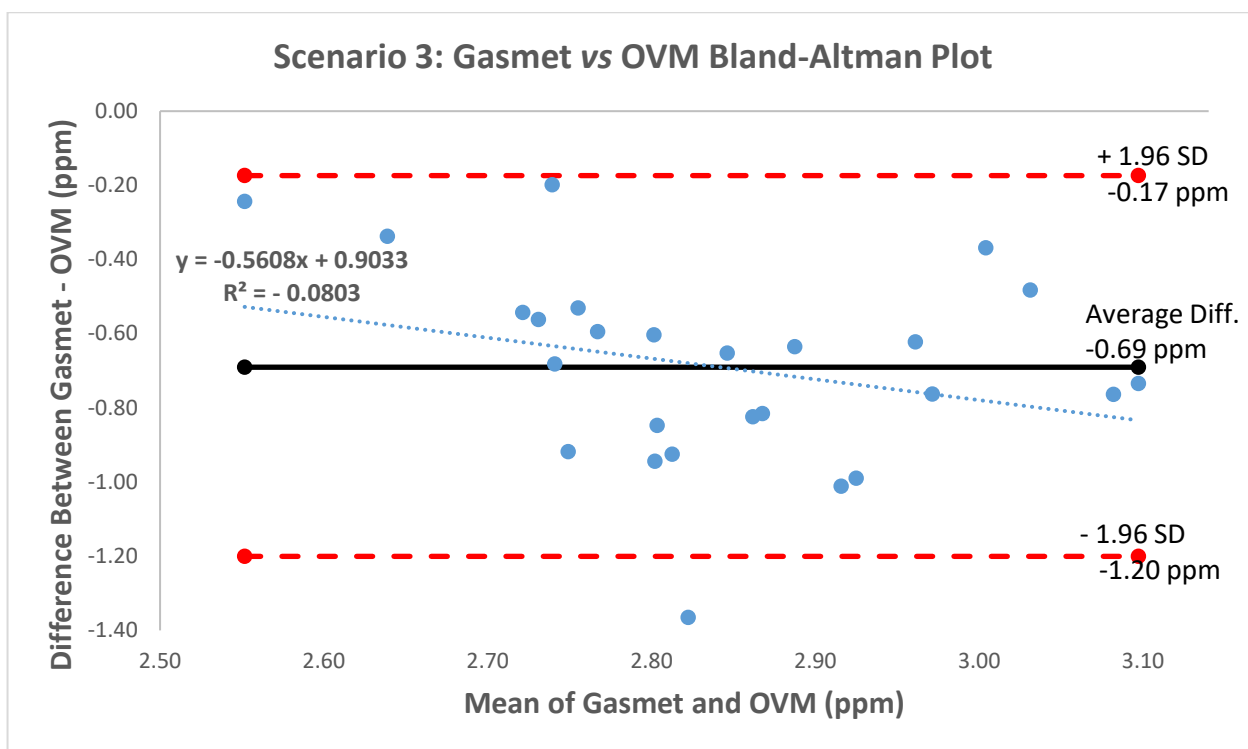


Figure 71: Scenario 3 plot of the average difference between Gasmet and OVM.

4.9.7 Scenario 3: Radiello® vs. OVM B-A Plot

Figure 72 shows the B-A plot for the performance of the Radiello® (Scenario 3) relative to the OVM at a 2.50 ppm target concentration. Greater than 95% of all differences between the two measurements lie between ± 1.96 times the data set's standard deviation. The average difference (bias) between the Gasmet and the OVM was 0.32 ppm. Linear regression was added to show how the data overestimated the measured benzene concentrations with increasing magnitude ($y = -0.1787x + 0.9217$). A minimal linear relationship ($R^2 = -0.01$) exists, downhill sloping, between the two variables indicating that they tend to move in opposite directions very slightly. Data values for individual samples have been included in Appendix J.

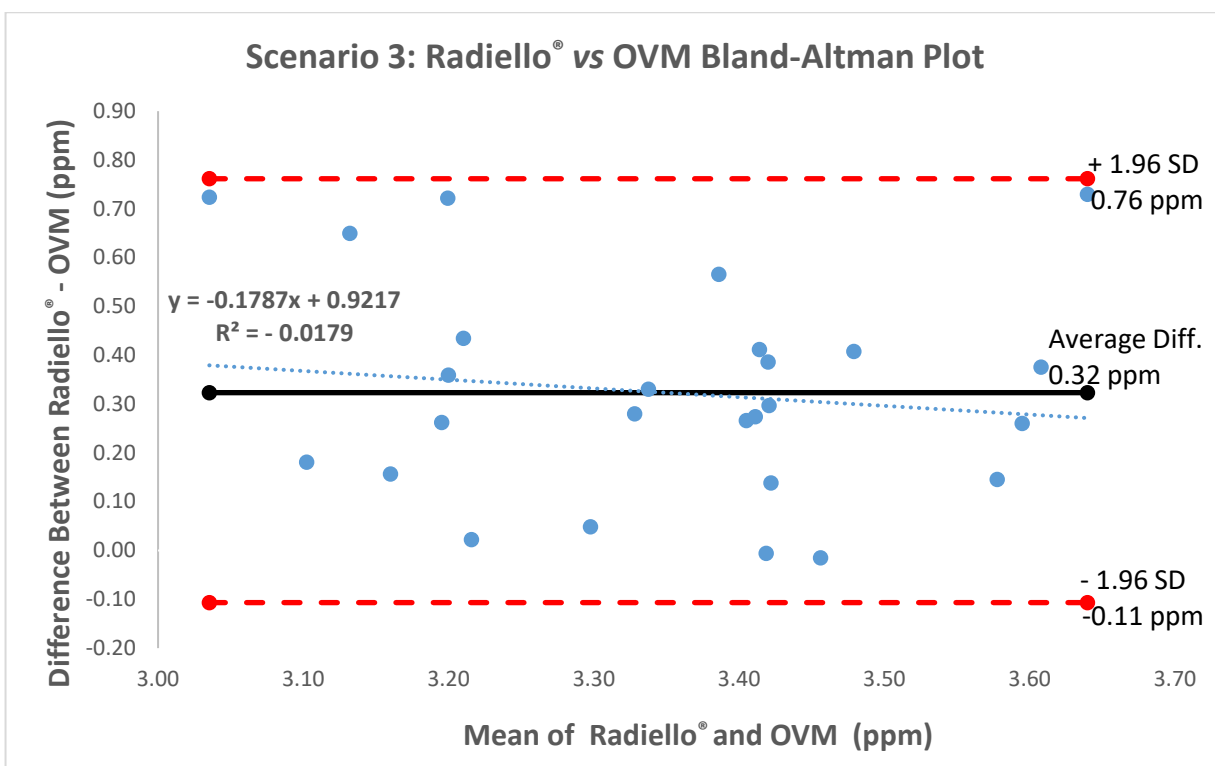


Figure 72: Scenario 3 plot of the average difference between Radiello® and OVM.

4.9.8 B-A Plots: Summary of Average Differences

Table 20 summarizes the average differences between each device type. Data values for individual samples have been included in Appendix J.

Table 20: B-A Plots: Summary of the average differences for three devices.

Gasmet - Radiello®		
Scenarios	Target Concentration (ppm)	Average Difference (ppm)
1	0.50	0.2
2	1.25	-0.55
3	2.5	-1.01

Gasmet - OVM		
Scenarios	Target Concentration (ppm)	Average Difference (ppm)
1	0.50	Not Detected
2	1.25	-0.07
3	2.5	-0.69

Radiello® - OVM		
Scenarios	Target Concentration (ppm)	Average Difference (ppm)
1	0.50	Not Detected
2	1.25	0.47
3	2.5	0.32

CHAPTER 5: DISCUSSION

5.1 COMPARISON OF RADIELLO® AND OVM TO REFERENCE INSTRUMENT

The Gasmet verified independent benzene concentrations were compared to two passive sampling devices in three different scenarios. Acceptable performance was defined with an average difference of 0.10 ppm or less (B-A Plots), a percent error (accuracy) of 30% or less, and a relative standard deviation of (precision) or 30 or less. The study found a significant difference ($p\text{-value} < 0.05$) between each pair of means. The OVM showed good agreement with the Gasmet reference with a relative error ranging from 8 to 28%. However, the OVM could not measure at the lowest benzene concentration of 0.50 ppm since the analytical method could not quantify benzene at this low concentration. This is a crucial point to consider since the 2022

ACGIH notice of intended changes is proposing a reduction of the STEL to 0.10 ppm. The OVM displayed acceptable performance at 1.25 parts per million, but performance decreased as concentrations increased. As concentrations increased, the average difference between the reference and the device increased, and the relative percent error (accuracy) also increased. This could mean the difference between complying or not since as the concentrations get larger, this device tends to overestimate the actual concentration.

Like the OVM, Radiello[®] sampler performance decreased at higher concentrations since the average difference and relative percent error increased. On the other hand, the Radiello[®] could measure the lowest target concentration of 0.50 ppm, although with a higher relative error that ranged from 40 to 43%. This could mean that this device would always tend to underestimate actual concentrations at low benzene concentrations (Scenario 1), which would be a less protective indicator of worker exposure.

5.2 CALIBRATION CURVE FOR AGILENT 7980B/5977B GC/MS

A nine-point calibration curve was used to calibrate the Agilent 7980B/5977B GC/MS. The spiked mass ranged from 233 to 5,330 ng, reflecting the expected mass that the sampler would collect during the sampling period at the concentrations of interest. Although a linear response was observed with an $R^2=0.99$, the relative error was evaluated to determine how accurate the measured values were to the actual value provided by the Gasmet. The relative error was highest when analyzing standards 1 (26%) and 2 (21%), with the percent error decreasing at the higher concentrations (Table 16). The linearity response was poor at these lower concentration standards due to the measured mass values approaching zero. This means that as you approach zero, any change can be proportionally large.

Injection-related problems could also have been a source of nonlinearity. Sample splitting was completed using the Markes Unity 2 with a 2,960:1 split ratio. A variety of different split ratios were tested to investigate the effect on the calibration curve's high and low ends. This was the best balance that could have been achieved for the extensive mass range investigated. If the split ratio were not high enough, there would not be good linearity on the top end. If the split ratio were too low, there would not be good linearity on the low end. It is possible that the split ratio was too high for the lower standards, which did not allow enough of the sample's mass to be introduced into the column for quantitative analysis. Insufficient mass introduced onto the column could have led to poor sensitivity. The analytical column used had a 0.25 mm inner diameter x 0.25 μ m film thickness which allowed for a capacity of 100 ng per component. Column capacity was utilized when determining the total split to prevent overloading. It is recommended that two different calibration curves be used for future studies. One calibration curve should utilize a lower split ratio that would be more effective at the lower masses, while the other should utilize a higher split ratio that would be more effective at the higher masses.

5.3 GASMET DX4040 REFERENCE INSTRUMENT

Several pilot studies were conducted using the Gasmet to monitor BTEX vapor concentrations in the chamber. Results recorded by the Gasmet during the pilot studies showed values that did not agree with the theoretically determined concentrations. The default wavelength values associated with each analysis area were used during this time. Theoretically, when the spectrum of an individual chemical is evaluated, it may show multiple peaks referred to as the wavelength numbers, and not all of the peaks will be useful for analysis.

During the pilot studies, it was also discovered that the Gasmet detected residual benzene readings of about 0.40 ppm of benzene while the syringe pump was in the off position. The

Gasmet was used to monitor these readings until zero ppm of benzene was achieved. An investigation revealed off-gassing benzene that had been absorbed by the PVC tubing connected from the Gasmet to the probe inlet. Benzene was also off-gassing from an internal PVC filter inside the Gasmet probe. The probe's filter was removed to prevent this reoccurrence, and PTFE (Teflon) hosing was installed. The material of the chamber also allowed benzene to be absorbed into its plastic material. Methods were adjusted to flush the chamber with UHP nitrogen for 15 minutes before taking samples. After changes in the approach were incorporated, several follow-up analyses were conducted, showing blank measurements for benzene.

5.4 SYRINGE PUMP INJECTION RATES

Achieving a sufficiently high injection rate was critical for producing stable chamber concentrations. Several options were considered to produce this injection rate, such as using a smaller syringe (0.5 μ L-50 mL), syringe material, adjusting the target concentration, and/or adding additional chemicals.

In light of the findings by Nelson (1992), who observed that when producing low injection rates (0.01 μ L/min), a syringe made of glass allowed benzene to escape, leading to high delivery errors, a gas-tight Hamilton 1000 Series Teflon-tipped plunger syringe was used (41). The syringe pump's mounting position in horizontal or vertical did not influence its performance. The syringe needed to be securely clamped into position so that the driving arm made firm contact with the plunger. It was challenging to achieve this firm contact for the smaller-sized syringes (0.5 μ L-10 mL), leading to significant delivery errors. An aluminum backing plate was used for the 25 mL and 50 mL Hamilton gas-tight syringes to help achieve firm contact (Figure 10).

Determining the appropriately sized syringe also required several pilot studies. The flow stability of a syringe pump is determined by the minimal movement of its motor. Since the movement of the piston and the volume of liquid injected from the syringe are correlated, a minimum movement of the piston results in a minimal injected volume. This minimal injected volume is also proportional to syringe diameter. A discrete phenomenon appears as oscillations or pulses at these low flow rates due to the motor step. Motor stepping allows for more stable positions (steps) per revolution, providing more torque. Therefore, the performance of the syringe becomes critical at a minimum flow rate of around 0.10 μL (41). A visual example of these oscillations at the low flow rate can best be described in Figure 73 (24). These examples used a 5mL syringe but varied the syringe's flow (injection) rate. At a flow rate of 0.10 μL , large oscillations were observed compared to a flow rate of 5.0 μL . These oscillations equate to varying chamber concentrations discovered during the pilot studies. Several changes were made to adjust the injection rate by choosing a different sized syringe, creating a mixture of BTEX, and increasing my lowest target concentration of benzene to 0.50 ppm.

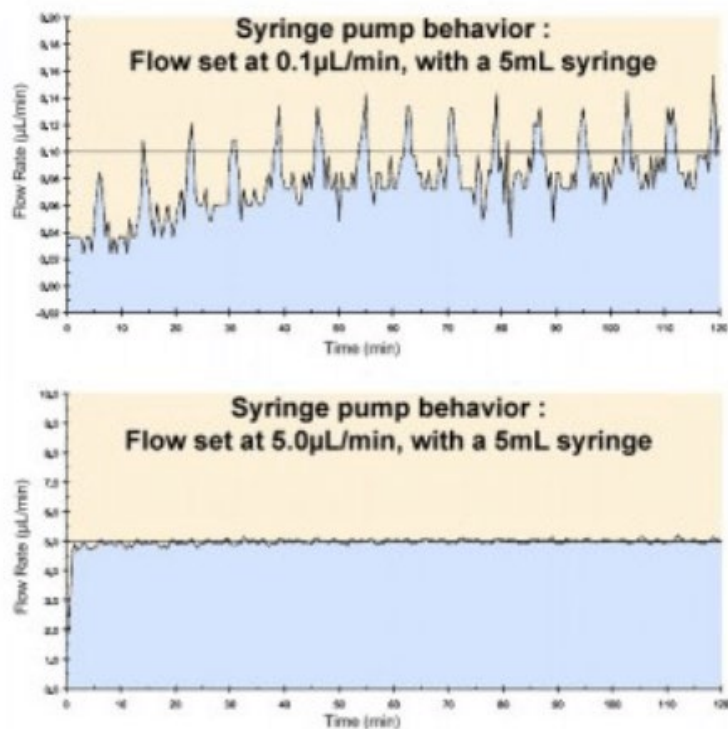


Figure 73: Syringe Pump Behavior with an adjusted flow rate using a 5 mL syringe (41).

5.5 STATISTICAL TESTS

Since an underlying assumption for many parametric statistical tests is that the data reasonably approximate a normal distribution, two statistical tests for normality were performed using SPSS: the Kolmogorov-Smirnov and Shapiro-Wilk tests. Both tests indicated p-values greater than 0.05, meaning that the data was normally distributed.

Histograms were included to provide a graphical representation of how the sample values were distributed in the data. The data showed a common bell-shaped curve pattern representing a normal distribution. Skewness values ranged from -0.68 to 0.51 across the three scenarios for all devices. A zero skewness means that the data is perfectly symmetrical as a reference. A skewness between -0.50 to 0.50 means that the distribution is approximately symmetrical. Boxplots were

also included in this study to help visualize the dispersion of the data across the three devices per scenario. These dispersion results were similar to what the histograms showed.

Several assumptions were made, which were verified before leading up to the one-way ANOVA. Some of these assumptions were that the samples would be normally distributed, the samples be independent of each other (based on study design), and homogeneity of variance (equal variance among the groups). A Levene's test effectively showed whether the variance was equal across the three devices by providing a p-value > 0.05 for Scenario 3 ($p = 0.405$). Since this scenario didn't identify a significant difference between the variances, a one-way ANOVA was used to investigate whether there was a significant difference between the sample means. The ANOVA showed a significant difference between the means ($p < 0.05$). A Sidak post-hoc test showed that all three sample means differed significantly ($p < 0.05$).

The Bland Altman plots provided a compelling visual display of these differences. The OVM showed good agreement with the Gasmeter reference. However, the OVM could not measure at the lowest benzene concentration of 0.50 ppm. The OVM also displayed acceptable performance at 1.25 ppm, but performance decreased as concentrations increased. Conversely, the Radiello[®] could measure the lowest target concentration of 0.50 ppm, although with a higher relative error that ranged from 40-to 43%. Like the OVM, sampler performance decreased at higher concentrations which can be seen by the negative trendline in the B-A plots (showing that the agreement decreases as concentration increases).

5.6 STUDY LIMITATIONS

This study was limited to only investigating one temperature and one relative humidity primarily due to budget constraints associated with obtaining enough OVMs to support additional testing parameters. Future work could also investigate benzene stability on the Radiello[®]

Carbograph 4 sorbent in more extreme temperatures that approximate temperatures in maritime ports such as Alaska (-35°C/77% RH) and Saipan (32°C/80% RH).

Several limitations were found in creating the calibration curve for the Agilent 7980B/5988B GC/MS. Errors in preparing the calibration standards are possible. Standards were prepared in 5 mL volumetric flasks with benzene in methanol. It is possible that evaporation of benzene could have occurred and affected standards 1 and 2 since such a small volume (microliters) of benzene was used to make those standards. It is also possible that there could have been user error when measuring benzene with the pipettes. This pipette error could have been attributed to not achieving optimum immersion depth or when the liquid was aspirated and dispensed.

Errors in preparing the spiked samples are also possible. Thermal desorption tubes with the Carbograph 4 sorbent were spiked with 1 microliter of each standard before being analyzed. It is possible that human error in the syringe technique could have been introduced when measuring this 1 microliter sample. Contamination of the standard between spiked samples was not likely since contamination was controlled by ensuring the syringe was clean and free of any residues. A cleaning process was used, with the final step requiring acetone. A Hamilton syringe cleaner was used to boil off any remaining acetone before the syringe was used to collect the following standard.

Initially, a stable target concentration of 0.25 ppm could not be achieved due to instrumentation limitations with the syringe pump. Future studies investigating the proposed benzene ACGIH TLV of 0.02 ppm or STEL of 0.10 ppm should consider other methods such as diffusion through tubes or a pressure-driven flow controller to achieve these very low target concentrations. This project was also limited to one reference instrument. It is recommended that

future studies use at least two reference instruments to verify chamber concentrations. If the proposed 2022 ACGIH TLVs or STELs are investigated, the Gasmeter DX4040 should not be used since it cannot detect 0.02 ppm.

Optimizing the Gasmeter reference instrument's analysis areas was a limitation of this study. Several in-house pilot studies were conducted, requiring the data to be sent to Gasmeter Technologies Oy where they further evaluated these wavelength numbers to select stronger bands that would improve accuracy and detection of the smaller benzene concentrations. A significant concern during these pilot studies was peak overlap since some of the BTEX chemicals show absorption of IR radiation at very similar wavelength numbers. For instance, if there were a BTEX component with low absorbance and strong absorbance from a different component of BTEX, the absorption by the component with stronger absorption at that wavenumber would obscure the absorption by the other component. Substantial overlap over the entire analysis areas could lead to cross interferences effects (bias). Gasmeter Technologies Oy reviewed and modified these analysis areas and selected peaks with as low intensity of overlapping components.

Several possibilities could explain why the Radiello[®] underestimated the target concentration of 0.50 ppm. During an overhaul of the Markes Unity 2, which is responsible for thermally desorbing the analytes trapped onto the sorbent, it was discovered that a fitting connecting the transfer line from the Markes Unity 2 to the GC/MS was not performing as intended. This could have led to a loss of sample, which can explain why the results showed an underestimation of the 0.50 ppm target concentration.

CHAPTER 6: CONCLUSION/FUTURE STUDIES

6.1 CONCLUSION AND RECOMMENDATIONS

Benzene is a volatile organic compound found in everyday consumer products, and research have shown no safe exposure level to it. Characterizing a maritime worker's exposure to benzene by combining passive sampling with thermal desorption could be an effective tool that could save lives. With passive sampling, the radial diffusive sampler offers the best option for low to high concentrations with short duration sampling since the radial design allows for a sizeable diffusive area relative to the adsorbing surface while still maintaining a small diffusive surface between the diffusive membrane and the adsorbent (15; 48). They also feature several desirable properties which could make them very effective in the field, such as intrinsic safety, ease of use, and the minimal training required for both workers who wear them and the technicians who perform the sampling. While more costly initially, the Radiello® sampler can be analyzed using thermal desorption, offering higher sensitivity and the ability for the sorbent to be re-used up to 200 times.

This study determined the level of agreement, precision and accuracy between two passive samplers when exposed to low benzene concentrations and a 15-minute sampling time. Although the OVM showed the best level of agreement in Scenarios 2 (1.25 ppm) and 3 (2.50 ppm), the OVM analytical method could not quantify benzene at the lowest benzene target concentration at Scenario 1 (0.50 ppm). The Radiello® was able to quantify benzene in all scenarios but with a lesser level of agreement and 40% relative error. Sample loss due to an instrumentation leak could be a reason for the high relative error makes this study inconclusive. Due to the OVMs lower uptake rate and solvent-based analysis, it is not a viable option for

sampling low concentrations of benzene over a short exposure period for comparison to the recently proposed short-term exposure limit of 0.10 ppm.

At this point, no recommendation can be made to the Coast Guard for the deployment of the Radiello® to determine short-term personal exposures to benzene. It is recommended that a future study reevaluate its performance at the proposed STEL of 0.10 ppm and a greater variety of temperatures and relative humidity levels that Coast Guard inspectors encounter in the field. Future studies should use two different reference instruments to verify and monitor chamber concentrations.

Studies investigating benzene's proposed ACGIH TWA and STEL (0.02 ppm and 0.10 ppm, respectively) should utilize another type of reference instrument since these values would fall outside the Gasmeter DX4040's limit of detection. When analyzing the proposed benzene concentrations, two calibration curves should be created to cover the lower masses more accurately at one split ratio and another at the higher masses with a second split ratio.

It is also recommended that future studies seeking to produce low benzene concentrations in a lab-based setting should use other methods such as diffusion through tubes or a pressure-driven flow controller. Diffusion methods allow the concentration to be controlled by adjusting the flow rate of the primary or secondary diluent gas. With a pressure-driven-flow controller, gas pressure is delivered to a flow controller, which feeds into the sealed reservoir containing benzene. The pressure created in the sealed reservoir would push benzene into the solvent vapor generator. Appendix K shows the performance of three different types of instruments to compare flow rate versus time (24).

REFERENCES

1. Aalborg Instruments & Controls Inc. 2019. Operating Manual GFM Mass Flow Meters. p. 40. Orangeburg, NY
2. Agilent Technologies Inc. 2013. Agilent 5977 Series MSD System Concepts Guide p. 66. Santa Clara, CA
3. Agilent Technologies Inc. 2019. Agilent 5977B Series MSD Troubleshooting and Maintenance Manual. p. 242. Santa Clara, CA
4. American Conference of Governmental Industrial Hygienists. 2019. 2019 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. p. 282. Cincinnati, OH: ACGIH
5. American Conference of Governmental Industrial Hygienists. 2022. *Introduction to the Chemical Substances TLVs®*. <https://www.acgih.org/science/tlv-bei-guidelines/tlv-chemical-substances-introduction/>
6. Andrews R, O'Connor PF. 2020. *NIOSH Manual of Analytical Methods (NMAM), 5th Edition*. National Institute for Occupational Safety and Health. 935 pp.
7. Assay Technology. 2011. Operating Manual Miller Nelson Model HCS-501 Flow-Temperature-Humidity Control System. Livermore, CA
8. Assay Technology. 2018. ChemDisk Monitor for Organic Vapors Technical Insert p. 1
9. Assay Technology. 2018. Title. Volume:In press
10. Assay Technology. 2018. Operating Manual Miller Nelson Model HCS-501 Flow-Temperature- Humidity Control System. p. 41. CA

11. Ballesta P, Grandesso E, Field R, Cabrerizo A. 2016. Validation and modeling of a novel diffusive sampler for determining concentrations of volatile organic compounds in air. *Analytica Chimica Acta* 908:11
12. Baur X, Budnik LT, Zhao Z, Bratveit M, Djurhuus R, et al. 2015. Health risks in international container and bulk cargo transport due to volatile toxic compounds. *Journal of Occupational Medicine and Toxicology* 10:19
13. Baur X, Poschadel B, Budnik LT. 2010. High frequency of fumigants and other toxic gases in imported freight containers--an underestimated occupational and community health risk. *Journal of Occupational Environmental Medicine* 67:207-12
14. Brown RH. 1993. The use of diffusive samplers for monitoring of ambient air (Technical Report). *Pure and applied chemistry* 65:1859-74
15. Bruno P, Caputi M, Caselli M, de Gennaro G, de Rienzo M. 2005. Reliability of a BTEX radial diffusive sampler for thermal desorption: field measurements. *Atmospheric environment (1994)* 39:1347-55
16. Budnik LT, Austel N, Gadau S, Kloth S, Schubert J, et al. 2017. Experimental outgassing of toxic chemicals to simulate the characteristics of hazards tainting globally shipped products. *PLoS One* 12:e0177363-e
17. C.R. Manning. 2019. Assay Technology: Evaluation of ChemDisk Organic Vapor Samplers. p. 12: Assay Technology
18. Centro di Ricerche Ambientali. 2019. Radiello User Manual 2019. ed. ICS Maugeri, p. 59. Italy
19. Cocheo V, Boaretto C, Sacco P. 1996. High Uptake Rate Radial Diffusive Sampler Suitable for Both Solvent and Thermal Desorption. *American Industrial Hygiene Association journal* 57:897-904

20. Cousins & Sears LLC. 2017. HTP.xw User Guide. p. 2. New York: SensorPush
21. Daniel WW, Cross CL. 2019. *Biostatistics : a foundation for analysis in the health sciences*. Hoboken, NJ: Wiley
22. Department of Homeland Security. 2019. *Cargo Security and Examinations*.
<https://www.cbp.gov/border-security/ports-entry/cargo-security>
23. Digi-Sense. 2021. User Manual Digi-Sense Thermohygrometer Indicator with NIST-Traceable Calibration Model 20250-30. p. 8: Digi-Sense
24. Elveflow. 2022. *Syringe Pumps and Microfluidics*.
<https://www.elveflow.com/microfluidic-reviews/microfluidic-flow-control/syringe-pumps-and-microfluidics/>
25. GASMET Technologies. 2016. GASMET White Paper FTIR Gas Analysis p. 8. Helsinki, Finland: GASMET Technologies
26. Gorecki T, Namiesnik J. 2002. Passive sampling. *TrAC, Trends in analytical chemistry (Regular ed.)* 21:276-91
27. Hamilton Company. 2017. Hamilton Syringe Care and Use Guide. Reno, NV
28. Harvard Apparatus. 2012. Pump 11 Elite & Pump 11 Pico Plus Elite User's Manual. p. 70. Massachusetts: Harvard Apparatus, Inc.
29. Infante PF. 2002. Benzene: an historical perspective on the American and European occupational setting. *Late lessons from early warnings: the precautionary principle 1896–2000*:38-51
30. International Agency For Research On Cancer. 2000. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. p. 563. Lyon, France: World Health Organization

31. International Agency For Research On Cancer. 2018. Benzene. p. 104. Lyon, France: World Health Organization
32. Jacobs W, Dubois D, Aerts D, Declerck P, Stranger M, et al. 2010. Monitoring of some major volatile organic compounds on board of chemical tankers. *Journal of Maritime Research* 7:20
33. Markes International. 2019. Calibration Solution Loading Rig. 4:16
34. Markes International. 2021. Empty Sorbent Tubes. United Kingdom: Markes International
35. Markes International. 2021. Gauze Retaining Springs. United Kingdom: Markes International
36. Markes International. 2016. Getting more out of your GC using thermal desorption. p. <https://youtu.be/TP9YcZcPs3Y>. youtube.com
37. Markes International. 2021. TubeMate Tool. United Kingdom: Markes International
38. McKernan JL, Grosse DW, Truesdale RS, Hayes HC, Dawson HE, et al. Passive Samplers for Investigations of Air Quality: Method Description, Implementation, and Comparison to Alternative Sampling Methods, 2015:
39. Miller-Nelson. 2011. Title. Volume:In press
40. Navy and Marine Corps Public Health Center. 2019. Industrial Hygiene Field Operations Manual. ed. Department of the Navy. Portsmouth, VA
41. Nelson GO. 1992. *Gas Mixtures: Preparation and Control*. Boca Raton, FL: CRC Press LLC. 294 pp.

42. Nilsson RI, Nordlinder R, Hörte LG, Järholm B. 1998. Leukaemia, lymphoma, and multiple myeloma in seamen on tankers. *Occupational and Environmental Medicine* 55:517-21
43. Pengelly I, Brown VM. 2019. A New Method for Workplace Monitoring of Airborne Diacetyl and 2,3-Pentanedione Using Thermal Desorption Tubes and Gas Chromatography-Mass Spectrometry. *Ann Work Expo Health* 63:407-14
44. Prezant B. 2012. Hazard Surveillance: Residual Chemicals in Shipping Containers. Unpublished
45. Ramírez N, Cuadras A, Rovira E, Borrull F, Marcé RM. 2010. Comparative study of solvent extraction and thermal desorption methods for determining a wide range of volatile organic compounds in ambient air. *Talanta* 82:719-27
46. Risepro. 2021. Risepro HT-9815 Thermometer Thermocouple Manual. p. 1. United States: Risepro
47. Snyder R. 1984. *The Benzene Problem in Historical Perspective*. pp 692-699. Piscataway, New Jersey Society of Toxicology
48. Stenerson KK, Desorcie J, Schultz K, Buchanan M. 2011. Benefits of Radiello Passive Sampling Devices. Sigma-Aldrich
49. Svedberg U, Johanson G. 2013. Work Inside Ocean Freight Containers—Personal Exposure to Off-Gassing Chemicals. *The Annals of Occupational Hygiene* 57:1128-37
50. Svedberg U, Johanson G. 2017. Occurrence of Fumigants and Hazardous Off-gassing Chemicals in Shipping Containers Arriving in Sweden. *Annals of Work Exposures and Health* 61:195-206

51. The American Industrial Hygiene Association. 2019. Important Instrumentation and Methods for the Detection of Chemicals in the Field. ed. P Smith, Cook, G., p. 290. Falls Church, Virginia: American Industrial Hygiene Association
52. The Madison Group. 2020. Back to Basics: Fourier Transform Infrared Spectroscopy. p. https://youtu.be/4WEK_M0V3uA. youtube.com
53. U.S. Coast Guard. 2020. Coast Guard Regulated Facility Compliance Program COMDTINST M166600.10. ed. DoH Security, p. 110. Washington D.C.
54. US Energy Information Administration. 2020. Petroleum Supply Annual, Volume 2.
55. Višnja M, Nenad G, Jan S, Diane E, Smilja K, et al. 2021. Assessment of Occupational Exposure to BTEX in a Petrochemical Plant via Urinary Biomarkers. *Sustainability (Basel, Switzerland)* 13:7178
56. Wilbur S, Keith S, Faroon O, Wohlers D, Stickney J, et al. 2007. Toxicological Profile for Benzene. ed. PHS US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, p. 438
57. Zefon International. 2021. *Passive vs. Active Air Sampling* <https://www.zefon.com/passive-vs-active-air-sampling>

APPENDIX A: SUMMARY OF THEORETICAL INJECTION RATES

Summary of the theoretical injection rates used for Scenarios 1, 2, and 3.

Theoretical Syringe Injection Rates and Syringe Volumes

Scenario # 1								
(C) Desired Analyte Concentration (ppm)	(M) Molecular Weight (g/mol)	(p) Density (g/mL)	(qD) Diluent Gas Flow Rate (L/min)	(P) Pressure (mmHG)	(T) Temperature (Kelvin)	(qL) Injection Rate (μL/min)	Volume (mL) in 100 mL	Volume (μL) in 100000 μL
BENZENE								
0.5	78.11	0.8765	40	758.19	294.45	0.074	0.900	899.84
TOLUENE								
15	92.11	0.8669	40	758.19	294.45	2.633	31.83	31833.84
ETHYLBENZENE								
12.5	106.167	0.8665	40	758.19	294.45	2.530	30.58	30576.70
m XYLENE								
15	106.16	0.8599	40	758.19	294.45	3.059	36.69	36689.62
TOTAL						8.295	100	100000
Scenario # 2								
(C) Desired Analyte Concentration (ppm)	(M) Molecular Weight (g/mol)	(p) Density (g/mL)	(qD) Diluent Gas Flow Rate (L/min)	(P) Pressure (mmHG)	(T) Temperature (Kelvin)	(qL) Injection Rate (μL/min)	Volume (mL) in 100 mL	Volume (μL) in 100000 μL
BENZENE								
1.25	78.11	0.8765	40	758.19	294.45	0.184	0.45	451.96
TOLUENE								
75	92.11	0.8669	40	758.19	294.45	13.163	31.98	31977.72
ETHYLBENZENE								
62.5	106.167	0.8665	40	758.19	294.45	12.649	30.71	30714.89
m XYLENE								
75	106.16	0.8599	40	758.19	294.45	15.294	36.86	36855.44
TOTAL						41.290	100	100000
Scenario # 3								
(C) Desired Analyte Concentration (ppm)	(M) Molecular Weight (g/mol)	(p) Density (g/mL)	(qD) Diluent Gas Flow Rate (L/min)	(P) Pressure (mmHG)	(T) Temperature (Kelvin)	(qL) Injection Rate (μL/min)	Volume (mL) in 100 mL	Volume (μL) in 100000 μL
BENZENE								
2.5	78.11	0.8765	40	758.19	294.45	0.368	0.45	451.96
TOLUENE								
150	92.11	0.8669	40	758.19	294.45	26.326	31.98	31977.72
ETHYLBENZENE								
125	106.167	0.8665	40	758.19	294.45	25.298	30.71	30714.89
m XYLENE								
150	106.16	0.8599	40	758.19	294.45	30.588	36.86	36855.44
TOTAL						82.580	100	100000

APPENDIX B: MARKES MAVERICK CONTROLLING METHOD

Controlling method used on Markes Maverick software for thermal desorption.

Controlling Method		
Step	Parameter	Value
Pre-Desorption		
	Pre-purge Time	1 min
	Split	On (checked)
	Flow	50 ml/min
Tube/Sample Desorption		
	Desorption temperature	315 °C
	Desorption time	10 min
	Trap in Line	Yes (checked)
	Trap Package	Tenax TA and Carbograph 1
	Trap Flow	12.0 ml/min
	Split	On (checked)
	Split Flow	200 ml/min
Trap Settings (Trap Desorb)		
	Pre-Trap Fire Purge	1 min
	Trap Flow	25.0 ml/min
	Flow	200 ml/min
	Trap Low Temperature	-15 °C
	Trap High Temperature	300 °C
	Heating Rate	Max °C/s
	Trap Hold	3 min
	Split	On (checked)
	Split Flow	200 ml/min
Auxiliary Parameters		
	Flow Path Temperature	160 °C
	Minimum Carrier Pressure	2.0 psi
	G.C. Cycle Time	12.0 min
Split Ratios		
	Inlet	17.7: 1
	Outlet	167.7: 1
	Total	2690: 1
Standby		
	Split on	On (checked)
	Flow	213 ml/min

APPENDIX C: MASSHUNTER DATA ANALYSIS SOFTWARE PARAMETERS

MassHunter Data Analysis: GC/MS operating parameters.

Sequence MiguelSplitRatioTestDay1.sequence.xml is running...

Running 1 of 29 Vial 1 D:\MassHunter\GCMS\1\data\Miguel\29MAR22 Test\Scenario 1 Blank (Edit... Data Analysis Pause

Instrument Control

Run Status: **PreRun**
Instrument Status: **Ready**

Sample Name: Scenario 1 Blank 01
Data File: Scenario 1 Blank 01.D

0.00
Run Time: 21.92

STOP

Sequence Method Instrument

40 Oven Temperature
200 Inlet-F Temperature
0.8 Column-1 Flow Calc.
250 Aux-2 Temperature
230 MS Source
150 MS Quad

Spectrum TIC

GC Acquisition

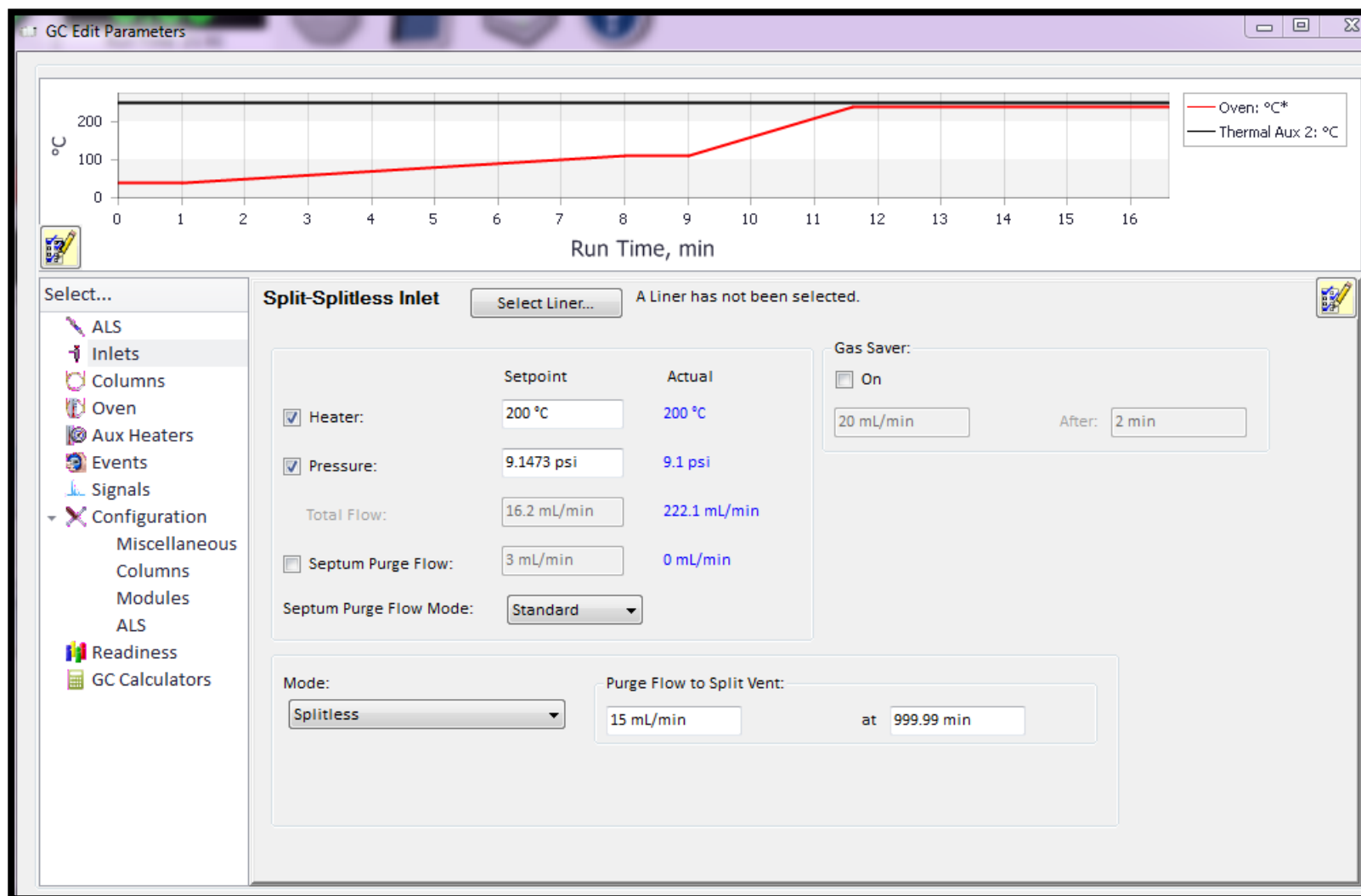
Waiting for remote start...
To manually override, click Start Run.

Start Run

Spectrum
MS Spectrum (Normalize)

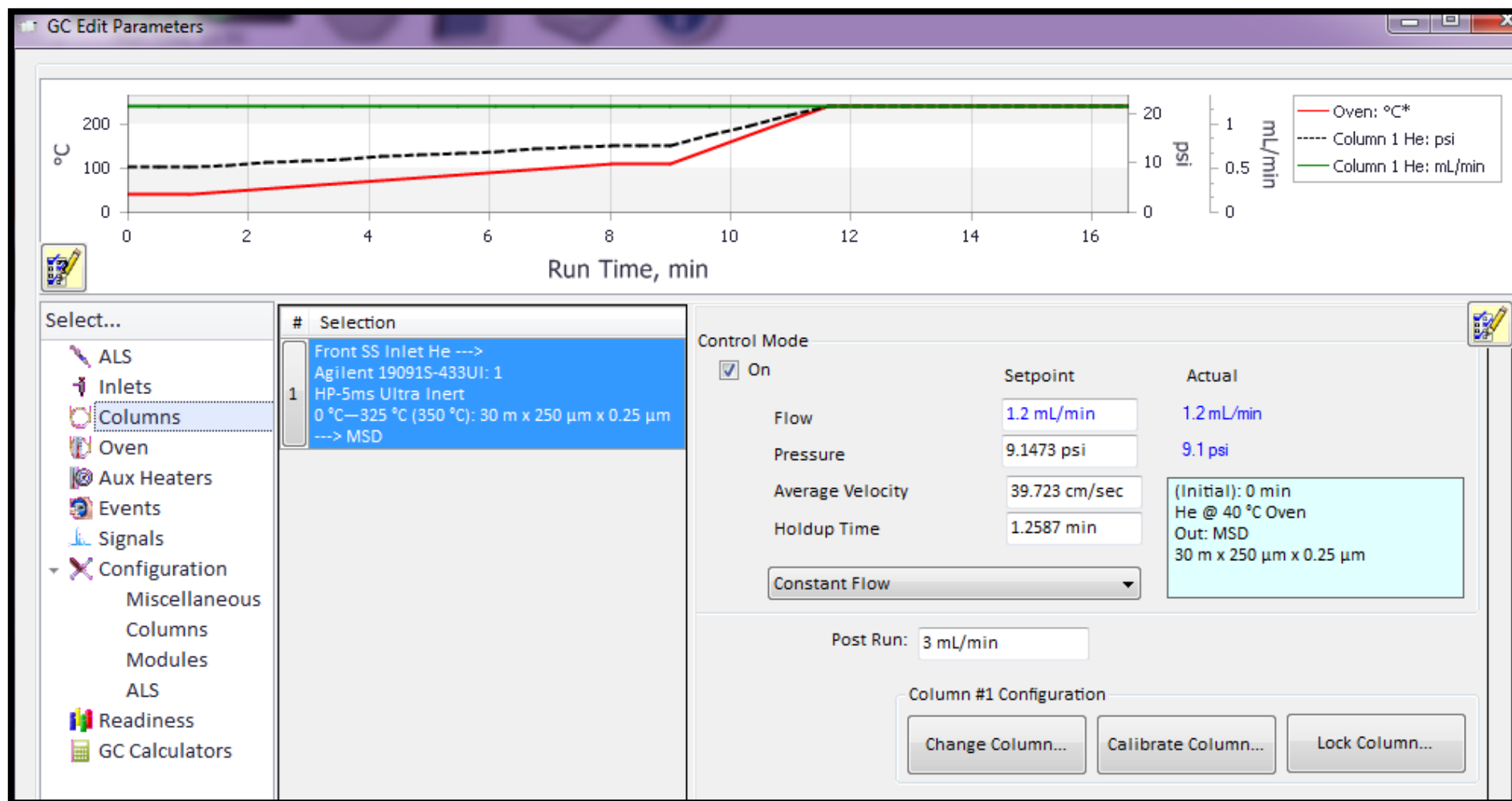
APPENDIX C: MASSHUNTER DATA ANALYSIS SOFTWARE PARAMETERS

MassHunter Data Analysis: GC/MS Software Parameters.



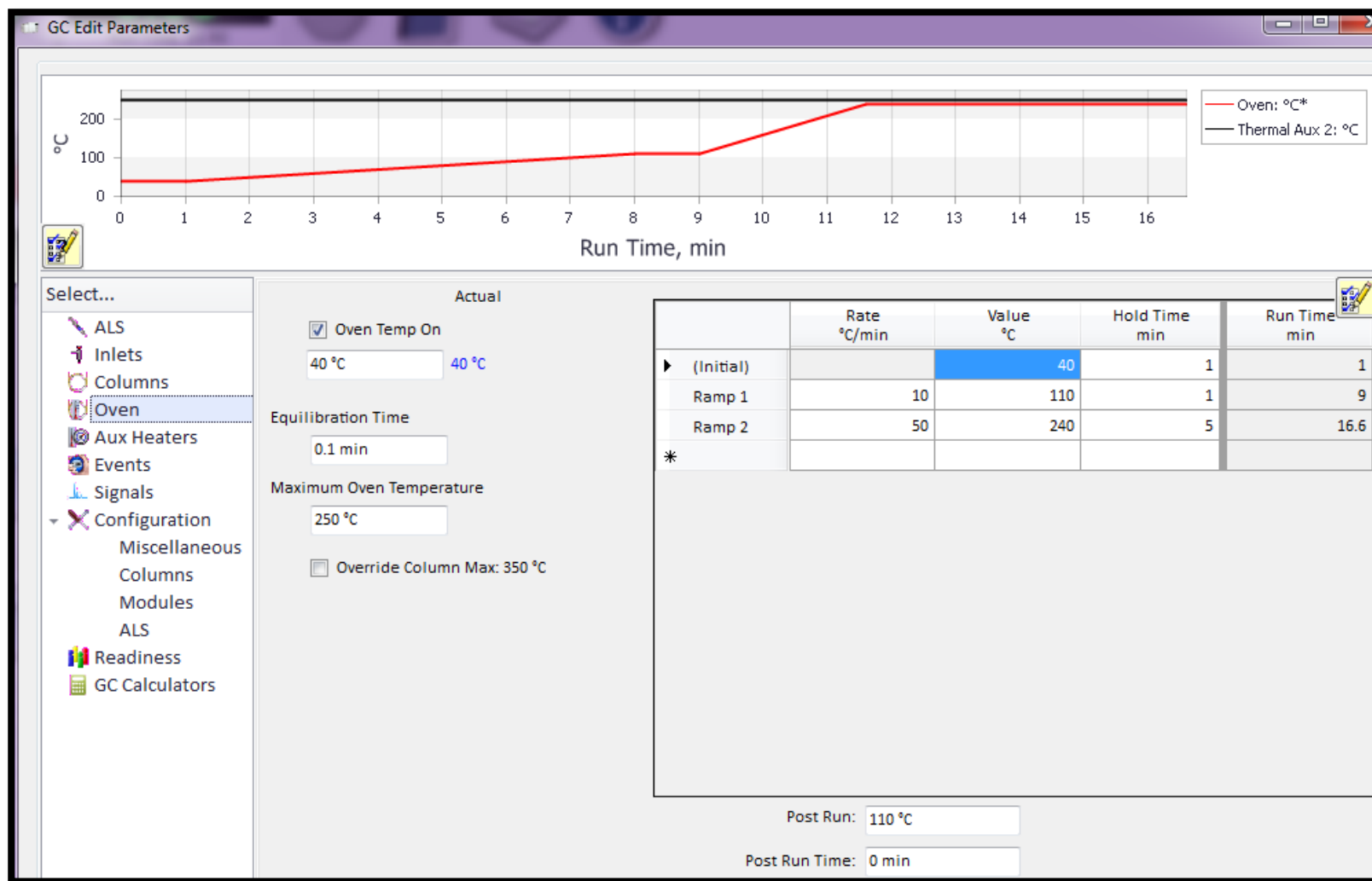
APPENDIX C: MASSHUNTER DATA ANALYSIS SOFTWARE PARAMETERS

MassHunter Data Analysis: GC/MS Software Parameters.



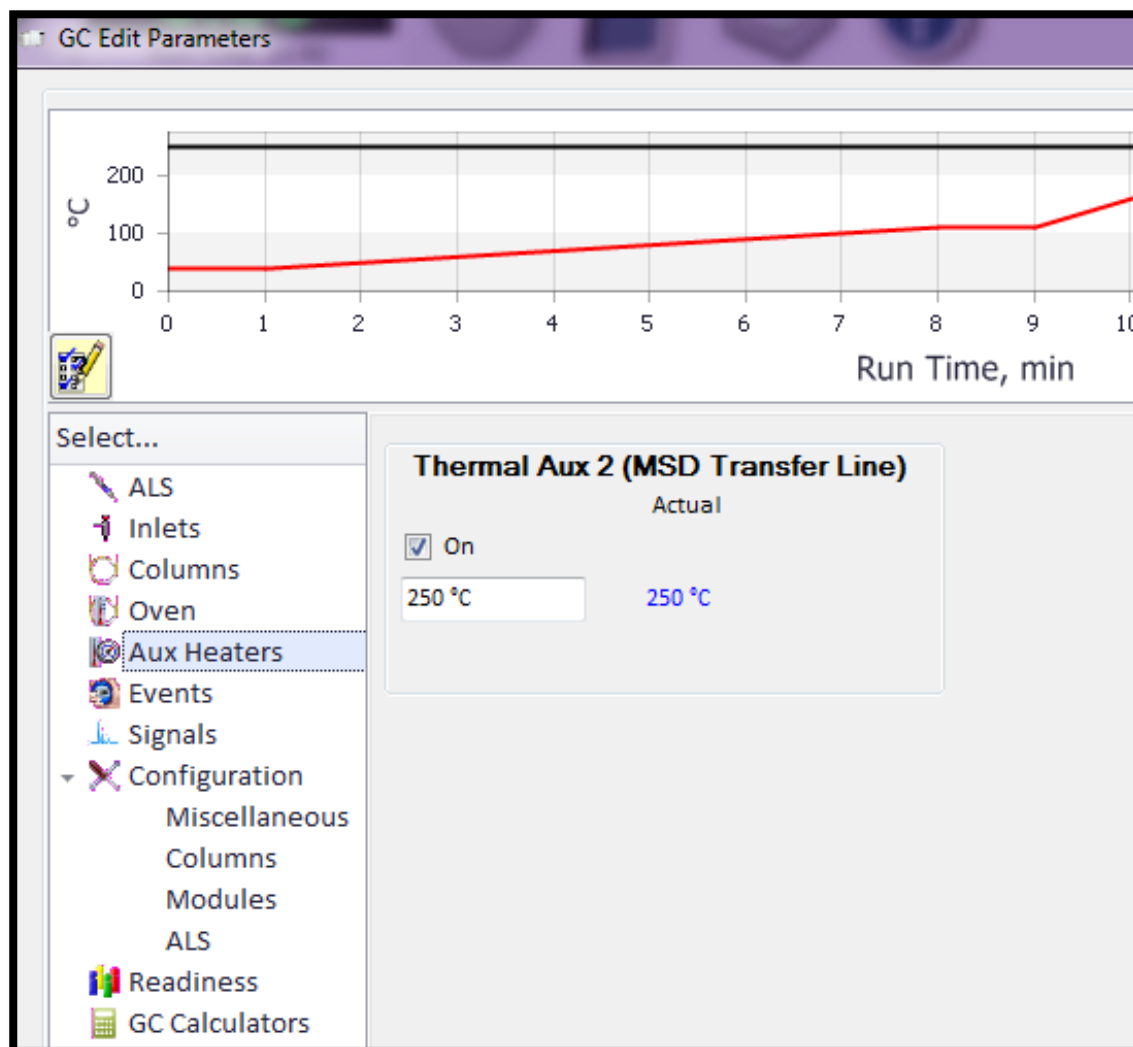
APPENDIX C: MASSHUNTER DATA ANALYSIS SOFTWARE PARAMETERS

MassHunter Software: GC/MS Software Parameters.



APPENDIX C: MASSHUNTER DATA ANALYSIS SOFTWARE PARAMETERS

MassHunter Software: GC/MS Software Parameters.



APPENDIX D: MARKES INTERNATIONAL MAVERICK SOFTWARE SETTINGS

Markes International Maverick Software: Controlling method parameters pre-desorption settings.

The screenshot displays the 'Method 2 (Controlling Method)' window. At the top, a dropdown menu is set to 'Standard 2(3) stage desorption'. To the right, under 'Standby', the 'Split On' checkbox is checked, and the 'Flow ml/min' is set to 213.0. Below this, there are three tabs: 'Pre-Desorption' (selected), 'Tube/Sample desorption', and 'Trap Settings'. The 'Pre-Desorption' tab contains a 'Purge' section with a large empty text area. Below this, 'Prepurge Time' is set to 1.0, and 'Flow ml/min' is set to 50.0. The 'Trap In Line' checkbox is unchecked, and the 'Split On' checkbox is checked. At the bottom, there are three input fields: 'Flow Path Temp' (160), 'Minimum Carrier Pressure' (2.0), and 'GC Cycle Time' (12.0). To the right of these is a 'Split Ratios' section with three rows: 'Inlet' (17.7 : 1), 'Outlet' (167.7 : 1), and 'Total' (2.96e03 : 1). A 'Confirm/Enter Flows' button is located to the right of the 'Split Ratios' section.

Parameter	Value
Flow Path Temp	160
Minimum Carrier Pressure	2.0
GC Cycle Time	12.0
Split Ratios Inlet	17.7 : 1
Split Ratios Outlet	167.7 : 1
Split Ratios Total	2.96e03 : 1

APPENDIX D: MARKES INTERNATIONAL MAVERICK SOFTWARE SETTINGS

Markes International Maverick Software: Controlling method parameters for tube/sample desorption settings.

The screenshot displays the 'Method 2 (Controlling Method)' window. At the top, a dropdown menu is set to 'Standard 2(3) stage desorption'. To the right, a 'Standby' section includes a checked 'Split On' checkbox and a 'Flow ml/min' value of 213.0. Below this are three tabs: 'Pre-Desorption', 'Tube/Sample desorption' (which is active), and 'Trap Settings'. The 'Tube/Sample desorption' tab contains a 'Tube Desorb' section with input fields for 'Time 1' (10.0), 'Temp 1' (315), 'Time 2' (0.0), and checkboxes for 'Trap In Line' and 'Split On' (both checked). It also includes 'Trap Flow ml/min' (12.0) and 'Split Flow ml/min' (200.0). At the bottom, there are three input fields: 'Flow Path Temp' (160), 'Minimum Carrier Pressure' (2.0), and 'GC Cycle Time' (12.0). To the right of these is a 'Split Ratios' section with 'Inlet' (17.7 : 1), 'Outlet' (167.7 : 1), and 'Total' (2.96e03 : 1). A 'Confirm/Enter Flows' button is located at the bottom right.

Tube Desorb	
Time 1	Temp 1
10.0	315
Time 2	
0.0	

Split Ratios	
17.7 : 1	Inlet
167.7 : 1	Outlet
2.96e03 : 1	Total

APPENDIX D: MARKES INTERNATIONAL MAVERICK SOFTWARE SETTINGS

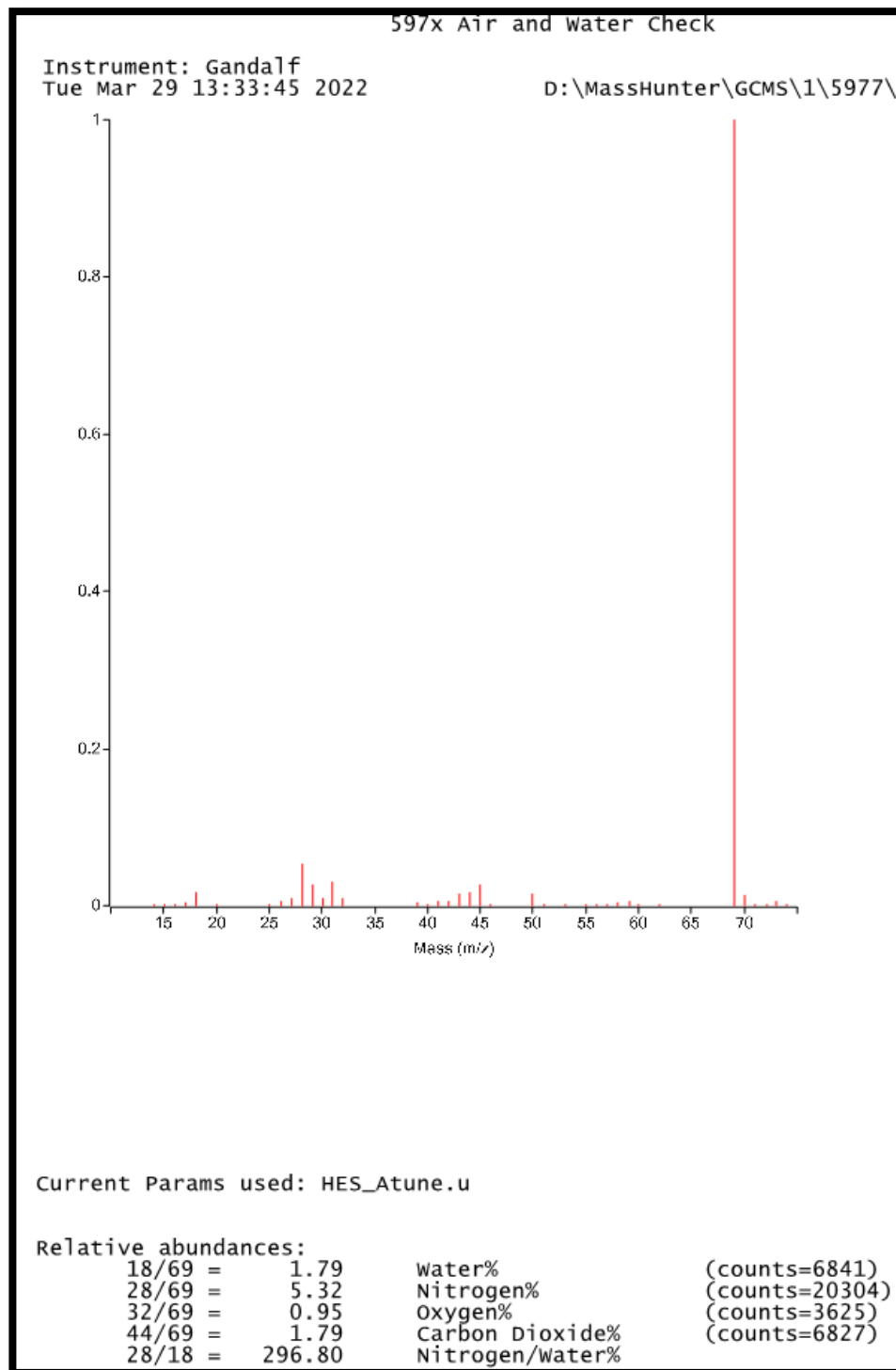
Markes International Maverick Software: Controlling method parameters for trap settings.

The screenshot shows the 'Method 2 (Controlling Method)' window. At the top, a dropdown menu is set to 'Standard 2(3) stage desorption'. To the right, under 'Standby', there is a checked 'Split On' checkbox and a 'Flow ml/min' value of 213.0. Below this, there are three tabs: 'Pre-Desorption', 'Tube/Sample desorption', and 'Trap Settings'. The 'Trap Settings' tab is active, showing a 'Trap Desorb' section with the following parameters: 'Pre-Trap Fire Purge/min' (1.0), 'Trap Flow ml/min' (25.0), 'Flow ml/min' (200.0), 'Trap Low /°C' (-15), 'Heating Rate °C/s' (MAX), 'Trap High /°C' (300), 'Trap Hold /min' (3.0), and 'Split Flow ml/min' (200.0) with a checked 'Split On' checkbox. At the bottom, there are three input fields: 'Flow Path Temp' (160), 'Minimum Carrier Pressure' (2.0), and 'GC Cycle Time' (12.0). To the right of these is a 'Split Ratios' section with 'Inlet' (17.7 : 1), 'Outlet' (167.7 : 1), and 'Total' (2.96e03 : 1). A 'Confirm/Enter Flows' button is located at the bottom right.

Parameter	Value
Pre-Trap Fire Purge/min	1.0
Trap Flow ml/min	25.0
Flow ml/min	200.0
Trap Low /°C	-15
Heating Rate °C/s	MAX
Trap High /°C	300
Trap Hold /min	3.0
Split Flow ml/min	200.0
Flow Path Temp	160
Minimum Carrier Pressure	2.0
GC Cycle Time	12.0
Split Ratios Inlet	17.7 : 1
Split Ratios Outlet	167.7 : 1
Split Ratios Total	2.96e03 : 1

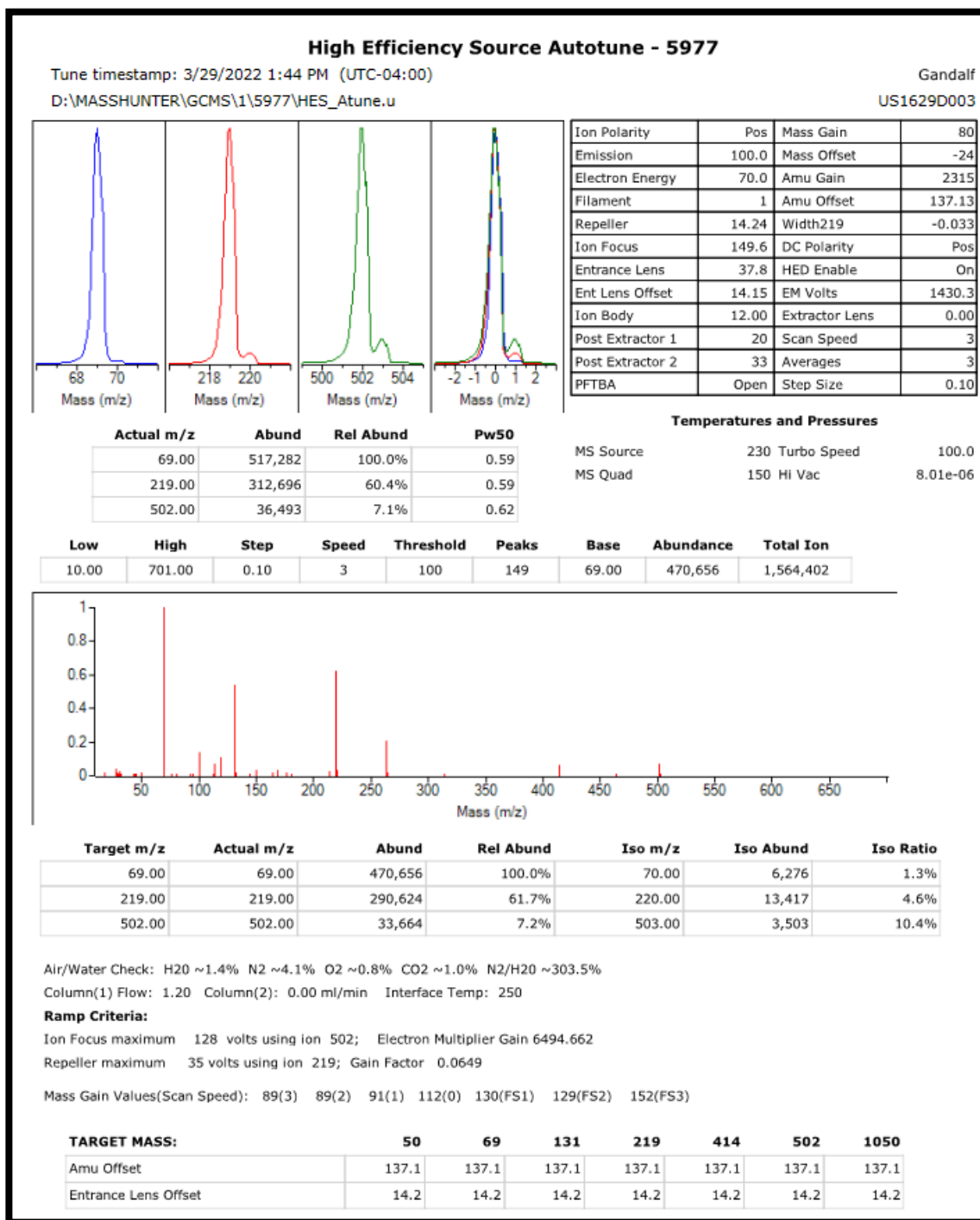
APPENDIX E: MASSHUNTER SOFTWARE PRE-CHECKS

MassHunter Software: Air and Water check.



APPENDIX E: MASSHUNTER SOFTWARE PRE-CHECKS

MassHunter Software: HES Autotune report.



APPENDIX E: MASSHUNTER SOFTWARE PRE-CHECKS

MassHunter Software: HES Autotune evaluation report.

System Verification - Tune (Detector Optimization) Portion		
Instrument Name	: Gandalf	
DC Polarity	: Positive	
Filament	1	
BasePeak should be 69 or 219		OK
Position of mass 69	69.00	OK
Position of mass 219	219.00	OK
Position of mass 502	502.00	OK
Position of isotope mass 70	70.00	OK
Position of isotope mass 220	220.00	OK
Position of isotope mass 503	503.00	OK
Ratio of mass 70 to mass 69(0.5 - 1.6%)	1.32	OK
Ratio of mass 220 to mass 219(3.2 - 5.4%)	4.57	OK
Ratio of mass 503 to mass 502(7.9 - 12.3%)	10.38	OK
Ratio of 219 to 69 should be > 40% and is	61.35	OK
Ratio of 502 to 69 should be > 2.4% and is	6.88	OK
Mass 69 Precursor (<= 3%)	1.49	OK
Mass 219 Precursor (<= 6%)	4.37	OK
Mass 502 Precursor (<= 12%)	6.68	OK
597x Air and Water Check		
Mon Mar 14 11:03:27 2022	Instrument: Gandalf	
D:\MassHunter\GCMS\1\5977\HES_Atune.u	US1629D003	
Testing for a leak in the system		
Ratio of 18 to 69 (<20%)	1.25	OK
Ratio of 28 to 69 (<10%)	4.59	OK
Electron Multiplier Voltage	1302	OK
Tune portion of System Verification passed.		

APPENDIX F: MASSHUNTER SOFTWARE SEQUENCE TABLE

MassHunter Software: Example of a sampling sequence table.

Sequence Table							
New Sample(s) X Tools							
	Name	Vial	Method Path	Method File	Data File	Type	
1	Scenario 1 Blank 01	1	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Blank 01	Blank	
2	Scenario 1 Sample #1	2	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #1	Sample	
3	Scenario 1 Sample #2	3	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #2	Sample	
4	Scenario 1 Sample #3	4	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #3	Sample	
5	Scenario 1 Sample #4	5	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #4	Sample	
6	Scenario 1 Sample #5	6	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #5	Sample	
7	Scenario 1 Sample #6	7	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #6	Sample	
8	Scenario 1 Sample #7	8	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #7	Sample	
9	Scenario 1 Sample #8	9	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #8	Sample	
10	Scenario 1 Sample #9	10	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #9	Sample	
11	Scenario 1 Sample #10	11	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #10	Sample	
12	Scenario 1 Sample #11	12	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #11	Sample	
13	Scenario 1 Sample #12	13	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #12	Sample	
14	Scenario 1 Sample #13	14	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #13	Blank	
15	Scenario 1 Blank 02	15	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Blank 02	Sample	
16	Scenario 1 Sample #14	16	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #14	Sample	
17	Scenario 1 Sample #15	17	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #15	Sample	
18	Scenario 1 Sample #16	18	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #16	Sample	
19	Scenario 1 Sample #17	19	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #17	Sample	
20	Scenario 1 Sample #18	20	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #18	Sample	
21	Scenario 1 Sample #19	21	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #19	Sample	
22	Scenario 1 Sample #20	22	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #20	Sample	
23	Scenario 1 Sample #21	23	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #21	Sample	
24	Scenario 1 Sample #22	24	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #22	Sample	
25	Scenario 1 Sample #23	25	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #23	Sample	
26	Scenario 1 Sample #24	26	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #24	Sample	
27	Scenario 1 Sample #25	27	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #25	Sample	
28	Scenario 1 Sample #26	28	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Sample #26	Sample	
29	Scenario 1 Blank 03	29	D:\MassHunter\GCMS1\methods	Miguel_BTEX.M	Scenario 1 Blank 03	Blank	

APPENDIX F: MASSHUNTER SOFTWARE SEQUENCE TABLE

MassHunter Software: Example of a start sequence.

Start Sequence MiguelSplitRatioTestDay1.sequence.xml Last Modified: Tue Mar 29 13:01:59 2022

Method Sections to Run

☒ Full Method

Sequence Barcode Options

☐ Disable barcode for this sequence.

☒ On mismatch, inject anyway.

☐ On mismatch, don't inject; continue the sequence.

☐ On mismatch, don't inject; stop the sequence.

☒ Overwrite Existing Data Files

Sequence Comment:

Operator Name:

Data File Directory:

Pre-Sequence Macros/Commands

Acquisition:

Data Analysis:

Post-Sequence Macros/Commands

Acquisition:

Data Analysis:

APPENDIX G: DESCRIPTIVE STATISTICS

Scenario 1 (0.50 ppm) descriptive statistics.

Descriptives				
Target Concentration			Statistic	Std. Error
0.5 Device Actual Concentration	Gasmet	Mean	0.5133	0.00508
		95% Confidence Interval for Mean	Lower Bound	0.5029
			Upper Bound	0.5237
		5% Trimmed Mean	0.5126	
		Median	0.5100	
		Variance	0.001	
		Std. Deviation	0.02783	
		Minimum	0.46	
		Maximum	0.58	
		Range	0.12	
		Interquartile Range	0.03	
		Skewness	0.484	0.427
		Kurtosis	0.192	0.833
	Radiello	Mean	0.3086	0.01326
		95% Confidence Interval for Mean	Lower Bound	0.2815
			Upper Bound	0.3358
		5% Trimmed Mean	0.3087	
		Median	0.3088	
		Variance	0.005	
		Std. Deviation	0.07140	
		Minimum	0.14	
		Maximum	0.48	
		Range	0.34	
		Interquartile Range	0.10	
		Skewness	-0.022	0.434
		Kurtosis	0.436	0.845

APPENDIX G: DESCRIPTIVE STATISTICS

Scenario 2 (1.25 ppm) descriptive statistics.

Descriptives				
Target Concentration			Statistic	Std. Error
1.25 Device Actual Concentration	Gasmet	Mean	1.2634	0.00750
		95% Confidence Interval for Mean	Lower Bound	1.2481
			Upper Bound	1.2788
		5% Trimmed Mean	1.2629	
		Median	1.2700	
		Variance	0.002	
		Std. Deviation	0.04038	
		Minimum	1.19	
		Maximum	1.35	
		Range	0.16	
		Interquartile Range	0.06	
		Skewness	0.097	0.434
		Kurtosis	-0.276	0.845
	Radiello	Mean	1.8105	0.02663
		95% Confidence Interval for Mean	Lower Bound	1.7559
			Upper Bound	1.8651
		5% Trimmed Mean	1.8114	
		Median	1.8031	
		Variance	0.020	
		Std. Deviation	0.14089	
		Minimum	1.51	
		Maximum	2.08	
		Range	0.57	
		Interquartile Range	0.22	
		Skewness	-0.002	0.441
		Kurtosis	-0.586	0.858
	OVM	Mean	1.3375	0.01773
		95% Confidence Interval for Mean	Lower Bound	1.3012
			Upper Bound	1.3738
		5% Trimmed Mean	1.3396	
		Median	1.3593	
		Variance	0.009	
		Std. Deviation	0.09547	
		Minimum	1.16	
		Maximum	1.49	
		Range	0.34	
		Interquartile Range	0.11	
		Skewness	-0.595	0.434
		Kurtosis	-0.404	0.845

APPENDIX G: DESCRIPTIVE STATISTICS

Scenario 3 (2.50 ppm) descriptive statistics.

Descriptives				
Target Concentration		Statistic		Std. Error
2.50 Device Actual Concentration	Gasmet	Mean	2.4965	0.03071
	95% Confidence Interval for Mean	Lower Bound	2.4333	
		Upper Bound	2.5598	
	5% Trimmed Mean		2.4968	
	Median		2.4650	
	Variance		0.025	
	Std. Deviation		0.15659	
	Minimum		2.14	
	Maximum		2.82	
	Range		0.68	
	Interquartile Range		0.20	
	Skewness		0.249	0.456
	Kurtosis		0.303	0.887
	Radiello	Mean	3.5103	0.03629
	95% Confidence Interval for Mean	Lower Bound	3.4355	
		Upper Bound	3.5850	
	5% Trimmed Mean		3.5027	
	Median		3.4968	
	Variance		0.034	
	Std. Deviation		0.18505	
	Minimum		3.19	
	Maximum		4.00	
	Range		0.81	
	Interquartile Range		0.23	
	Skewness		0.513	0.456
	Kurtosis		0.755	0.887
	OVM	Mean	3.1869	0.04109
	95% Confidence Interval for Mean	Lower Bound	3.1023	
		Upper Bound	3.2715	
	5% Trimmed Mean		3.1966	
	Median		3.2174	
	Variance		0.044	
	Std. Deviation		0.20954	
	Minimum		2.67	
	Maximum		3.50	
	Range		0.83	
	Interquartile Range		0.24	
	Skewness		-0.682	0.456
	Kurtosis		0.238	0.887

APPENDIX H: RELATIVE PERCENT ERROR

Scenario 1: Gasmeter vs. Radiello®

Sample No.	True Value of Benzene Concentration (ppm) (Gasmeter)	Observed Benzene Concentration (ppm) (Radiello®)	Relative Error (%)
1	0.49	0.14	71
2	0.46	0.25	46
3	0.51	0.19	63
4	0.50	0.27	46
5	0.52	0.24	54
6	0.50	0.29	42
7	0.50	0.25	49
8	0.53	0.32	40
9	0.50	0.23	55
10	0.54	0.34	38
11	0.50	0.24	51
12	0.54	0.33	39
13	0.48	0.24	50
14	0.57	0.30	47
15	0.49	0.31	37
16	0.50	0.38	25
17	0.53	0.35	34
18	0.52	0.37	29
19	0.55	0.28	50
20	0.53	0.36	32
21	0.51	0.31	40
22	0.50	0.43	15
23	0.50	0.33	34
24	0.55	0.40	27
25	0.48	0.35	27
26	0.58	0.34	42
27	0.47	0.37	21
28	0.53	0.28	47
29	0.51	0.48	7
Average Relative Error (%):			40

APPENDIX H: RELATIVE PERCENT ERROR

Scenario 2: Gasmeter vs. Radiello®			
Sample No.	True Value of Benzene Concentration (ppm) (Gasmeter)	Observed Benzene Concentration (ppm) (Radiello®)	Relative Error (%)
1	1.22	1.69	39
2	1.28	1.75	37
3	1.25	1.73	38
4	1.28	1.69	32
5	1.28	1.63	27
6	1.29	1.86	44
7	1.27	1.76	39
8	1.31	1.86	42
9	1.26	1.79	42
10	1.26	1.88	49
11	1.23	1.85	50
12	1.27	1.89	49
13	1.34	2.08	55
14	1.19	1.92	61
15	1.22	1.99	63
16	1.19	1.91	61
17	1.31	2.03	55
18	1.35	2.00	48
19	1.29	1.99	54
20	1.21	1.79	48
21	1.23	1.67	36
22	1.27	1.66	31
23	1.25	1.67	34
24	1.28	1.63	27
25	1.24	1.51	22
26	1.22	1.73	42
27	1.30	1.89	45
28	1.30	1.81	39
Average Relative Error (%):			43

APPENDIX H: RELATIVE PERCENT ERROR

Scenario 2: Gasmet vs. OVM

Sample No.	True Value of Benzene Concentration (ppm) (Gasmet)	Observed Benzene Concentration (ppm) (OVM)	Relative Error (%)
1	1.22	1.31	8
2	1.28	1.33	4
3	1.25	1.34	7
4	1.28	1.36	6
5	1.28	1.31	3
6	1.29	1.45	12
7	1.27	1.36	7
8	1.31	1.40	7
9	1.26	1.29	3
10	1.26	1.40	11
11	1.23	1.43	16
12	1.27	1.29	2
13	1.34	1.49	12
14	1.19	1.45	22
15	1.22	1.38	13
16	1.19	1.45	22
17	1.31	1.38	5
18	1.35	1.38	2
19	1.29	1.45	12
20	1.21	1.31	9
21	1.23	1.29	5
22	1.27	1.29	1
23	1.25	1.20	4
24	1.28	1.18	8
25	1.24	1.16	7
26	1.22	1.16	5
27	1.30	1.16	11
28	1.30	1.39	7
29	1.25	1.39	11
Average Relative Error (%):			8

APPENDIX H: RELATIVE PERCENT ERROR

Scenario 3: Gasmet vs. Radiello®

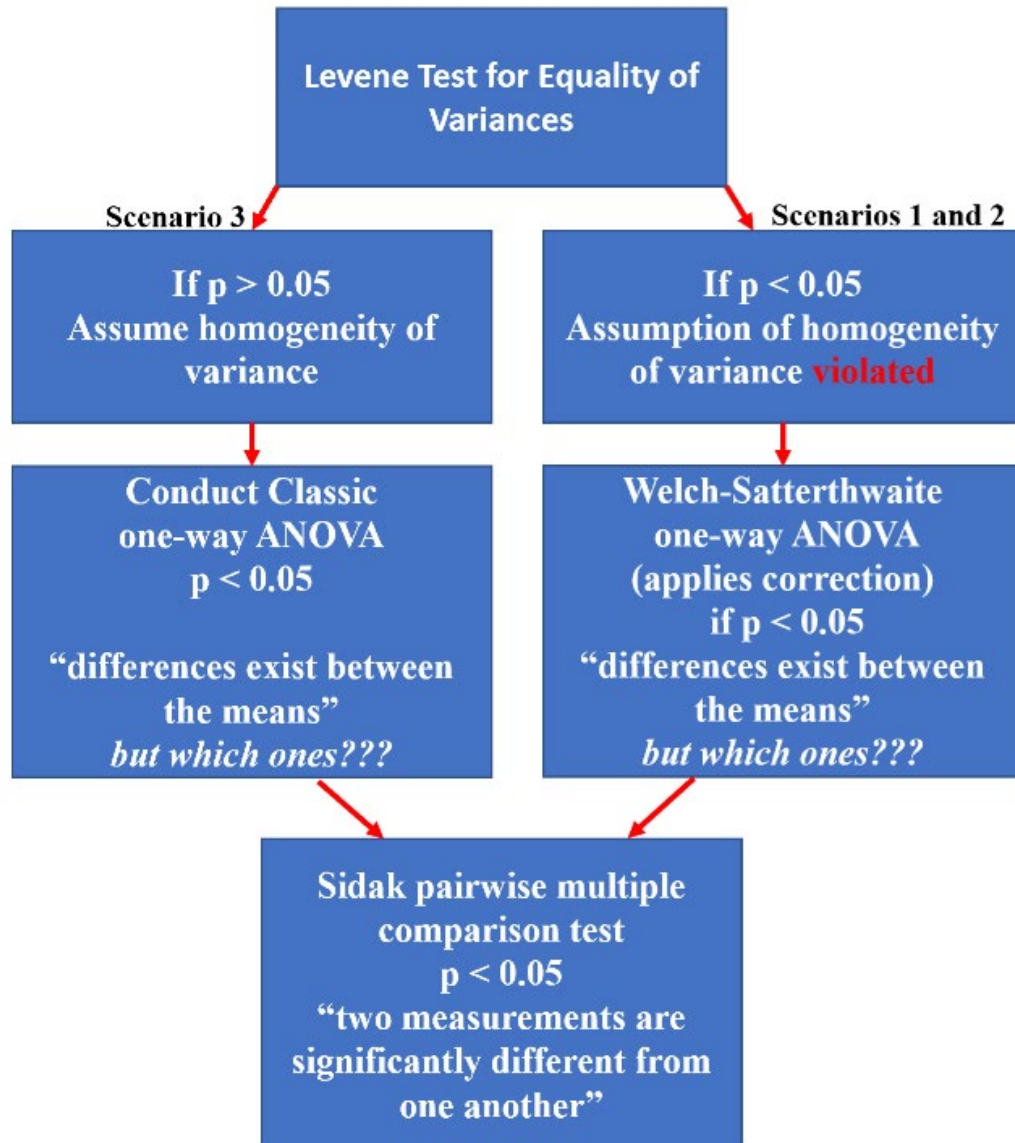
Sample No.	True Value of Benzene Concentration (ppm) (Gasmet)	Observed Benzene Concentration (ppm) (Radiello®)	Relative Error (%)
1	2.38	3.61	52
2	2.29	3.62	58
3	2.41	3.42	42
4	2.59	3.49	35
5	2.45	3.32	36
6	2.14	3.65	71
7	2.70	3.45	28
8	2.35	3.68	57
9	2.73	3.72	36
10	2.79	3.57	28
11	2.33	3.55	52
12	2.46	4.00	63
13	2.43	3.80	56
14	2.65	3.54	34
15	2.45	3.19	30
16	2.64	3.56	35
17	2.45	3.43	40
18	2.57	3.23	26
19	2.40	3.24	35
20	2.49	3.38	36
21	2.43	3.40	40
22	2.52	3.50	39
23	2.82	3.47	23
24	2.47	3.46	40
25	2.50	3.67	47
26	2.47	3.33	35
Average Relative Error (%):			41

APPENDIX H: RELATIVE PERCENT ERROR

Scenario 3: Gasmet vs. OVM

Sample No.	True Value of Benzene Concentration (ppm) (Gasmet)	Observed Benzene Concentration (ppm) (OVM)	Relative Error (%)
1	2.38	3.23	36
2	2.29	3.21	40
3	2.41	3.42	42
4	2.59	3.35	29
5	2.45	3.27	34
6	2.14	3.50	64
7	2.70	3.46	28
8	2.35	3.27	39
9	2.73	3.46	27
10	2.79	3.27	17
11	2.33	3.27	41
12	2.46	3.28	33
13	2.43	3.42	41
14	2.65	3.27	23
15	2.45	3.01	23
16	2.64	2.84	8
17	2.45	2.99	22
18	2.57	3.20	25
19	2.40	3.08	28
20	2.49	3.02	21
21	2.43	2.67	10
22	2.52	3.17	26
23	2.82	3.19	13
24	2.47	2.81	14
25	2.50	3.10	24
26	2.47	3.06	24
Average Relative Error (%):			28

APPENDIX I: LEVENE TEST FOR EQUALITY OF VARIANCES



APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 1: Gasmeter vs Radiello® B-A Plot Data (ppm)			
Gasmeter	Radiello®	Average	Difference
0.49	0.14	0.32	0.35
0.46	0.25	0.35	0.21
0.51	0.19	0.35	0.32
0.50	0.27	0.39	0.23
0.52	0.24	0.38	0.28
0.50	0.29	0.40	0.21
0.50	0.25	0.38	0.25
0.53	0.32	0.42	0.21
0.50	0.23	0.36	0.27
0.54	0.34	0.44	0.20
0.50	0.24	0.37	0.26
0.54	0.33	0.44	0.21
0.48	0.24	0.36	0.24
0.57	0.30	0.44	0.27
0.49	0.31	0.40	0.18
0.50	0.38	0.44	0.12
0.53	0.35	0.44	0.18
0.52	0.37	0.44	0.15
0.55	0.28	0.41	0.27
0.51	0.36	0.43	0.15
0.50	0.31	0.40	0.19
0.50	0.43	0.46	0.07
0.55	0.33	0.44	0.22
0.48	0.40	0.44	0.08
0.58	0.35	0.46	0.23
0.47	0.34	0.40	0.13
0.53	0.37	0.45	0.16
0.51	0.28	0.40	0.23
0.51	0.48	0.49	0.03
Avg. Diff			0.20
Lower			0.064
Upper			0.336

APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 2: Gasmeter vs Radiello® B-A Plot Data (ppm)			
Gasmeter	Radiello®	Average	Difference
1.22	1.69	1.46	-0.47
1.28	1.75	1.52	-0.47
1.25	1.73	1.49	-0.48
1.28	1.69	1.48	-0.41
1.28	1.63	1.46	-0.35
1.29	1.86	1.57	-0.57
1.27	1.76	1.51	-0.49
1.31	1.86	1.59	-0.55
1.26	1.79	1.53	-0.53
1.26	1.88	1.57	-0.62
1.23	1.85	1.54	-0.62
1.27	1.89	1.58	-0.62
1.34	2.08	1.71	-0.74
1.19	1.92	1.56	-0.73
1.22	1.99	1.61	-0.77
1.19	1.91	1.55	-0.72
1.31	2.03	1.67	-0.72
1.35	2.00	1.68	-0.65
1.29	1.99	1.64	-0.70
1.23	1.79	1.51	-0.56
1.27	1.67	1.47	-0.40
1.25	1.66	1.46	-0.41
1.28	1.67	1.47	-0.39
1.24	1.63	1.44	-0.39
1.22	1.51	1.36	-0.29
1.30	1.73	1.52	-0.43
1.30	1.89	1.59	-0.59
1.25	1.81	1.53	-0.56
		Avg. Diff	-0.55
		Lower	-0.807
		Upper	-0.279

APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 2: Gasmet vs OVM B-A Plot Data (ppm)			
Gasmet	OVM	Average	Difference
1.22	1.31	1.27	-0.09
1.28	1.33	1.31	-0.05
1.25	1.34	1.29	-0.09
1.28	1.36	1.32	-0.08
1.28	1.31	1.30	-0.03
1.29	1.45	1.37	-0.16
1.27	1.36	1.32	-0.09
1.31	1.40	1.36	-0.09
1.26	1.29	1.28	-0.03
1.26	1.40	1.33	-0.14
1.23	1.43	1.33	-0.20
1.27	1.29	1.28	-0.02
1.34	1.49	1.42	-0.15
1.19	1.45	1.32	-0.26
1.22	1.38	1.30	-0.16
1.19	1.45	1.32	-0.26
1.31	1.38	1.35	-0.07
1.35	1.38	1.37	-0.03
1.29	1.45	1.37	-0.16
1.21	1.31	1.26	-0.10
1.23	1.29	1.26	-0.06
1.27	1.29	1.28	-0.02
1.25	1.20	1.22	0.05
1.28	1.18	1.23	0.10
1.24	1.16	1.20	0.08
1.22	1.16	1.19	0.06
1.30	1.16	1.23	0.14
1.30	1.39	1.34	-0.09
1.25	1.39	1.32	-0.14
Avg. Diff			-0.07
Lower			-0.267
Upper			0.122

APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 2: Radiello® vs OVM B-A Plot Data (ppm)			
Radiello®	OVM	Average	Difference
1.69	1.31	1.50	0.38
1.75	1.33	1.54	0.42
1.73	1.34	1.53	0.39
1.69	1.36	1.52	0.33
1.63	1.31	1.47	0.32
1.86	1.45	1.65	0.41
1.76	1.36	1.56	0.40
1.86	1.40	1.63	0.46
1.79	1.29	1.54	0.50
1.88	1.40	1.64	0.48
1.85	1.43	1.64	0.43
1.89	1.29	1.59	0.60
2.08	1.49	1.79	0.58
1.92	1.45	1.68	0.47
1.99	1.38	1.69	0.61
1.91	1.45	1.68	0.46
2.03	1.38	1.71	0.65
2.00	1.38	1.69	0.62
1.99	1.45	1.72	0.55
1.79	1.31	1.55	0.48
1.67	1.29	1.48	0.38
1.66	1.29	1.48	0.38
1.67	1.20	1.43	0.47
1.63	1.18	1.41	0.46
1.51	1.16	1.33	0.35
1.73	1.16	1.45	0.58
1.89	1.16	1.52	0.73
1.81	1.39	1.60	0.43
		Avg. Diff	0.47
		Lower	0.271
		Upper	0.679

APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 3: Gasmeter vs Radiello® B-A Plot Data (ppm)

Gasmeter	Radiello®	Average	Difference
2.38	3.61	3.00	-1.23
2.29	3.62	2.95	-1.33
2.41	3.42	2.91	-1.01
2.59	3.49	3.04	-0.90
2.45	3.32	2.89	-0.87
2.14	3.65	2.90	-1.51
2.70	3.45	3.07	-0.75
2.35	3.68	3.02	-1.33
2.73	3.72	3.23	-0.99
2.79	3.57	3.18	-0.78
2.33	3.55	2.94	-1.22
2.46	4.00	3.23	-1.54
2.43	3.80	3.11	-1.37
2.65	3.54	3.09	-0.89
2.45	3.19	2.82	-0.74
2.64	3.56	3.10	-0.92
2.45	3.43	2.94	-0.98
2.57	3.23	2.90	-0.66
2.40	3.24	2.82	-0.84
2.49	3.38	2.93	-0.89
2.43	3.40	2.91	-0.97
2.52	3.50	3.01	-0.98
2.82	3.47	3.14	-0.65
2.47	3.46	2.96	-0.99
2.50	3.67	3.08	-1.17
2.47	3.33	2.90	-0.86
Avg. Diff			-1.01
Lower			-1.504
Upper			-0.522

APPENDIX J: BLAND-ALTMAN PLOT DATA

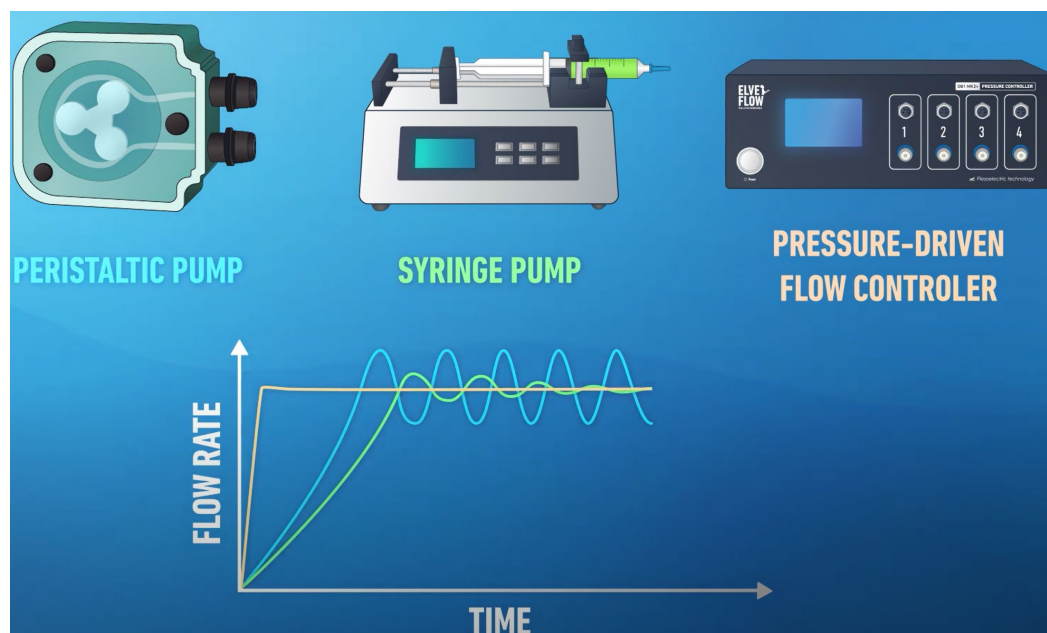
Scenario 3: Gasmet vs OVM B-A Plot Data (ppm)

Gasmet	OVM	Average	Difference
2.38	3.23	2.80	-0.85
2.29	3.21	2.75	-0.92
2.41	3.42	2.92	-1.01
2.59	3.35	2.97	-0.76
2.45	3.27	2.86	-0.82
2.14	3.50	2.82	-1.36
2.70	3.46	3.08	-0.76
2.35	3.27	2.81	-0.92
2.73	3.46	3.10	-0.73
2.79	3.27	3.03	-0.48
2.33	3.27	2.80	-0.94
2.46	3.28	2.87	-0.82
2.43	3.42	2.92	-0.99
2.65	3.27	2.96	-0.62
2.45	3.01	2.73	-0.56
2.64	2.84	2.74	-0.20
2.45	2.99	2.72	-0.54
2.57	3.20	2.89	-0.63
2.40	3.08	2.74	-0.68
2.49	3.02	2.76	-0.53
2.43	2.67	2.55	-0.24
2.52	3.17	2.85	-0.65
2.82	3.19	3.00	-0.37
2.47	2.81	2.64	-0.34
2.50	3.10	2.80	-0.60
2.47	3.06	2.77	-0.59
Avg. Diff			-0.69
Lower			-1.200
Upper			-0.174

APPENDIX J: BLAND-ALTMAN PLOT DATA

Scenario 3 Radiello® vs OVM B-A Plot Data (ppm)			
Radiello®	OVM	Average	Difference
3.61	3.23	3.42	0.39
3.62	3.21	3.41	0.41
3.42	3.42	3.42	-0.01
3.49	3.35	3.42	0.14
3.32	3.27	3.30	0.05
3.65	3.50	3.58	0.15
3.45	3.46	3.46	-0.02
3.68	3.27	3.48	0.41
3.72	3.46	3.59	0.26
3.57	3.27	3.42	0.30
3.55	3.27	3.41	0.27
4.00	3.28	3.64	0.73
3.80	3.42	3.61	0.38
3.54	3.27	3.40	0.27
3.19	3.01	3.10	0.18
3.56	2.84	3.20	0.72
3.43	2.99	3.21	0.43
3.23	3.20	3.22	0.02
3.24	3.08	3.16	0.16
3.38	3.02	3.20	0.36
3.40	2.67	3.04	0.72
3.50	3.17	3.34	0.33
3.47	3.19	3.33	0.28
3.46	2.81	3.13	0.65
3.67	3.10	3.39	0.57
3.33	3.06	3.20	0.26
		Avg. Diff	0.32
		Lower	-0.107
		Upper	0.762

APPENDIX K: SYRINGE PUMP BEHAVIOR



Syringe pump behavior across three different devices (41).