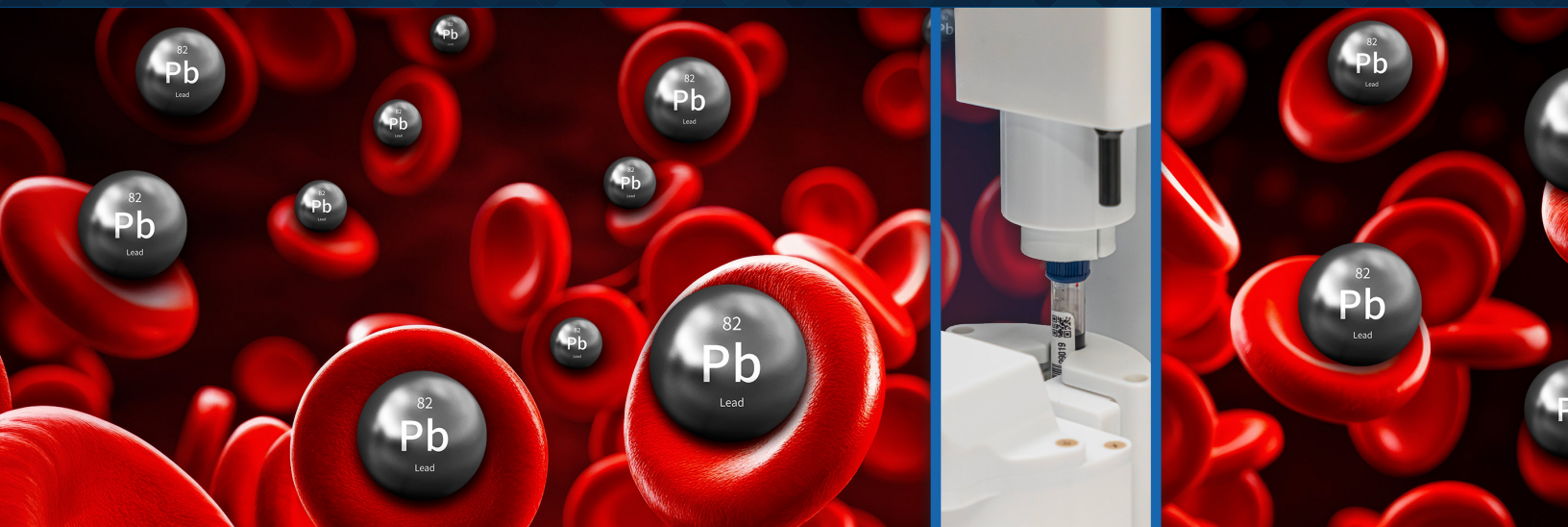




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TRAXStation Clinical – Fully Automated Preparation of Whole Blood Samples for the Analysis of Lead

Introduction

Trace element analysis plays a critical role in modern clinical diagnostics, providing essential information for evaluating nutritional status, toxic exposures, and metabolic disorders. Traditionally, the workflow for preparing and analyzing clinical samples by inductively coupled plasma mass spectrometry (ICPMS) has relied heavily on manual liquid handling steps. These steps – such as uncapping, rocking, pipetting, and dilution are time-consuming, prone to operator variability, and present ongoing risks of contamination, especially at trace and ultra-trace concentrations. As clinical demand grows, laboratories processing hundreds to thousands of patient samples per day face the mounting pressure to increase throughput while maintaining uncompromising analytical quality.

The **TRAXStation** Automated Multifunctional Liquid Handling System directly addresses these challenges by automating routine sample preparation tasks within a controlled, contamination free environment. Constructed from chemically inert materials, the platform is engineered to reliably process complex clinical matrices while minimizing external contamination and manual handling variability. Advanced capabilities including automated vial uncapping, liquid-level

detection, barcode tracking, sample mixing, and precise dilution routines ensure consistent and reproducible preparation across large sample sets.

In addition, the integrated SampleConfirm™ functionality verifies each aspiration event in real time, detecting incomplete or failed liquid handling steps and preventing compromised samples from advancing to analysis. For high-volume laboratories, this combination of automation and verification improves reproducibility, reduces operator workload, and provides a reliable, traceable pathway from raw sample to analysis-ready specimen.



Figure 1. TRAXStation Clinical 422.

Introduction (Continued)



Figure 2. TRAXStation Clinical takes up a whole blood aliquot for automated preparation in a 96-well microplate.

TRAXStation Clinical automates the full preparation workflow for whole blood samples collected in metal free collection tubes. The compact platform integrates all key steps into a single system, improving laboratory efficiency, traceability, and operator safety while ensuring

high-quality, reproducible results. By replacing labor-intensive manual steps, TRAXStation Clinical reduces errors, shortens turnaround times, and increases throughput while maintaining strict regulatory compliance and sample integrity.

TRAXStation Clinical Workflow

Barcode Reading & Sample Tracking

Integrated barcode scanning provides complete traceability and seamless connection to instruments and LIMS.

Sample Tube Rocker

Gentle rocking of tubes prior to processing guarantees homogeneous samples for accurate downstream analysis.

Automated Uncapping

Hands-free uncapping reduces manual handling, contamination risk, and biohazard exposure.

Sample Level Detecting

Sound waves are used to detect sample liquid levels. The probe will aspirate from just below the liquid surface.

SampleConfirm™

Sample integrity and verification function designed to confirm sample presence and total sample volume.

Precision Sampling & Dilution

High-accuracy pipetting enables aliquoting into tubes or 96-well plates with programmable dilutions for flexible assay workflows.

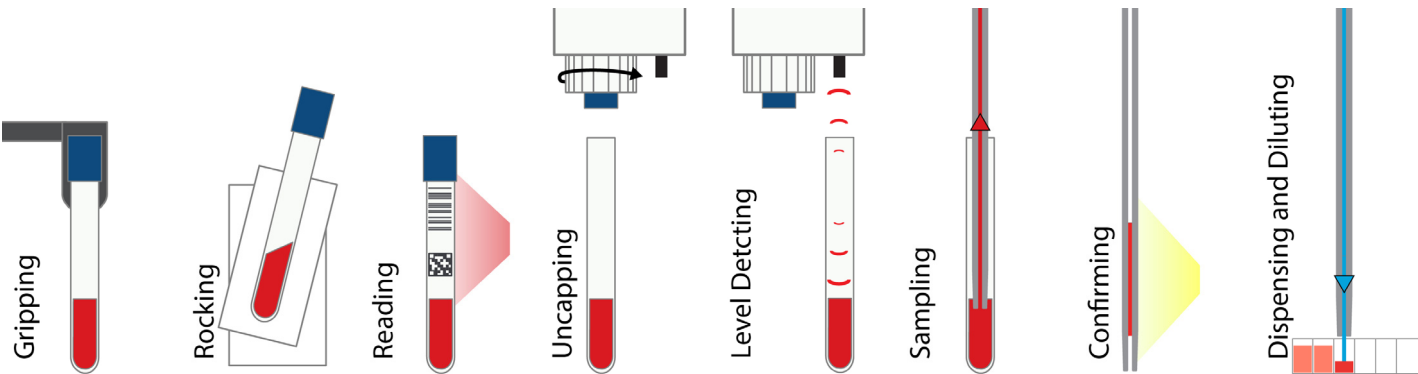


Figure 3. TRAXStation Clinical automated workflow for whole blood sample preparation.

Background

Blood lead testing is a critical public health measure that helps identify and prevent lead poisoning, particularly in vulnerable populations such as children and working adults. Lead is a toxic metal that can cause serious health effects even at very low concentrations. In children, elevated blood lead levels can impair brain development, reduce IQ, and cause behavioral and learning problems that may persist throughout life. In adults, chronic exposure can lead to hypertension, kidney damage, reproductive issues, and neurological symptoms. Laboratory testing provides the only reliable means of detecting exposure, as symptoms are often subtle or nonspecific.

Common Sources of Lead Exposure in Children

Children can be exposed to lead through a variety of environmental and household sources. One of the most significant is lead-based paint and dust, commonly found in homes built before 1978. As paint deteriorates or during renovation activities, lead dust can become airborne or settle on surfaces where children can easily ingest or inhale it. Contaminated household dust and soil also present a major risk, as lead particles can accumulate on floors, toys, or in soil near older buildings and roadways due to historical use of leaded paint and gasoline. Drinking water may contribute additional exposure, particularly in older homes with lead pipes, solder, or brass plumbing fixtures that can leach lead into tap water.

Parental occupational exposure can introduce lead into the home environment when adults inadvertently bring lead dust home on their skin, clothing, or shoes.

Lead is especially harmful to children because their brains and nervous systems are still developing, and they absorb lead more easily than adults. This can result in permanent damage to cognitive development, including reduced IQ, attention problems, behavioral issues, and learning difficulties – even at very low exposure levels.

Common Sources of Lead Exposure in Adults

Adults are most frequently exposed to lead through occupational settings, particularly in industries such as construction, painting, plumbing, battery manufacturing or recycling, metal smelting, and auto repair – where direct contact with lead-containing materials or dust is common. Home renovation of older buildings also presents a high risk, since sanding, scraping, or demolishing lead-based paint can release fine lead dust into the air and surrounding surfaces.

Drinking water remains a concern in areas with aging plumbing systems that still contain lead pipes, solder, or brass fittings, allowing lead to leach into tap water. Finally, take-home exposure is an important but often overlooked pathway. Workers in lead-related occupations can inadvertently bring lead dust home on their clothing, skin, or footwear, posing a secondary exposure risk to family members.

Table 1. Lead in whole blood reference ranges.

	Reference Range	Interpretation/Information
CDC	Children <6 y/o, <3.5 µg/dL	This value represents the 97.5 th percentile of blood lead levels among children in the U.S. It does not represent a safety threshold as there is no known safe blood lead level.
CDC	Adults – None Established	No reference range for adults has been established but health concerns and recommendations start at values greater than or equal to 5 µg/dL.
OSHA	<40 µg/dL	OSHA does not define "normal" blood lead levels. They use enforceable action thresholds. This value represents when workers are allowed to continue or return to work. Please see 29 CFR 1910.1025 and 29 CFR 1926.62 for list of blood lead levels and action requirements.
WHO	<5 µg/dL	WHO and other public health sources explicitly state that there is no known safe blood lead level, and even low concentrations can be associated with adverse effects such as decreased intelligence and learning problems, particularly in children.

Experimental – TRAXStation Automated Sample Prep

Operating conditions and parameters of **TRAXStation** preparation & ICPMS measurement for precision (repeatability and reproducibility) and accuracy (bias vs. assigned concentrations) for lead. Samples were measured across the clinical range using three pooled sample levels: Level 1 (at or below normal population levels), Level 2 (indicates significant exposure), and Level 3 (critical levels that may require immediate intervention).

Table 2. Materials and manual preparations.

Item	Description
Matrix	Bovine Whole Blood EDTA (pooled)
Pool Levels	Level 1, Level 2, Level 3 (based on reference range)
Target Conc.	Level 1 ≈ 3.5 µg/dL Level 2 ≈ 15.0 µg/dL Level 3 ≈ 45.0 µg/dL
Aliquoting	Aliquot each pool into 25 identical tubes
Calibrators	Aqueous – 6 Levels from 1.0 µg/dL to 100.0 µg/dL
Diluent	1% Nitric Acid (v/v) 2% Methanol (v/v) 10 ppb Bismuth (Internal Standard)
Additional Materials	UPW, Calibration Standards, Blanks, and Negative

Data Analysis Criteria

For clinical lead in whole blood testing, good precision and accuracy are demonstrated through rigorous statistical validation consistent with CLIA, CAP, and CLSI guidelines. Precision is evaluated by repeated analysis of whole blood pools at low, mid, and high concentrations, with 25 replicates per level over 25 runs/batches and expressed as coefficient of variation (%CV). For metals such as lead, intra-assay and inter-assay %CVs should generally be ≤5% at normal and high levels and ≤10% at low levels. Accuracy is verified by comparison with mean recovery required to fall within ±10% of target values. According to CLIA proficiency testing criteria, the allowable total error (TEa) is ±10% or 4 µg/dL, whichever

Table 3. Run structure and experimental design.

Item	Description
Samples per Run	83 (25 each level + Calibration)
Total Runs	25 (1875 data points) Multiple runs per day
Run Format	Blank, Calibrators, Negative, 25 Low, 25 Mid, 25 High
Data Collection	Accuracy and Precision monitored within and across runs
Data Analysis	Inter and Intra Assay Performance presented as a percent CV. (See Data Analysis Criteria below)

Table 4. TRAXStation Clinical sample automation.

Item	Description
Rinse 1	0.4% TMAH, 1% EtOH, 0.05% TritonX
Rinse 2	1% Nitric Acid
Diluent	(See Table 2 for prep) Connect and prime system
“Source” Samples	Load all calibrators and blood samples to “source” racks
Destination Racks	Load all destination racks with 12 mL plastic conical tubes
Dilution Factor	100x
Aspiration Volume	25 µL sample
Diluent Volume	2475 µL

is greater. Both short-term and long-term reproducibility must be assessed across runs, days, and operators to ensure robustness. Adherence to Good Laboratory Practice (GLP) principles and use of trace-element-free collection and processing materials are essential to minimize contamination. Additionally, a carryover study will be performed to verify that high-concentration samples do not contaminate subsequent low-level samples. All together, these statistical and procedural controls ensure that samples prepared by the **TRAXStation** for the analysis of lead in whole blood are analytically valid, reproducible, and compliant with regulatory standards for clinical testing.

Instrument Prep and Parameters

All samples were prepared using **TRAXStation Clinical**, and analyzed using 4DXCi SampleSense *FAST* UHT-C in combination with a single quad ICPMS.

Table 5. Instrument information.

Parameter	Value
Sample Introduction System	ESI 4DCXi Autosampler SampleSense <i>FAST</i> UHT-C TRAXStation Clinical
Instrument	Single Quad ICPMS
Valve	Magnetically-Coupled Inert 6-Port Valve
Probe	Carbon Fiber 0.8 mm ID Probe SC-5037-3755-100
Nebulizer	High Solids PFA Microflow Nebulizer ES-2030-79
Rinse 1	1% Nitric Acid
Rinse 2	1% Nitric Acid
Carrier	1% Nitric Acid (v/v) 2% MEOH (v/v)
Method Time	24 sec/sample analysis

Table 6. Instrument parameters.

Parameter	Value
Analytes	Pb (m/z 208 + 207 + 206)
ISTD	Bi (m/z 209)
ICPMS Mode	Standard Mode
Sweeps per Replicate	20
Replicates per Sample	3
Dwell	50 ms

Figure 4. The AutoBench4 platform provides an integrated and organized workspace for ICPMS analysis, combining the autosampler, rinse stations, and fluid management components into a single, controlled sampling environment. This design simplifies system setup, improves laboratory ergonomics, and helps maintain consistent sample handling during extended analytical runs. By centralizing key sampling components, the AutoBench platform supports stable operation, efficient workflow, and reliable performance in high-volume clinical and public health laboratories.



Lead Calibration – Analytical Measurement Range (AMR) 1-100 µg/dL

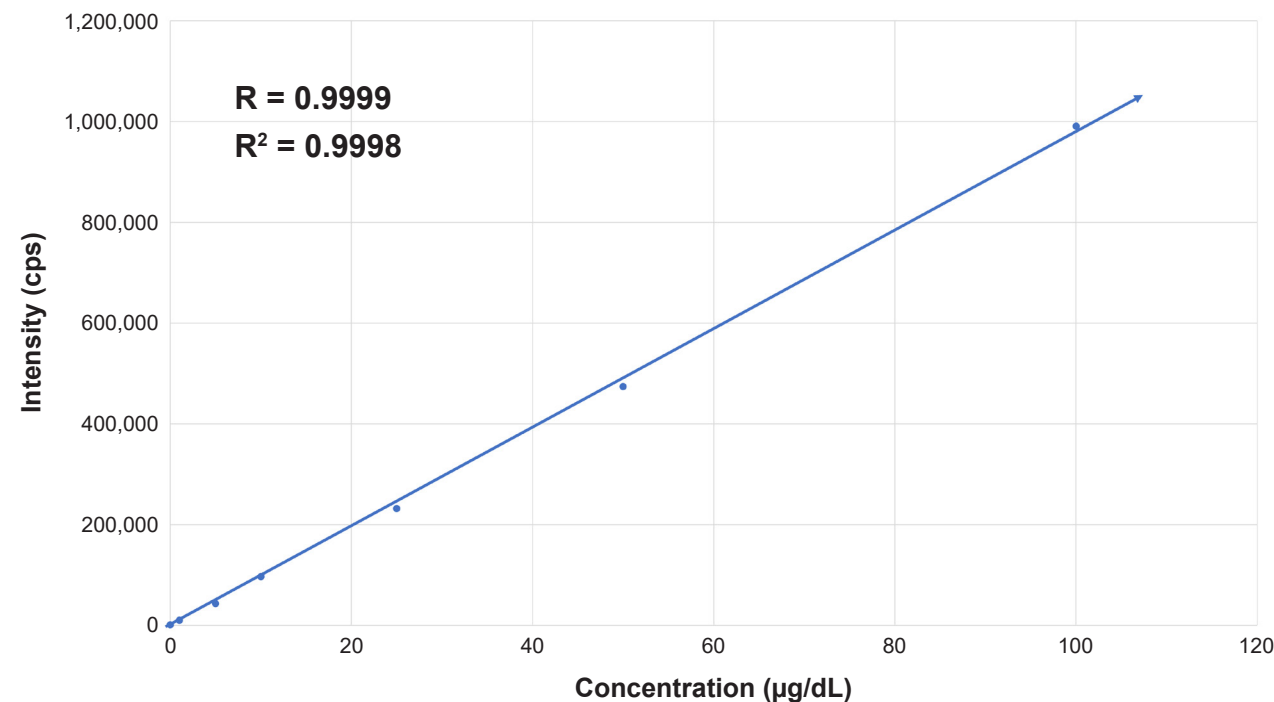


Figure 5. Calibration results demonstrated excellent precision and accuracy for lead when aqueous calibrators were pipetted and prepared using the **TRAXStation Clinical** automated platform. Measured concentrations closely matched target values, and all Correlation Coefficients were 0.999 or better, indicating minimal bias and strong agreement with expected results. Together, these findings validate that **TRAXStation** delivers consistent, contamination-free preparation, ensuring reliable quantitation of lead in clinical testing workflows.

The SampleSense *FAST* UHT-C is engineered for ultra-high-throughput ICPMS analysis while maintaining precise and contamination-controlled sample introduction. Rapid sampling cycles enable fast sample-to-sample analysis, while integrated SampleSense technology verifies sample presence prior to aspiration to prevent missed or incomplete uptake. Optimized rinse routines minimize carryover between samples, supporting accurate measurement across a wide concentration range during long, unattended analytical sequences.



Figure 6. SampleSense *FAST* UHT-C.

Results Summary

The **TRAXStation Clinical** and SampleSense *FAST* UHT-C delivered outstanding accuracy and precision in quantitative testing. Across multiple analytical runs and clinical matrices, results consistently met or exceeded target recoveries, with relative standard deviations well within accepted method criteria. This high level of reproducibility reflects the platform's robust automation, contamination-free fluidics, and stable sample handling – ensuring dependable data quality for high-throughput, ultra-trace ICPMS analyses in demanding clinical laboratory environments.

Additionally, the **TRAXStation Clinical** and SampleSense *FAST* UHT-C demonstrated excellent performance in

carryover and memory-effect studies. Across repeated runs of high-concentration samples followed by negative whole blood samples, both systems maintained extremely low residual signal levels that was well below defined thresholds for clinical trace-element testing.

This performance confirms the system's superior fluidic design, optimized rinse protocols, and effective sample pathway isolation, ensuring negligible cross-contamination even under high-throughput conditions. These findings highlight the platform's reliability for ultra-trace ICPMS applications where accuracy, precision, and contamination control are critical.

Table 7. Lead in whole blood results.

	Level 1 Concentration	Level 2 Concentration	Level 3 Concentration
Average (µg/dL)	3.29	15.00	43.85
Standard Deviation (µg/dL)	0.06	0.40	1.24
Intra-Assay Precision	2.29% CV	1.62% CV	1.52% CV
Inter-Assay Precision	1.85% CV	2.66% CV	2.83% CV

Table 8. Carryover results.

	Spiked Concentration	Negative Concentration	Washout
Carryover	200 µg/dL	15.00 µg/dL	>1000 fold

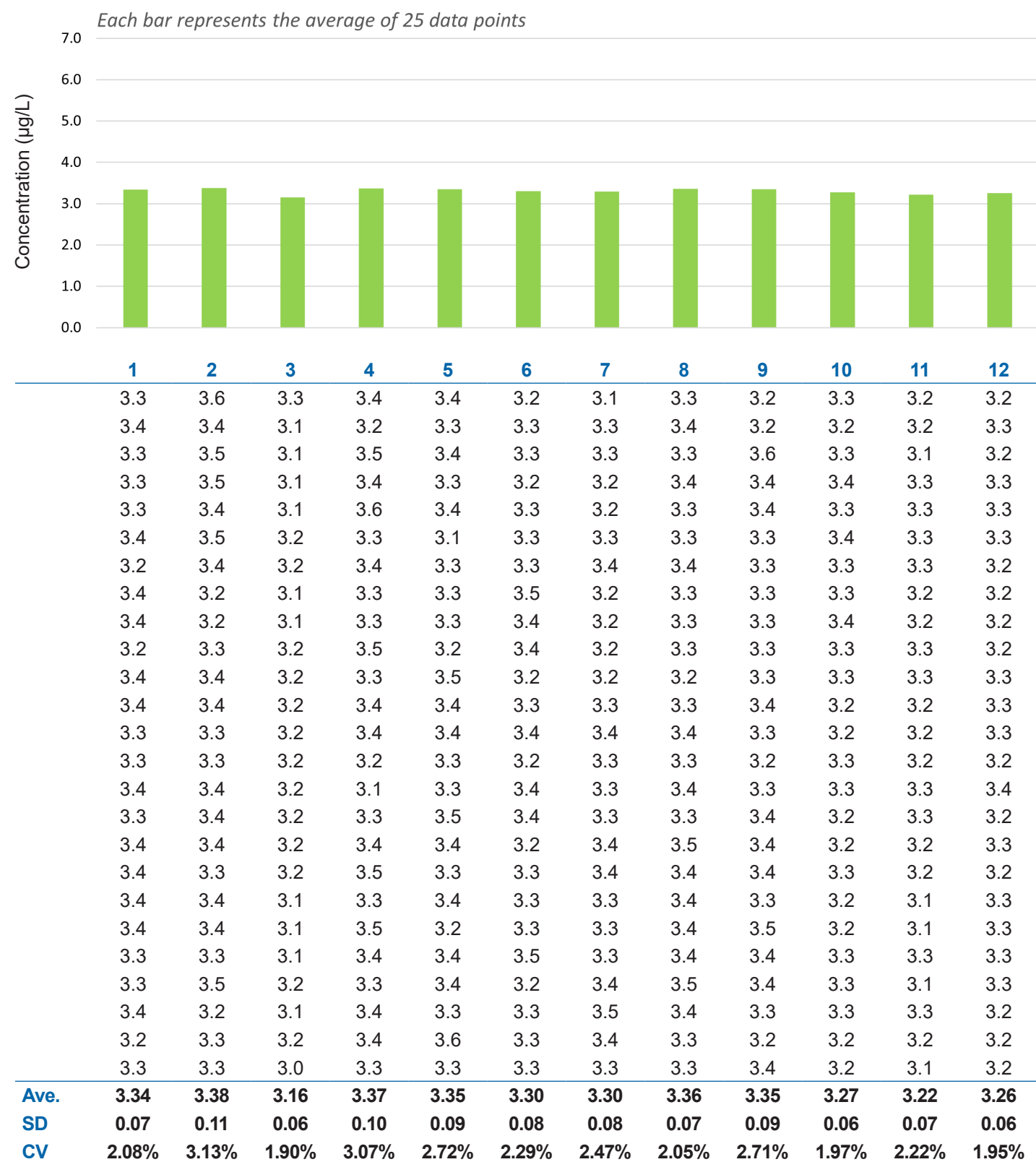
The **TRAXStation Clinical 221** platform is also available. This compact version delivers the full power of automated sample preparation in a small footprint – ideal for laboratories with limited bench space. It automates uncapping, mixing, pipetting, and dilution steps to eliminate manual variability, improve reproducibility, and protect sample integrity through contamination-free, metal-inert processing. With intuitive LabSymphony software, barcode tracking, and flexible rack configurations, the **TRAXStation Clinical 221** integrates seamlessly into existing ICPMS workflows while reducing labor, consumable costs, and operator exposure. Despite its small size, it provides high-throughput performance, superior consistency, and enhanced laboratory safety – all in a compact, efficient design.



Figure 7. **TRAXStation Clinical 221.**

See raw data on the following pages.

Lead Inter and Intra-Assay Data – Level 1 Concentrations (625 data points)



Lead Inter and Intra-Assay Data – Level 1 Concentrations (Continued)

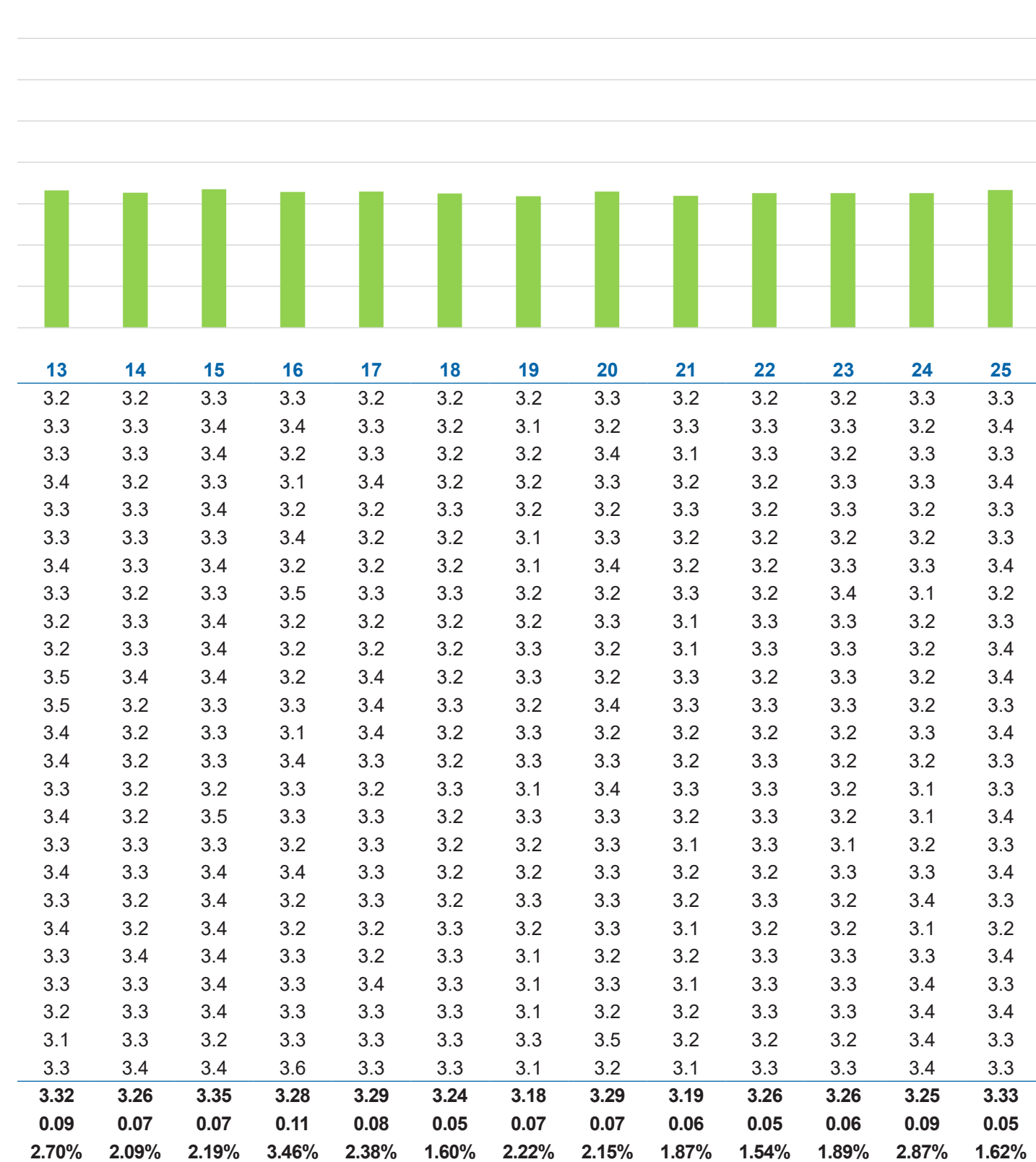
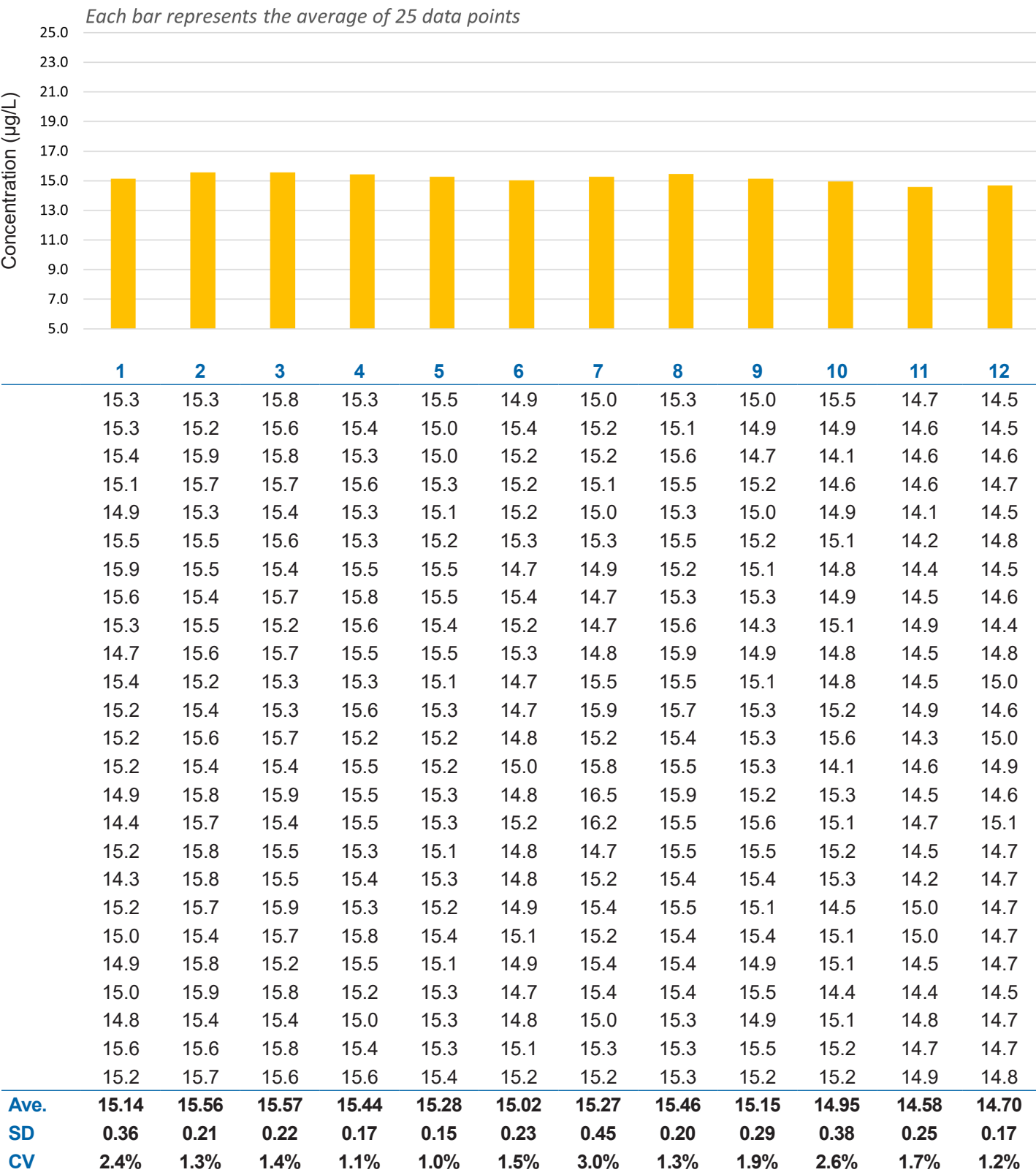


Figure 8. Level 1 concentrations for lead measured by ICPMS (m/z 208 + 207 + 206). Each number 1-25 corresponds to a batch. The graph above shows the average, and the numbers below show the individual sample data from the batch.

Lead Inter and Intra-Assay Data – Level 2 Concentrations (625 data points)



Lead Inter and Intra-Assay Data – Level 2 Concentrations (625 data points) (Continued)

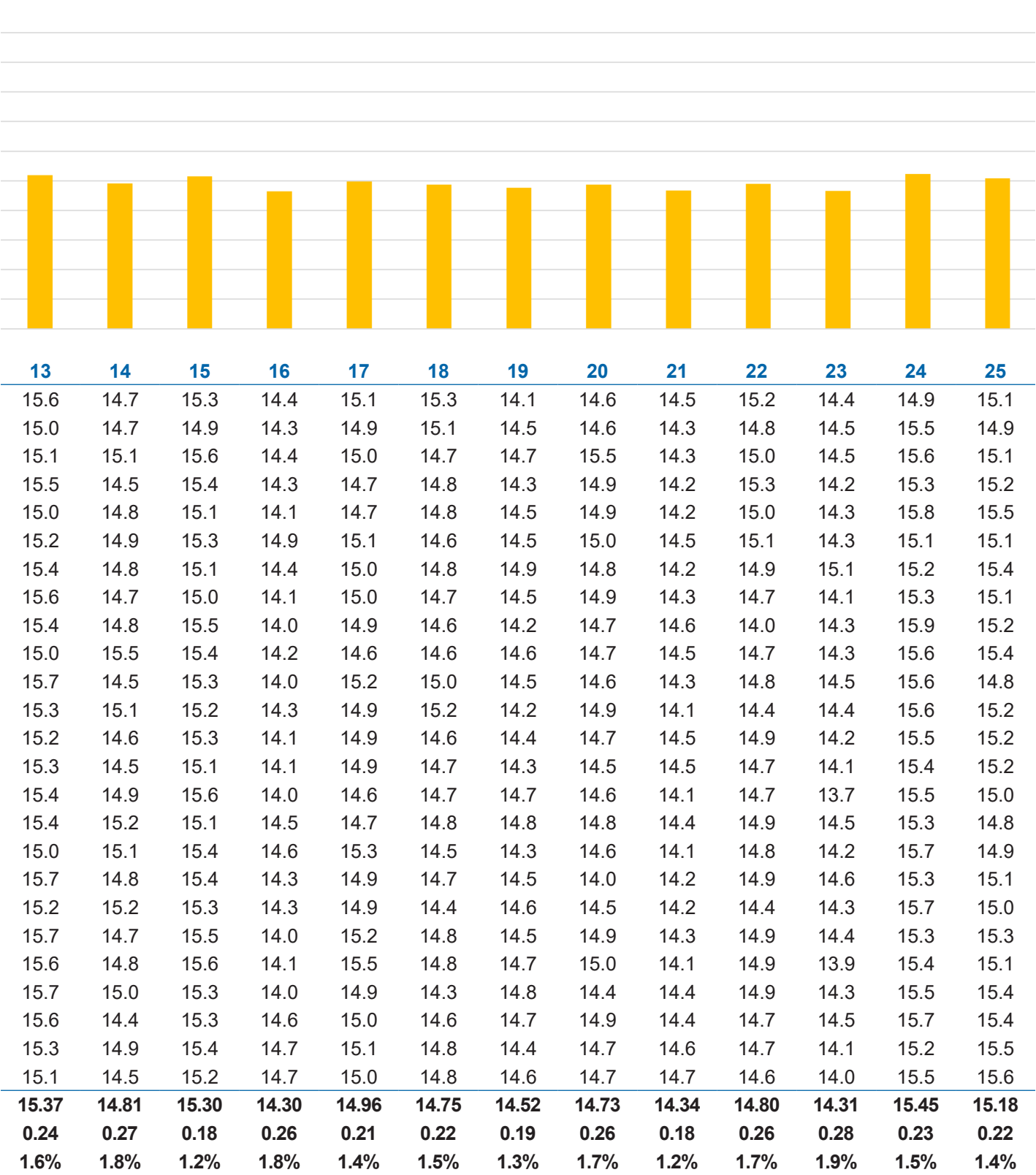
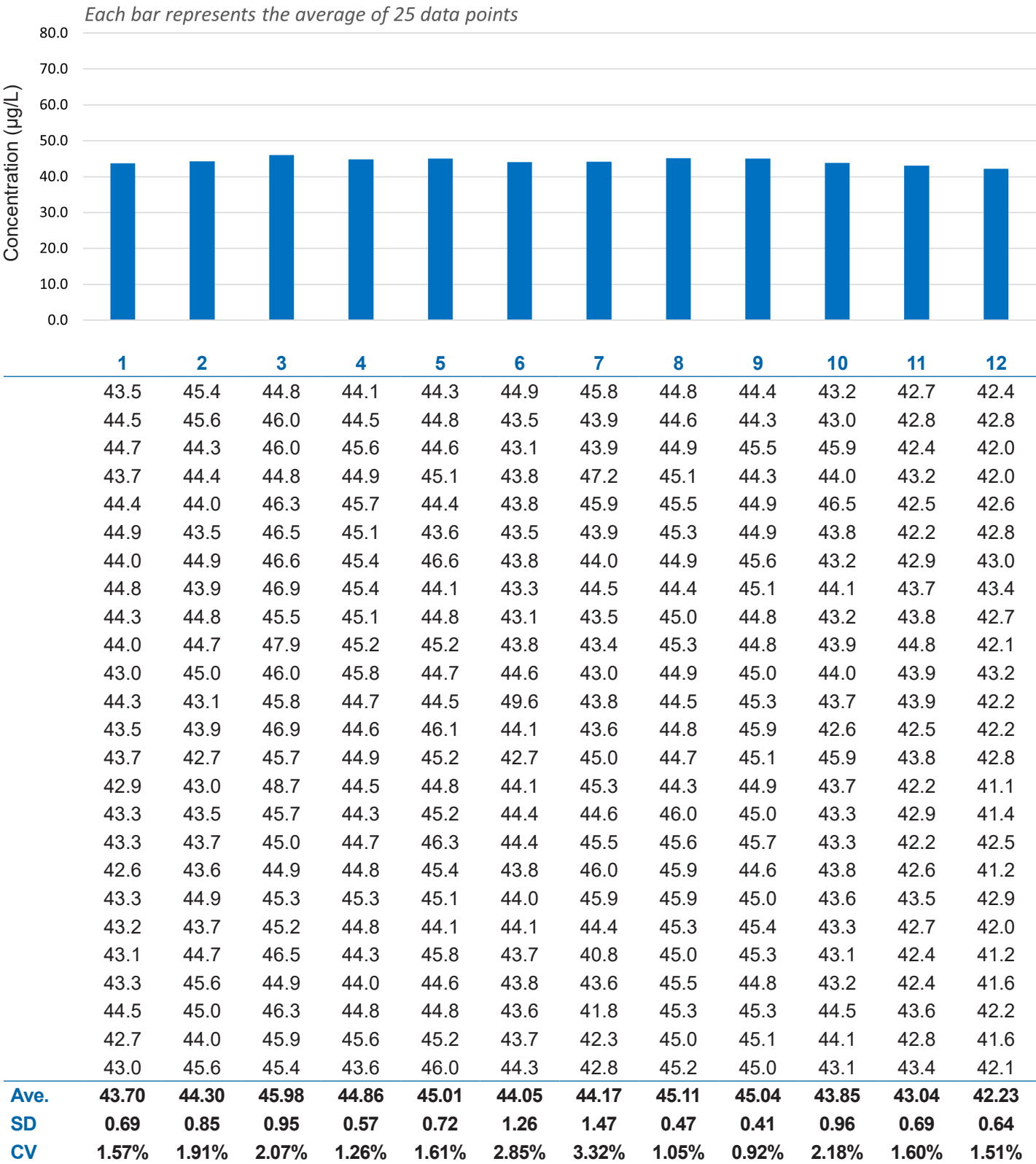


Figure 9. Level 2 concentrations for lead measured by ICPMS (m/z 208 + 207 + 206). Each number 1-25 corresponds to a batch. The graph above shows the average, and the numbers below show the individual sample data from the batch.

Lead Inter and Intra-Assay Data – Level 3 Concentrations (625 data points)



Lead Inter and Intra-Assay Data – Level 3 Concentrations (625 data points) (Continued)

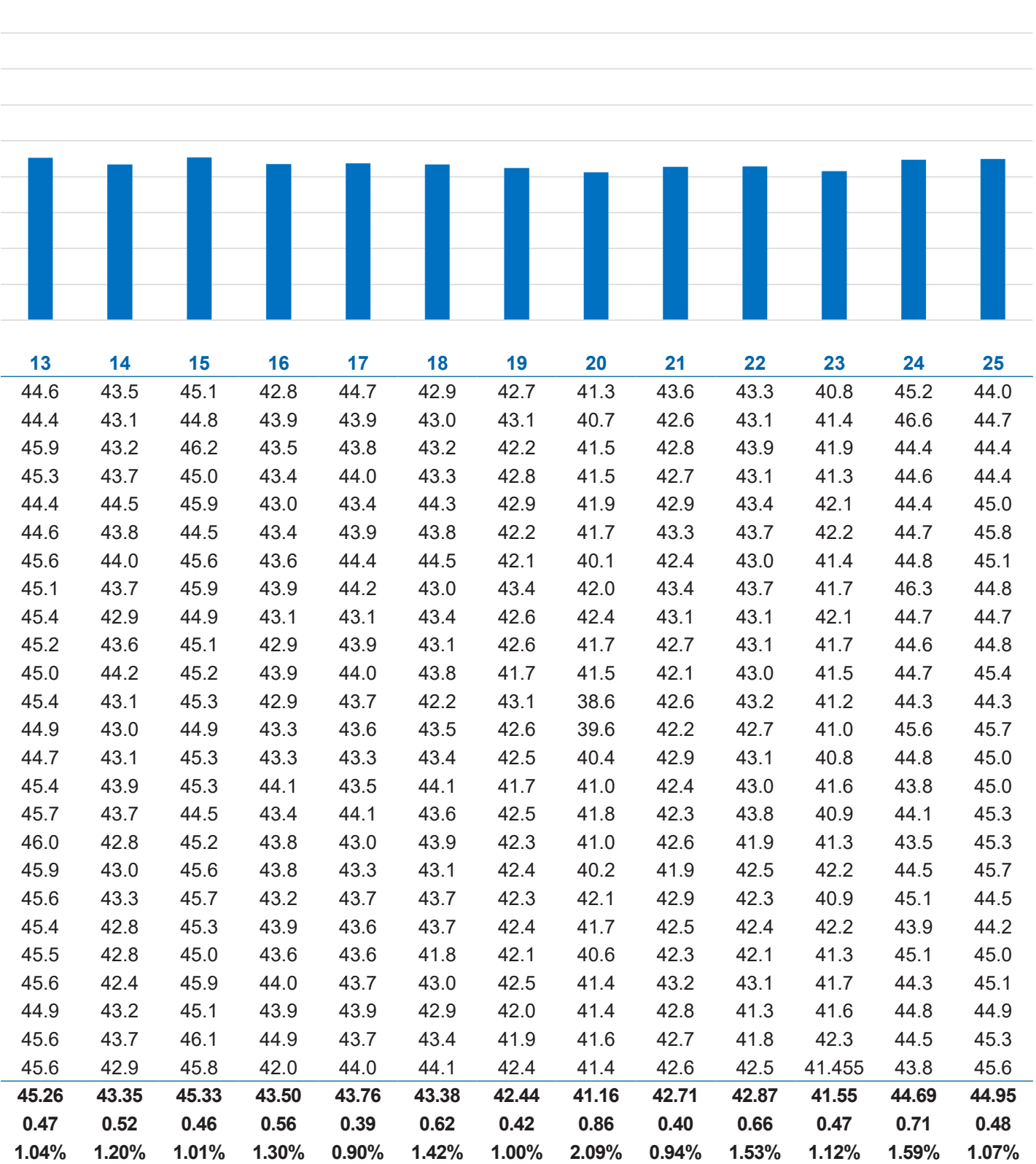


Figure 10. Level 3 concentrations for lead measured by ICPMS (m/z 208 + 207 + 206). Each number 1-25 corresponds to a batch. The graph above shows the average, and the numbers below show the individual sample data from the batch.

Carryover Evaluation

Carryover, or memory effect, represents one of the most critical performance parameters in trace-element analysis by ICPMS. When testing clinical samples at ultra-trace concentrations, even minute residual material from a preceding high-concentration sample can lead to artificially elevated results in subsequent specimens. To ensure analytical integrity, a formal carryover study was performed to assess how effectively the instrument's sample introduction and rinsing systems eliminate residual analytes between each sample analysis.

This study evaluates the **TRAXStation Clinical** and **SampleSense FAST UHT-C** platforms under high-throughput operating conditions typical of clinical trace-metal testing. By challenging the system with high-level spiked whole blood followed by negative blood samples, the carryover performance demonstrates the efficiency of the autosampler's fluidic design, rinse sequence, and sample path isolation. The results provide clear evidence of the system's ability to maintain baseline signals even after exposure to concentrated specimens – confirming that it meets stringent CLIA and CAP validation criteria for analytical specificity and contamination control.

The carryover evaluation was conducted by spiking 26 whole blood samples to a concentration of 200 µg/dL, a level well above the analytical measurement range and representative of an extremely toxic, clinically rare condition. Each spiked sample was processed using the **TRAXStation Clinical** for automated sample preparation and immediately followed by a negative whole blood sample to assess potential residual contamination. Analytical measurements were performed by ICPMS utilizing the **SampleSense FAST UHT-C**.

The measured values for all negative samples are shown in the graph. They represent potential carryover with an average of 0.15 µg/dL, which represents a signal more than 1,000-fold lower than the spiked sample concentration and well below the method's lower reporting limit of 1 µg/dL. These results demonstrate that the **TRAXStation Clinical** and **SampleSense FAST UHT-C** systems provide exceptionally effective and rapid rinsing performance, ensuring minimal memory effects and high analytical integrity even when challenged with extreme sample concentrations.

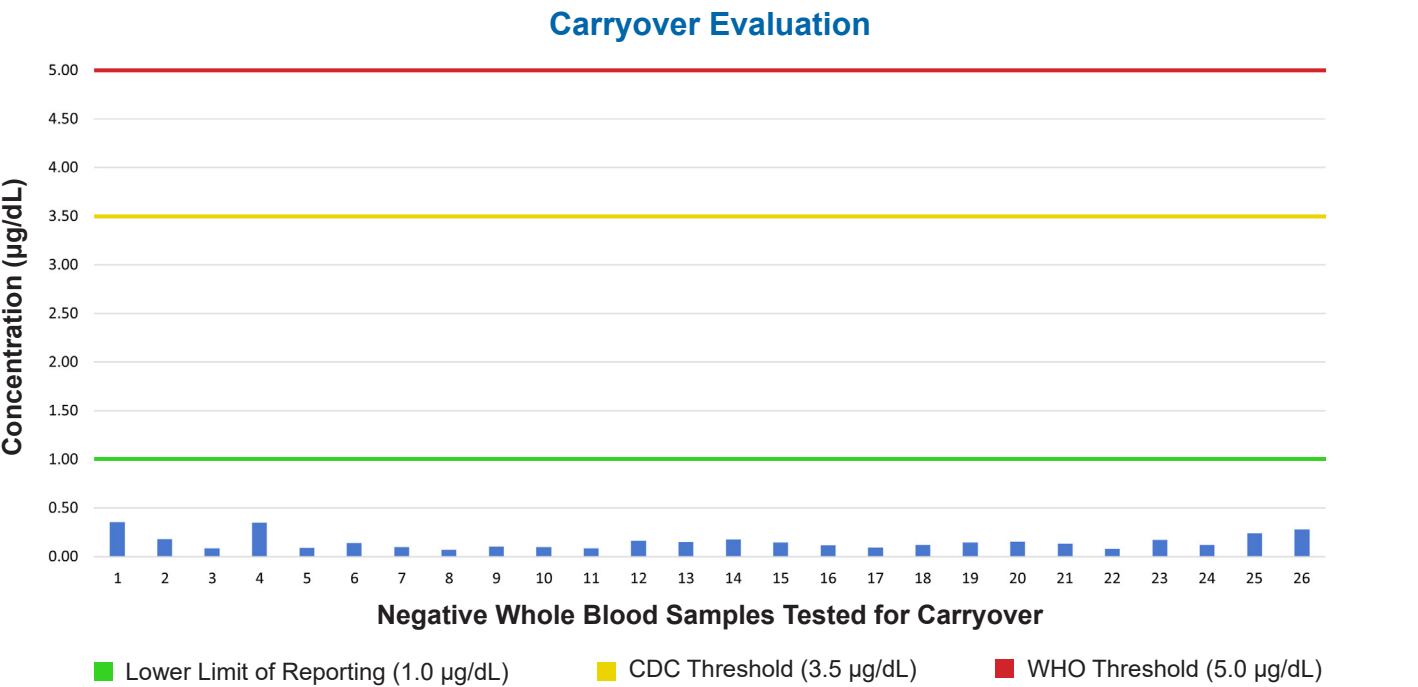


Figure 11. Carryover assessment following high-concentration of lead in whole blood samples.

Conclusion

The **TRAXStation Clinical Automated Multifunctional Liquid Handling System** demonstrated performance that surpassed expected analytical targets for both accuracy and precision. Measured values consistently aligned with target concentrations over extended periods of time, indicating minimal systematic error and confirming high method accuracy. Replicate analyses showed very low variability, with relative standard deviations well below

acceptance criteria, reflecting exceptional precision. Carryover evaluation further demonstrated no detectable sample-to-sample carryover, confirming effective contamination control throughout the automated workflow. Collectively, the data provides strong evidence of method robustness and reliability, exceeding established quality benchmarks and reinforcing confidence in both the measurement process and resulting conclusions.

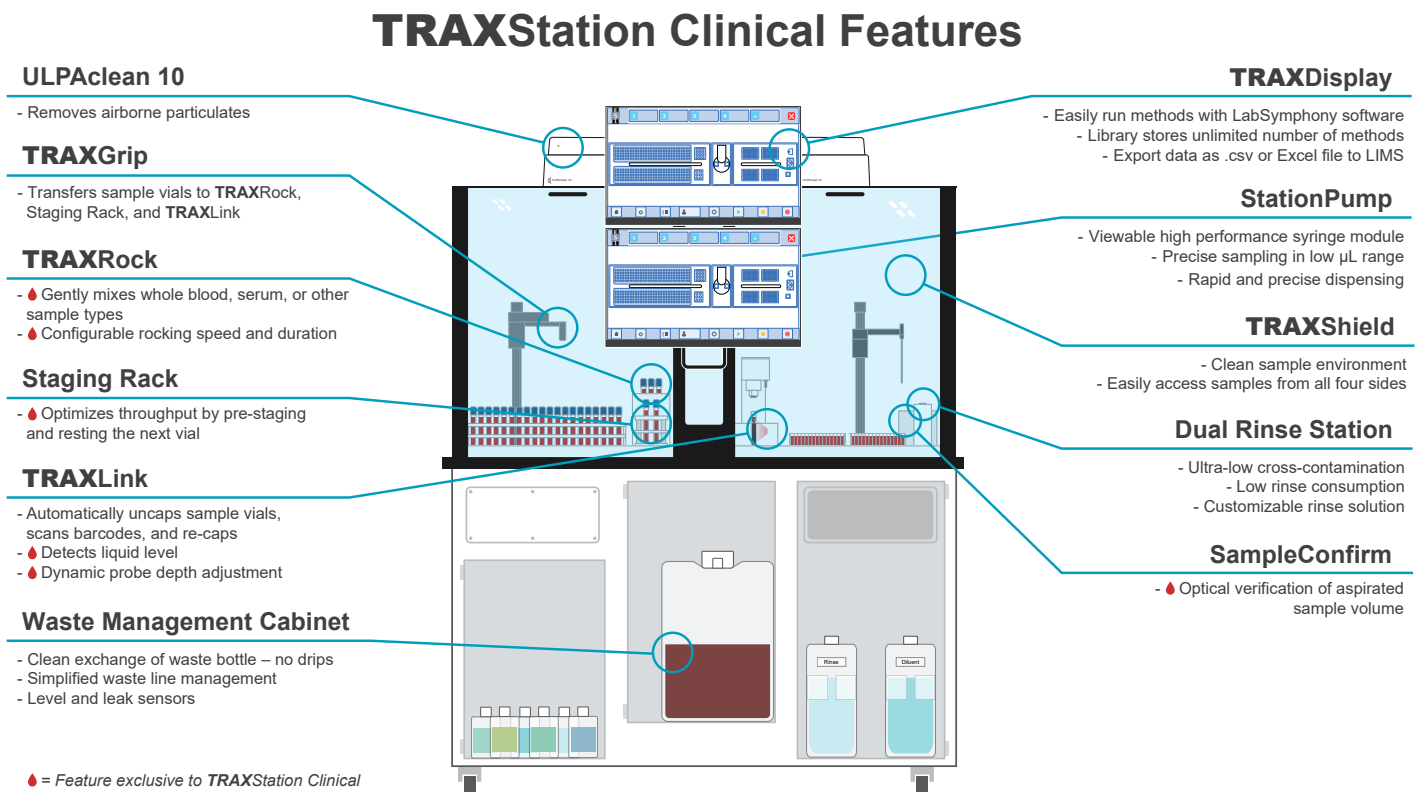


Figure 12. **TRAXStation Clinical** features diagram. **TRAXStation Clinical** is available in several models and configurations to match laboratory methods and throughput requirements. These include **TRAXStation 221**, **422**, and **442** models.



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