CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW240006

II. Parent Document Number

K240402

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

CytoChip Inc.

V. Proprietary and Established Names

Cito CBC System

VI. Measurand (analyte)

WBC, RBC, HGB, HCT, MCV, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, and BASO%/#

VII. Sample Type(s)

Venous whole blood anticoagulated with K_2EDTA

VIII. Type of Test

Complete blood count (WBC, RBC, HGB, HCT, MCV, PLT) and leukocyte 5-part differential (NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, and BASO%/#)

IX. Test System Description

A Overview

The Cito CBC system is an automated hematology analyzer that is intended to analyze K_2EDTA venous human whole blood, and report results of 16 hematology parameters. The system consists of a tabletop analyzer, the Cito CBC Analyzer, and a disposable test cartridge, the Cito CBC

Cartridge. The analyzer includes software with Graphic User Interface to guide users through the test procedure. To perform a test, the test cartridges and other test consumables are provided as a test kit. The Cito CBC system utilizes the principle of fluorescent flow cytometry for cell count and cell classification. A laser is used as the light source, and fluorescence and light scattering signals are detected for the measurements. For fluorescent labeling, blood cells are treated with a fluorescent dye that has high affinity binding to nucleic acid. Additionally, the analyzer utilizes the principle of two-wavelength photometry for the measurement of the hemoglobin. Blood cells are lysed to release hemoglobin. Meanwhile, the light scattering signal measured from the flow cytometry and the light absorption signals measured from the photometry are both used to quantify the hematocrit and mean cell volume.

B Test System Components

- Cito CBC Analyzer: a tabletop instrument
- Cito CBC Cartridge Kit:
  - Cartridge (individually packaged in a foil pouch, self-contained, disposable and single use)
  - Dispenser
  - Alcohol Pad
  - Sealing Card

C Results Interpretation

The Cito CBC System provides an option to obtain a printout of patient results at the completion of each sample analysis. Results are printed along with the reference range for the indicated age of the patient by the analyzer system. Analyzer reference ranges are defined by the manufacturer and cannot be modified by the operator. The operator is instructed to provide the results to the clinician; therefore, no result interpretation is performed by the operator. The clinician makes a decision on the triage and treatment of the patient based on interpretation of the results and within the context of the patient's clinical presentation. The Cito CBC System provides the following results for all specimens: Normal result or Suppressed result.

The Cito CBC System software uses various rules that regulate result suppression. These rules include:

- Suppression of parameter results when a sample flag is present that potentially affects accuracy of the parameter.
  - System analysis of the test results will detect the presence of some pre-analytical sample conditions such as lipemia, abnormal RBC scattergram, etc. When the condition is detected, the system generates a flag, and the associated results are suppressed.
- Suppression of parameter results when a value is out of reportable range, as shown in the table below.

Reference ranges, Suppressed Low, and Suppressed High values are illustrated in the table below.

Parameter	Suppressed Low	Reference Range	Suppressed High
WBC (10^3/μL)	< 3.00	4.17–10.54	> 50.0
RBC (10^6/μL)	< 2.00	4.00–5.74	> 8.25
PLT (10^3/μL)	< 100	179–413	> 750
HGB (g/dL)	< 10.0	11.1–16.8	> 24.0
HCT (%)	< 25.0	35.5–49.8	> 70.0
MCV (fL)	< 65.0	82.4–96.8	> 115
NEUT (10^3/μL)		1.65–6.75	
LYMPH (10^3/μL)		1.10–3.50	
MONO (10^3/μL)		0.29–1.00	
EO (10^3/μL)		0.04–0.42	
BASO (10^3/μL)		0.00–0.11	
NEUT% (%)		37.3–72.8	
LYMPH% (%)		17.4–49.1	
MONO% (%)		4.9–13.5	
EO% (%)		0.6–5.8	
BASO% (%)		0.1–1.6	

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

The table below demonstrates how the Cito CBC System is simple per the FDA guidance *Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices (FDA, 2020)*.

Guidance Criteria	How Addressed on the Cito CBC System
Is a fully automated instrument or a unitized or self-contained test.	The device uses a self-contained cartridge with on-board reagent for the test. The cartridge is inserted into the analyzer for automated sample analysis.
Uses direct unprocessed specimens, such as capillary blood (fingerstick), venous whole blood, nasal swabs, throat swabs, or urine.	The system uses venous whole blood from standard vacuum blood collection tubes with K_2EDTA anticoagulant.
Needs only basic, non-technique-dependent specimen manipulation, including any for decontamination.	User follows basic operations including: - invert blood tube to mix the sample. - insert a dispenser tip through the tube cap. - dispense blood by pressing the dispense tip at cartridge inlet. - wipe cartridge inlet with an alcohol wipe. - close the inlet seal by swiping. - insert cartridge into the analyzer to start a test. - remove cartridge from the analyzer after test.
Needs only basic, non-technique-dependent reagent manipulation, such as "mix reagent A and reagent B".	All reagents are pre-packaged in the cartridge. No reagent manipulation is needed by the user.
Needs no operator intervention during the analysis steps.	After the cartridge is inserted into the analyzer, sample analysis is completed without operator intervention.

Guidance Criteria	How Addressed on the Cito CBC System
Needs no technical or specialized training with respect to troubleshooting or interpretation of multiple or complex error codes.	Technical or specialized training is not required for troubleshooting or error code interpretation. If an error code is shown, simple on-screen instructions are provided to the operator.
Needs no electronic or mechanical maintenance beyond simple tasks, e.g., changing a battery or power cord.	There is no maintenance required other than basic cleaning of the external surfaces of the analyzer. No electronic or mechanical maintenance is required.
Produces results that require no operator calibration, interpretation, or calculation.	System provides direct readout of quantitative results, and the operator never performs calibration or calculation. Results are printed with the associated reference intervals with no operator involvement. The reference intervals are not editable by the operator.
Produces results that are easy to determine, such as 'positive' or 'negative', a direct readout of numerical values, the clear presence or absence of a line, or obvious color gradation.	Results are printed as numeric values or percentages.
Includes quick reference instructions (Quick Reference Guide, Operator's Instrument Manual (if applicable), etc.) that are written at no higher than a 7th grade reading level.	The Quick Reference instructions are written at a 7th grade comprehension level.

In addition, the table below demonstrates how the Cito CBC System is simple by not having the following characteristics.

Guidance Criteria	How Addressed on the Cito device
Sample manipulation is required to perform the assay. Sample manipulation includes processes such as centrifugation, complex mixing steps, or evaluation of the sample by the operator for conditions such as hemolysis or lipemia.	The system requires only that the specimen to be collected using correct phlebotomy technique, and the blood inside the blood collection tube to be mixed properly following on-screen prompts.
Measurement of analyte could be affected by conditions such as sample turbidity or cell lysis	Some patient samples will generate a flag caused by sample abnormalities. In such cases, a warning message of the flag will be presented, and the affected parameter results will be suppressed.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   A risk analysis was performed and focused on the following: human factor/operator errors, specimen integrity, cartridge integrity, hardware and electronics integrity, software integrity, test flow integrity, stability of external QCs and internal controls, and environmental factors. All risks of harm to the patient or operator were mitigated to an acceptable level and were supported by flex studies and/or operator instructions.

2. Fail-Safe and Failure Alert Mechanisms:

Based on the risk analysis, a series of fail-safe and failure alert mechanisms have been implemented as risk control measures, which are organized into the following categories:

A. Instrument Design
   - Mechanical guide to prevent inserting cartridge in wrong orientation.
   - Mechanical push seal to close cartridge inlet to mitigate the risk of inlet seal not being closed by user.
   - Sensor to alert if insufficient blood volume collected in cartridge and abort test.
   - Sensor to detect if the cartridge insertion lid is not closed or opened during test and abort test.
   - Sensor to monitor environmental temperature and suppress test function if temperature out of range.

B. Cartridge Design
   - Cartridge sample collection is only one-time use to prevent reuse of cartridges.
   - Capillary valve at the blood collection channel to prevent blood overloading.
   - Barcode with expiration date to prevent use of expired cartridge.
   - Filter in pneumatic ports to prevent aerosol leak from cartridge into instrument

C. System Self-Check
   - System performs self-check periodically and locks out test function if self-check fails.
   - System checks key hardware parameters during each test run, and abort test if failure detected (e.g., pneumatic build time).
   - System checks cartridge before each test run, and abort test if failure is detected (e.g., sensing window scratched or dirty).

D. Cartridge Built-In QC
   - Cartridge contains micro beads as build-in QC, and check if detection module works properly.
   - Failure of QC beads detection will suppress test result.

E. External QC Design
   - Barcode with expiration date to prevent use of expired QC controls.

F. Test Flow Monitoring
   - System uses sensors to monitor the test flow inside the cartridge for each test run.
   - Monitoring checks a series of key steps of the test flow (e.g., flow time, excessive bubbles, mixing uniformity, etc.).
   - Abnormality in any key step will either abort the test run or suppress the test result.

G. Result Suppression Rule
   - System checks the quality of the measurement signals (e.g., baseline fluctuation of cytometer signal) for each test run.
   - Abnormality of signal will suppress the impacted test result.
   - System will suppress the test result if sample abnormalities are detected (for example: significant hemolysis, lipemia, etc.)

H. Software Design

For each risk category, the implemented fail-safe and failure alert mechanisms are summarized below:

i. Human Factor/Operator Errors
   - Instrument Design
   - Cartridge Design
   - System Self-Check

ii. Specimen Integrity
   - Result Suppression Rules

iii. Cartridge Integrity
   - Cartridge Design
   - System Self-Check

iv. Hardware and Electronics Integrity
   - Cartridge Design
   - System Self-Check
   - Cartridge Built-in QC

v. Test Flow Integrity
   - Test Flow Monitoring
   - Result Suppression Rules

vi. Stability of QC Controls and Internal Controls
   - External QC Design

vii. Environmental Factors
   - Instrument Design

The fail-safe and failure alert mechanisms also included points to consider based on the 2020 CLIA Waiver Guidance, which includes the following:

- Lock-out functions that do not allow output of results if controls or system checks are not successfully completed
- Lock-out functions that do not allow output if expired reagents are used
- Lock-out functions that do not allow output of results if the device was mishandled (e.g., dropped) and the device detects damage during internal electronic system checks
- Physical features to ensure correct placement of components, such as strips or cartridges
- Monitors of environmental conditions (e.g., indicator desiccants) incorporated into the test system or the kit container to alert the user to environmental conditions that are outside of the recommended storage conditions
- Battery checks
- Internal procedural controls to flag procedural problems such as improper sample flow, incorrect use of components, or improper addition of specimen. (However, procedural

controls generally provide limited problem detection and, by themselves, are generally not sufficient to serve as a failure alert mechanism.)
- Internal non-procedural controls (e.g., for checking the integrity of the reagents)
- Controls to check that electronic features of the device are within specifications

3. Flex Studies:

Flex studies were conducted in order to assess how effectively the instrument operational checks, the quality control requirements, and the flagging/suppression rules would prevent release of erroneous results.

Acceptance Criteria

Based on the study design, the various flex studies were conducted using QCs or whole blood samples. For each study condition, the results for each parameter must fall within the acceptable limits. Criteria for QCs or whole blood samples required that the test conditions versus the control or baseline result fall within the acceptance criteria in the table below:

Parameter	Acceptance Criteria (%bias)
WBC ($x10^3/\mu L$)	±5%
RBC ($x10^6/\mu L$)	±5%
HGB (g/dL)	±5%
HCT (%)	±5%
PLT ($x10^3/\mu L$)	±5%
MCV (fL)	±5%
Parameter	**Acceptance Criteria (Total error)**
NEUT ($\times10^3/\mu L$)	±15% if CM>4.7 ±0.7 if CM≤4.7
LYMPH ($\times10^3/\mu L$)	±15% if CM>3.3 ±0.5 if CM≤3.3
MONO ($\times10^3/\mu L$)	±0.5
EO ($\times10^3/\mu L$)	±0.5
BASO ($\times10^3/\mu L$)	±0.5

* CM = comparator method

Category 1: Operator error/Human factors

Flex Study 1: Incorrect Sample Dispensing
To dispense blood from blood tube to test cartridge, the Quick Reference Guide (QRG) instructs users to "apply downward pressure on the vial to release the sample, until it fills up to the [blue triangle] marker on the view window". This study was performed to evaluate the risk of erroneous results when incorrect blood dispensing procedures were conducted.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (remove vial before sample filled in the view window), all replicates of two samples triggered result suppression and one sample reported either acceptable or suppressed results (e.g. triggered the fail-safe mechanism for "under-fill").
- For experiment group 2 (remove vial after the blood filled in the view window but before filled up to the marker), all samples reported either acceptable or suppressed results.
- For experiment group 3 (remove vial 30 seconds after the blood filled up to the marker), all samples reported either acceptable or suppressed results.
- For the over-fill evaluation group (purposely pushing sample past the marker), all samples triggered result suppression (e.g. triggered the fail-safe mechanism for "over-fill").

The results demonstrate that incorrect sample dispensing procedures poses insignificant risks of erroneous results. Additionally, the results also validate the fail-safe mechanism for impropriate user operation of "under-fill" and "over-fill".

Flex Study 2: Multiple Blood Drops Dispensing
The Quick Reference Guide (QRG) instructs users to "apply downward pressure on the vial to release the sample, until it fills up to the [blue triangle] marker on the view window". This instruction utilizes one-time dispensing. This study was performed to evaluate the risk of variation for multiple times of dispensing, under following conditions:

- Control group: User performed the blood dispensing step once according to QRG.
- Experiment group 1: User performed the blood dispensing step twice.
- Experiment group 2: User performed the blood dispensing step three times.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (dispensing for two times), all samples reported acceptable results.
- For experiment group 2 (dispensing for three times), all samples reported acceptable results.

The results demonstrate that dispensing blood samples multiple times on the cartridge inlet port poses insignificant risks of erroneous results.

Flex Study 3: Sample Volume
The Quick Reference Guide (QRG) instructs users to "apply downward pressure on the vial to release the sample, until it fills up to the [blue triangle] marker on the view window". This dispensing step would normally dispense 15 to 20 µL blood on the cartridge inlet port. This study was performed to evaluate the risk of volume variation that too much or too little blood was dispensed.

Results
Three samples (one normal, two abnormal) are tested, evaluated against a control group, for 5 replicates for each group.
- For experiment group 1 (dispensing 60 µL of blood sample), all three samples reported acceptable results.

- For experiment group 2 (dispensing 7 μL of blood sample), all three samples reported suppressed results.

These results demonstrate that the variation of the dispensed sample volume (7 μL to 60 μL) poses insignificant risk of erroneous results.

Flex Study 4: Incorrect Inlet Port Wiping
After blood dispensing, the QRG instructs users to perform a wiping step that removes blood residue from the Inlet Port. The instructed wiping action is to perform one wipe with the alcohol pad included in the test kit. The purpose of this study is to evaluate the variation of this wiping step.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (no wipe), all three samples reported acceptable results.
- For experiment group 2 (wipe for 2 times), all three samples reported acceptable results.
- For experiment group 3 (wipe for 5 times), all three samples reported acceptable results.

The results demonstrate that variation of the wiping step poses insignificant risks of erroneous results.

Flex Study 5: Incorrect Inlet Port Sealing
After wiping the inlet port to remove blood sample residue, the Quick Reference Guide (QRG) instructs users to seal the inlet port by the following procedures: 1) remove the plastic liner from the inlet seal, and 2) use the sealing card (provided in the cartridge kit box) to seal the inlet. This study was performed to evaluate the risk when users perform incorrect sealing procedures.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (not removing the plastic liner), all three samples either reported acceptable results or suppressed results.
- For experiment group 2 (sealing the inlet port by gentle finger pressing), all three samples either reported acceptable results or suppressed results.
- For experiment group 3 (sealing the inlet port by excessive finger pressing), all three samples either reported acceptable results or suppressed results.

The results demonstrate that performing incorrect inlet port sealing procedures poses insignificant risks of erroneous results.

Flex Study 6: Delay to Start Testing After Readying Cartridge
After completing the inlet port sealing procedures, the cartridge is ready for testing and the QRG instructs users to insert cartridge into the analyzer to start the testing. This study was performed to evaluate the risk of variation in time gap between readying cartridge and starting test.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (wait for 2 minutes to start testing), all samples reported either suppressed or acceptable results.
- For experiment group 2 (wait for 5 minutes to start testing), all samples reported either suppressed or acceptable results.
- For experiment group 3 (wait for 10 minutes to start testing), all samples reported either suppressed or acceptable results.

The results demonstrate that variation in time gap between preparing the cartridge and starting the test (up to 10 minutes) poses insignificant risks of erroneous results.

Flex Study 7: Slow Analyzer Lid Closing
After inserting the cartridge into the analyzer, QRG instructs users to close the analyzer lid in a quick motion to start the test. The action of closing the lid normally takes less than 3 seconds. The purpose of this study is to evaluate the risk of slower lid closing motion.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For group 1 (lid closing within 5–10 seconds), all three samples reported acceptable results.
- For group 2 (lid closing within 10–20 seconds), all three samples reported either acceptable or suppressed results.

The results demonstrate that slower lid closing poses insignificant risks of erroneous results.

Category 2: Specimen Integrity and Handling

Flex Study 8: Incorrect Sample Mixing
Before dispensing sample from the blood vial, the Quick Reference Guide (QRG) instructs users to “invert the vial 10 times to mix the sample”. This study was performed to evaluate the risk of using the blood samples that were inverted for incorrect times.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (invert for 0 time), the test results of all samples failed the acceptance criteria.
- For experiment group 2 (invert 5 times), the test results of all samples passed the acceptance criteria.
- For experiment group 3 (invert 15 times), the test results of all samples passed the acceptance criteria.
- For experiment group 4 (invert 50 times), the test results of all samples passed the acceptance criteria.

The results demonstrate that testing performed using blood samples that are inverted 5 to 50 times poses insignificant risks of erroneous results. However, using blood samples that are not inverted before sample dispensing may cause erroneous results and should be avoided. To mitigate the risk, the following mitigations are implemented: 1) the QRG provide step-to-step guidance for the test procedure, and one step requires users to invert the blood vial 10 times before test; 2) the software Graphic User Interface (GUI) provides step-by-step guidance, and one step reminds users to invert the blood vial 10 times before test; 3) the QRG require new operators to pass QC test first, which relies on correct mixing, to be qualified for patient sample testing (flex study 27).

Flex Study 9: Delay Between Sample Mixing and Dispensing
After mixing the samples, the Quick Reference Guide instructs users to dispense blood sample on the cartridge inlet port, which normally takes less than 1 minute. This study was performed to evaluate the risk of a delay between sample mixing and dispensing.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (dispensing samples 5 minutes after mixing), all 3 samples reported acceptable results.
- For experiment group 2 (dispensing samples 15 minutes after mixing), all 3 samples reported acceptable results.
- For experiment group 3 (dispensing samples 30 minutes after mixing), 1 sample reported either acceptable or suppressed results, and 2 samples reported results not meeting acceptance criteria.

The results demonstrate that using blood samples that are dispensed with delay (e.g. within 15 minutes) from sample mixing poses insignificant risks of erroneous results. However, dispensing blood samples with prolonged delay (e.g. after more than 30 minutes) may cause erroneous results and should be avoided. To mitigate this risk, the following mitigation is implemented: 1) the software Graphic User Interface (GUI) provide step-to-step guidance, and one step reminds users to dispense the samples within 5 minutes after mixing, and 2) a software timer is used to track if the delay exceeds 5 minutes, which triggers the GUI to report an error alert that requires user to start a new test.

Flex Study 10: Cold Sample
The QRG instructs users to either store samples at room temperature or to warm up samples at room temperature for at least 10 minutes if the samples are stored in a 2–8°C. This study was performed to evaluate the risk of using refrigerated samples without adequate warm-up at room temperature before testing.

Results
Three samples (one normal, two abnormal) were tested for each experiment group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to that of the control group. All three samples reported acceptable results for WBC, RBC, PLT, HGB, HCT, MCV, and WBC Diff in the experiment group. The results demonstrate that testing

refrigerated samples without adequate warm-up at room temperature poses an insignificant risk of erroneous results.

Flex Study 11: Sample Freeze-and-Thaw
The Cartridge Insert instructs users to store the blood sample either at room temperature or at 2°C-8°C refrigerator. The purpose of this study is to evaluate the risk of using samples improperly stored at freezing condition.

Results
Three samples (one normal, two abnormal) were tested for each experiment group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to that of the control group. All test replicates of three samples reported suppressed results for WBC, RBC, PLT, HGB, HCT, MCV, and WBC Diff in the experiment group. The study demonstrates that using samples subjected to one freeze-thaw cycle leads to result suppression and poses insignificant risks of erroneous results.

Flex Study 12: Sample stability
The Quick Reference Guide (QRG) instructs users to test blood specimens within 8 hours from blood draw, and the blood specimens should be stored at room temperature or refrigerated temperature. To evaluate the risk of using aged specimens, blood specimens were tested after storage for different time durations at room and refrigerated temperatures.

Results
Three samples (one normal, two abnormal) were tested for each group. The samples were tested for 5 replicates, and the test results of the experiment groups were compared to that of the control group.

For samples stored at room-temperature condition (15–25°C), both group 1-1 (8.5-hour storage) and group 1-2 (10.5-hour storage) reported acceptable results. For samples stored at refrigerated-temperature condition (2–8°C), both group 2-1 (8.5-hour storage) and group 2-2 (10.5-hour storage) reported either acceptable or suppressed results.

Results from this study demonstrate that using the aged specimens (up to 10.5 hours from blood draw) that are stored at room temperature or refrigerated temperature poses insignificant risks of erroneous results.

Flex Study 13: Improper Anticoagulant
The Quick Reference Guide (QRG) instructs users to use venous whole blood with K_2EDTA anticoagulant. This study was conducted to evaluate the risk of using samples collected in blood tubes with improper anticoagulants.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (blood samples collected in K_3EDTA anticoagulant blood collection tubes), all three samples reported acceptable results.

- For experiment group 2 (blood samples with sodium citrate blood collection tubes), the reported results exceed the acceptance criteria for WBC, PLT and NEUT.
- For experiment group 3 (blood samples with sodium heparin blood collection tubes), the reported results exceed the acceptance criteria for PLT.
- For experiment group 4 (blood samples with serum separator tubes), all three samples reported suppressed results, which is acceptable.

These results demonstrate that 1) blood tube anticoagulated with K_3EDTA pose insignificant risk of erroneous results; and 2) using other types of blood collection tubes should be avoided (i.e., sodium citrate, sodium heparin and serum separator). To reduce the risk of using an incorrect blood collection tube type, the following mitigations have been implemented: 1) QRG requires users to use only K_2EDTA anticoagulated blood tube, 2) the test workflow in the QRG includes a step that requires the user to check the blood collection tube type (i.e., the tube cap is purple in color, with K_2EDTA as anticoagulant); 3) the Graphic User Interface of the software includes a step that requires users to check the blood collection tube type (i.e., the tube cap is purple in color, with K_2EDTA as anticoagulant).

Category 3: Reagent Integrity

Flex Study 14: Cartridge Drop on the Floor
The Cartridge Insert instructs the users not to use cartridges that are dropped on the floor. This study was performed to evaluate the risk of using dropped cartridges.

Results
Three samples (one normal, two abnormal) were tested for each experiment group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (cartridge drop before loading blood sample), all three samples reported acceptable results.
- For experiment group 2 (cartridge drop after loading blood sample), all three samples reported acceptable results.

The results demonstrate that using cartridges dropped on the floor (e.g. from bench height) before or after loading blood samples poses insignificant risks of erroneous results.

Flex Study 15: Cartridge Freeze and Thaw
The Cartridge Insert instructs users to store cartridges at room temperature and do not freeze the cartridges. This study was performed to evaluate the risk of using cartridges improperly stored at freezing condition.

Results
Three samples (one normal, one abnormally low, and one abnormally high) were tested for the experiment group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to that of the control group. All three samples reported either acceptable or suppressed results in the experiment group. The results demonstrate that using cartridges that are subjected to one freeze-thaw cycle poses insignificant risks of erroneous results.

Flex Study 16: Cold Cartridge
The Cartridge Package Insert instructs users to store cartridges in room temperature. This purpose of this study is to evaluate the risk of using cold cartridges stored in refrigeration temperature.

Results
Three samples (one normal, two abnormal) were tested for each group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to those of the control group. All three samples reported acceptable results. The results demonstrate that cold cartridges (e.g. stored at 2–8°C) poses insignificant risks of erroneous results.

Flex Study 17: Cartridge Open-Pouch Stability
The test cartridge is individually packaged in a foil pouch for humidity protection. The Cartridge Insert instructs the users to use cartridges promptly once the cartridge pouch is opened. This study was performed to evaluate the risk of using cartridges that are left for a time duration after having been taken out from the foil pouch.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (left in normal humidity for 5 minutes), all samples reported either acceptable or suppressed results.
- For experiment group 2 (left in normal humidity for 2 hours), all samples reported either acceptable or suppressed results.
- For experiment group 3 (left in high humidity for 5 minutes), all samples reported either acceptable or suppressed results.
- For experiment group 4 (left in high humidity for 2 hours), all samples reported suppressed results.

The results demonstrate that testing performed with cartridges that are left for 2 hours after having been taken out from the cartridge pouch poses insignificant risks of erroneous results.

Flex Study 18: Air Bubble in Cartridge
Air bubbles may be introduced in the liquid reagent storage chambers of the test Cartridge. This study was performed to evaluate the risk caused by the air bubbles in the cartridge.

Results
Three samples (one normal, two abnormal) were tested for each group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to that of the control group. All three samples reported acceptable results in the experiment group. The study results demonstrates that the air bubbles in cartridge's liquid reagent chambers (e.g. introduced by forcefully shaking the cartridge) pose insignificant risks of erroneous results.

Flex Study 19: Cartridge Box Stacking
This study was conducted to evaluate the risk of using cartridges from the cartridge box that has been stacked during storage at use site.

Results
Three samples (one normal, two abnormal) were tested for each group. Each sample was tested with 5 replicates. The test results of the experiment group were compared to that of the control group. All three samples reported acceptable results in the experiment group. Results from this study show that the testing performance of cartridges from a cartridge box that has been stacked during storage is acceptable, demonstrating that cartridge box stacking poses insignificant risks of erroneous results.

Category 4: Environmental factors

Flex Study 20: Operating Temperature
The Instrument Manual instructs the users to operate analyzer at ambient temperature (15–25°C). This study was performed to evaluate the risk of operating analyzer at varied temperatures.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (testing performed at 12–14°C), the analyzer failed system self-check at power-on, and the sample testing function was disabled. The message read "Error Code: Environment is too cold.; Suggested Action: Please heat up the room and maintain the room temperature between 15–25°C (59–77°F). Reboot to run the system self-check". No tests were performed.
- For experiment group 2 (testing performed at 17–19°C), all samples reported either acceptable or suppressed results.
- For experiment group 3 (testing performed at 23–25°C), all samples reported either acceptable or suppressed results.
- For experiment group 4 (testing performed at 28–30°C), the analyzer failed to pass system self-check, and the sample testing function was disabled. The message read "Error Code: Environment is too hot.; Suggested Action: Please cool down the room and maintain the room temperature between 15–25°C (59–77°F). Reboot to run the system self-check". No tests were performed.

The results demonstrate that performing testing at ambient temperature range poses insignificant risks of erroneous results. When the environment temperature exceed the specification (e.g. at 12–14°C, or at 28–30°C) the system cannot pass self-check, and sample testing function will be disabled.

Flex Study 21: Operating Altitude
The Instrument Manual instructs users to operate analyzer within a maximum altitude of 2500 feet above sea level. This study was performed to evaluate the risk of performing CBC testing at altitude levels higher than 2500 feet above the sea level.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (testing at the ambient pressure equivalent to 2,800 feet above sea level), all samples reported either acceptable or suppressed results.

- For experiment group 2 (testing at the ambient pressure equivalent to 10,000 feet above sea level), the analyzer failed system self-check, and the sample testing function was disabled. The error message read "Error Code: S623; Suggested Action: Reboot system and perform QC test". The instrument manual provides additional guidance that "If the error persists after following the On-Screen Suggested Actions, record the error code and contact Manufacturer for technical assistance".

The results demonstrate that performing testing at low ambient pressure equivalent to an altitude of 2,800 feet above sea level poses insignificant risks of erroneous results. At low ambient pressure equivalent to an altitude of 10,000 feet, analyzer cannot pass system self-check and the sample testing function is disabled.

Flex Study 22: Analyzer Tilt
The Instrument Manual instructs the users to place the analyzer on a horizontal surface. This study was performed to evaluate the risk of operating the analyzer on a non-horizontal surface.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (analyzer tilted with a 5° angle), the test results of all samples met the acceptance criteria.
- For experiment group 2 (analyzer tilted with a 10° angle), the test results of all samples met the acceptance criteria.
- For experiment group 3 (analyzer tilted with a 25° angle), the test results of all samples met the acceptance criteria.
- For experiment group 4 (analyzer tilted with a 30° angle), the reported results for leftward tilt exceed the acceptance criteria for PLT and RBC. The test results of all other samples met the acceptance criteria.
- For experiment group 5 (analyzer tilted with a 35° angle), the reported results for leftward tilt exceed the acceptance criteria for PLT and WBC. The test results of all other samples met the acceptance criteria.

The results demonstrate that operating the analyzer on a non-horizontal surface (e.g. with an angle less than 25°) poses insignificant risks of erroneous results. For tilts up to 30° and 35°, the degree of tilt is so severe that it is unlikely to happen in practical use, so the risk is considered acceptable.

Flex Study 23: Environmental Vibration
This study is to evaluate the risk when a vibration source (common vibration sources in a CLIA-waived site, e.g., centrifuge and sonication machine) is near the analyzer.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates.

- For experiment group 1 (centrifuge vibration), all three samples reported either acceptable or suppressed results.

- For experiment group 2 (sonicator vibration), all three samples reported either acceptable or suppressed results.

The results demonstrate that having a vibration source near the analyzer, e.g. centrifuge (operating at 3,000 rpm/minute) and sonicator (e.g. operating at a frequency of 40 kHz), poses insignificant risks of erroneous results.

Flex Study 24: Power Interruption
This study was conducted to evaluate the risk of analyzer malfunction caused by power interruption during testing.

Results
One sample was tested for 5 replicates for each group, evaluated against a control group.

- For group 1 (pneumatic pump interruption), the Analyzer passed the system self-check when powered back on and there was no result saved or reported on the Analyzer.
- For group 2 (pneumatic valve interruption), the Analyzer passed the system self-check when powered back on and there was no result saved or reported on the Analyzer.
- For group 3 (cytometry signal collection interruption), the Analyzer passed the system self-check when powered back on and there was no result saved and reported on the Analyzer.
- For group 4 (photometry signal collection interruption), the Analyzer passed the system self-check when powered back on and there was no result saved and reported on the Analyzer.

Results from this study demonstrate that power interruption during testing poses insignificant risk of erroneous results. Additionally, it does not impact normal analyzer function after the power is resumed.

Flex Study 25: Robustness of Cleaning
For the maintenance of the Analyzer, the Quick Reference Guide (QRG) instructs users to clean and disinfect the analyzer exterior daily. This study was conducted to evaluate the risk of multiple cleaning and disinfection cycles during the Analyzer's typical life span of 5 years.

Results
Three samples (one normal, two abnormal) were tested for each group, evaluated against a control group. Each sample was tested with 5 replicates on the Analyzer after the cleaning and disinfection cycles. The CBC results of all samples tested meet pre-defined acceptance criteria. Results from this study show that the Analyzer's performance the cleaning and disinfection (e.g. up to 2,625 cycles, which is the worst-case estimation in a typical life span of 5 years) poses insignificant risk of erroneous results.

Category 5: Sample Challenge

Flex Study 26: Sample Challenge
To evaluate the risk of testing abnormal samples, 309 abnormal samples were tested on both the Cito CBC system and the comparative method, Sysmex XN hematology analyzer. Venous whole blood samples were used in this study.

The correlation of CBC results and the flagging agreement (positive/negative for abnormal samples) are compared between the Cito CBC system and the Comparative Method. Both the correlation performance and the flagging agreement meet the pre-defined acceptance criteria. The number of samples and the sample abnormality types included in this study are shown in the table below.

Sample abnormality and potential interfering substance	Number of samples included
Leukocytosis (WBC: 12-50)	10
Leukocytopenia (WBC: <3.5)	15
Neutrophilia (NEUT: >7.7)	10
Neutropenia (NEUT: <1.5)	12
Lymphocytosis (LYMPH: >4)	6
Thrombocytosis (PLT: 500-800)	6
Thrombocytopenia (PLT: <150)	16
Low RBC (RBC: <3)	10
High RBC (RBC: 6-8)	5
Hypochromia (MCHC: <31)	9
Microcytosis (MCV: <80)	10
Macrocytosis (MCV: >100)	8
Immature Granulocytes (IG) Present (IG%: >5%)	10
Chronic inflammation	5
Hemoglobinopathies / hereditary RBC diseases (including Sickle Cell, Ion Deficiencies, Hb variants)	4
Leukemia (including Acute myeloid leukemia, Acute lymphocytic leukemia, Chronic myeloid leukemia, Chronic lymphocytic leukemia)	26
Lymphoma	7
Myelodysplastic syndromes	3
Parasitic infection	3
Acute inflammation	6
Allergic reaction	15
B12 or folate deficiency	4
Bacterial infection	3
Benign leukopenia	5
Respiratory diseases	5
Viral infection	7
WBC Abnormal Scattergram	6
Atypical lymphocytes/Blasts/Abnormal Lymphocyte	5
NRBC	5
RBC Abnormal Distribution (e.g. dual RBC population)	4
PLT abnormal distribution	5
PLT clumps	5
Large/Giant PLT	5
In vivo hemolysis	9
RBC inclusions	3
WBC fragment/agglutinates	3
Cold agglutinins, warm agglutinins	8

Sample abnormality and potential interfering substance	Number of samples included
Fragmented RBCs	9
High lipids	3
Hyperglycemia	5
Hypernatremia, Hyponatremia	3
Sample Coagulation	5
Immunoglobulin therapy	6
Immunosuppressive drugs	8
Microorganisms (bacteria or fungi)	5

Results
Sample challenge data demonstrate that the Cito CBC Analyzer appropriately suppressed results and avoided the reporting of erroneous results.

Category 6: Control Material Integrity and Handling

Flex Study 27: QC Sample Inadequate Mixing
Before dispensing QC sample to a test cartridge, the QRG instructs users to invert the QC vial at least 10 times to mix the QC sample. This study was conducted to evaluate the risk of insufficient QC mixing, e.g. using QC vial inverted less than the required 10 times.

Results
One set of QC vials (one low-level, one normal-level, and one high-level) are tested for 5 replicates per level in each study group, evaluated against a control group.

- For control group (10 times inversions), all QC tests (5 replicates for low level, 5 replicates for normal level, and 5 replicates for high level) report QC Pass.
- For experiment group 1 (no inversion), all QC tests (5 replicates for low level, 5 replicates for normal level, and 5 replicate for high level) report QC Fail, and the function of patient sample test was properly disabled. This result meets the acceptance criteria.
- For experiment group 2 (5 times inversions), the results of 14 QC tests (5 replicates for low level, 5 replicates for normal level, and 4 replicate for high level) report QC Fail, and the function of patient sample test was properly disabled; the result of 1 QC test (1 replicate for high-level) replicate reports QC Pass. This result meets the acceptance criteria.

Results from this study demonstrate that proper mixing (e.g. inversion 10 times) is required for the QC test:

- Failure to mix the QC material (no vial inversion) triggers QC Fail and disables the function of patient sample test.
- Insufficient mixing of the QC material (5 times inversion, the minimal times required for patient sample test) triggers QC Fail most of the time, leaving insignificant margin of error if the user does not adhere to the mixing instruction.

To mitigate the risk of user not properly mixing the QC material, the following mitigations are implemented: 1) the QRG provide step-to-step guidance for the QC test procedure, and one step requires users to invert the QC vial 10 times before test; 2) the software Graphic User Interface

(GUI) provides step-by-step guidance, and one step reminds users to invert the QC vial 10 times before test.

Flex Study 28: Expired QC Sample
The QRG instructs users to use unexpired QC material. The analyzer requires users to register a QC lot before QC vials from this lot can be used for QC test. This study was conducted to evaluate the risk if expired QC materials are used.

Result
One set of QC material from an expired lot was used for testing in each of the condition groups. 5 replicates are performed for each condition group:

- For Group 1 (QC lot registered and expired), all QC tests cannot be initiated and a prompt message on screen alerts users to register an unexpired lot of QC Samples.
- For Group 2 (registering an expired QC lot), the QC registration cannot be initiated and a prompt message on screen alerts that QC samples have expired and instructs users to register an unexpired lot of QC Samples.

Study results show that expired QC samples cannot be tested or registered. The fail-safe mechanisms can be properly triggered to prevent the usage variation of QC expiration.

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

1. Clinical Study Design

   A clinical study was conducted to evaluate the performance of the Cito CBC System in the hands of the intended users when performed in a CLIA waived setting.

   Study Sites
   Testing was performed at three CLIA waived testing sites. Sites had a diverse population of patients and covered a wide range of specialties including family practice, internal medicine, OB/GYN, pediatrics, and specialty care/psychiatry.

   Operators
   Nine untrained operators participated in the clinical study. Operators had no laboratory training or prior knowledge of the system operation and included medical assistants, laboratory assistants, and office staff. The work experience of the untrained operators ranged from < 1 year to 20 years and their education level ranged from high school to graduate school (Masters). The operators performed the testing using the Quick Reference Guide and the prompts on the software user interface; no additional training was provided to the operators.

   Subjects (patients)
   A total of 481 subjects were included in the study; of the 481 subjects, there were 197 female (41%), 284 male (59%). One K_2EDTA venous whole blood sample was collected from each subject. Each specimen was tested on the Cito CBC System at the CLIA waived testing sites by untrained operators.

2. Comparative Method

Testing with the comparative method (CM), the Sysmex XN-Series Automated Hematology Analyzer, was performed in duplicate in clinical laboratory testing sites by laboratory professionals.

3. Allowable Total Error (ATE) and Limit of Erroneous Results (LER)

The allowable total error for each hematology parameter was set to values presented in the table below.

Parameter	ATE
WBC ($\times 10^3/\mu L$)	±10%
RBC ($\times 10^6/\mu L$)	±4%
PLT ($\times 10^3/\mu L$)	±15%
HGB (g/dL)	±4%
HCT (%)	±5%
MCV (fL)	±7%
NEUT ($\times 10^3/\mu L$)	±15% if CM >4.7 ±0.7 if CM≤4.7
LYMPH ($\times 10^3/\mu L$)	±15% if CM >3.3 ±0.5 if CM≤3.3
MONO ($\times 10^3/\mu L$)	±0.5 (absolute value)
EO ($\times 10^3/\mu L$)	±0.5 (absolute value)
BASO ($\times 10^3/\mu L$)	±0.5 (absolute value)
NEUT%	±7.5 (absolute value)
LYMPH%	±7.5 (absolute value)
MONO%	±5.0 (absolute value)
EO%	±3.0 (absolute value)
BASO%	±2.0 (absolute value)

Limit of erroneous results (LER) for each hematology parameter was set by two regions described as (comparator method (CM)=Low and subject device (SD)=High) and (CM=High and SD=Low) where Low and High were defined based on the Sysmex XW-100 (CW170012) public decision summary and are related to the reference interval for adults (≥21 years old) for XW-100. Although slightly different, this aligns similarly with the reference interval for the Cito CBC System (see table below).

Parameter	LER Zone
WBC ($\times 10^3/\mu L$)	(CM≤3.9 and SD≥10.4) or (CM≥10.4 and SD≤3.9)
RBC ($\times 10^6/\mu L$)	(CM≤3.71 and SD≥5.52) or (CM≥5.52 and SD≤3.71)
PLT ($\times 10^3/\mu L$)	(CM≤147 and SD≥382) or (CM≥382 and SD≤147)
HGB (g/dL)	(CM≤10.9 and SD≥16.7) or (CM≥16.7 and SD≤10.9)

Parameter	LER Zone
HCT (%)	(CM≤32.4 and SD≥49.4) or (CM≥49.4 and SD≤32.4)
MCV (fL)	(CM≤82.5 and SD≥98.0) or (CM≥98.0 and SD≤82.5)
NEUT ($\times 10^3/\mu L$)	(CM≤2.2 and SD≥7.1) or (CM≥7.1 and SD≤2.2)
LYMPH ($\times 10^3/\mu L$)	(CM≤0.9 and SD≥3.4) or (CM≥3.4 and SD≤0.9)
MONO ($\times 10^3/\mu L$)	(CM≤0.2 and SD≥1.2) or (CM≥1.2 and SD≤0.2)
EO ($\times 10^3/\mu L$)	(CM≤0.2 and SD≥1.2) or (CM≥1.2 and SD≤0.2)
BASO ($\times 10^3/\mu L$)	(CM≤0.2 and SD≥1.2) or (CM≥1.2 and SD≤0.2)

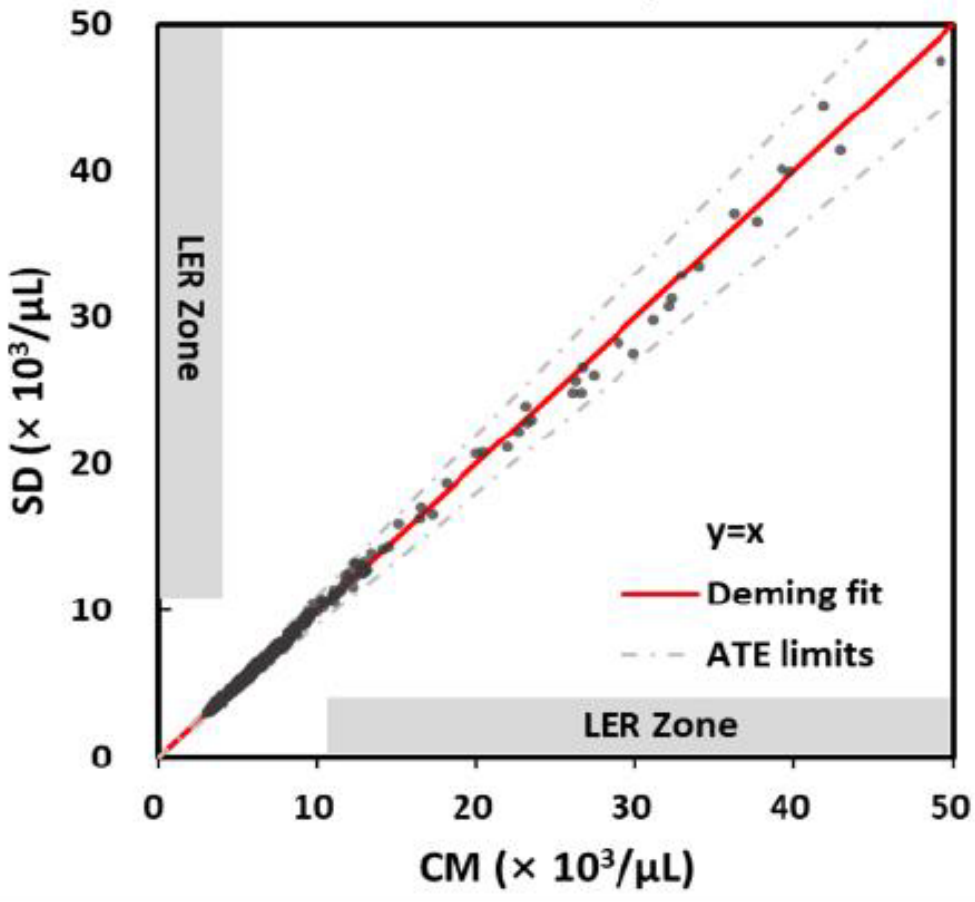
At least 95% of the tested samples fall within the ATE limits and no tested samples should fall into the LER zone.

4. Data Analysis of the Clinical Study

For each hematology parameter, the following data analyses were performed:

- Scatter plot of the data with ATE and LER.
- Percent of Cito CBC System results within ATE and LER.
- Total error (an interval for the 95% differences or relative differences between the Cito CBC System result and CM result (an average of two replicates)) was calculated. Deming weighted regression analysis was performed and biases at the Lower Limit of the Reference Interval (LL of RI) and Upper Limit of the Reference Interval (UL of RI) for adults (≥21 years old) were calculated along with 95% confidence intervals.

WBC (x 10^3/µL)



ATE = ± 10% Percent of samples inside of ATE	LER Percent of samples inside of LER
100.0% (480/480) 95% CI: (99.2%; 100.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

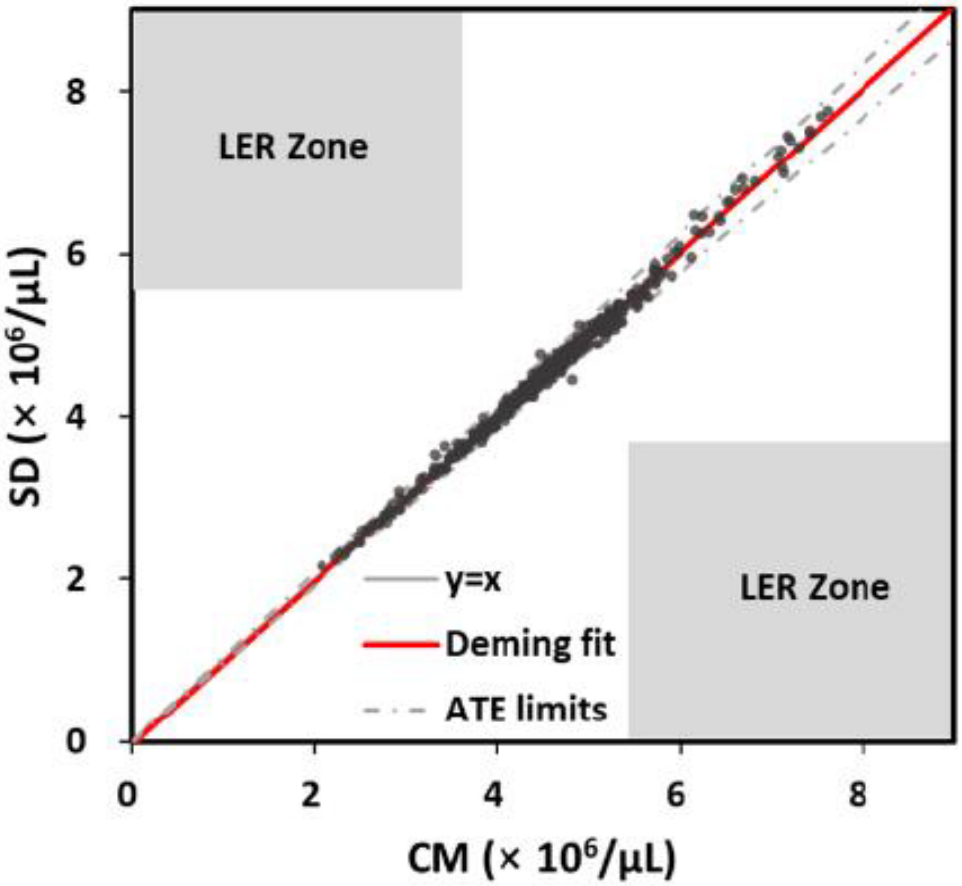
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±10%)
		2.5th Percentile	97.5th percentile	
[3.00, 5.7]	179	-5.0%	5.2%	100.0%
[5.7, 7.55]	149	-4.7%	4.4%	100.0%
[7.55, 50.00]	152	-5.3%	5.5%	100.0%
[3.00 to 50.00]	480	-4.9%	5.1%	100.0%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.00 (0.99, 1.01)	-0.02 (-0.07, 0.03)	4.2	-0.3% (-1.2%, 0.6%)	10.5	-0.02% (-0.3%, 0.3%)

RBC (x 10^6/µL)



ATE = ± 4% Percent of samples inside of ATE	LER Percent of samples inside of LER
98.1% (469/478) 95%CI: (96.5%, 99.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

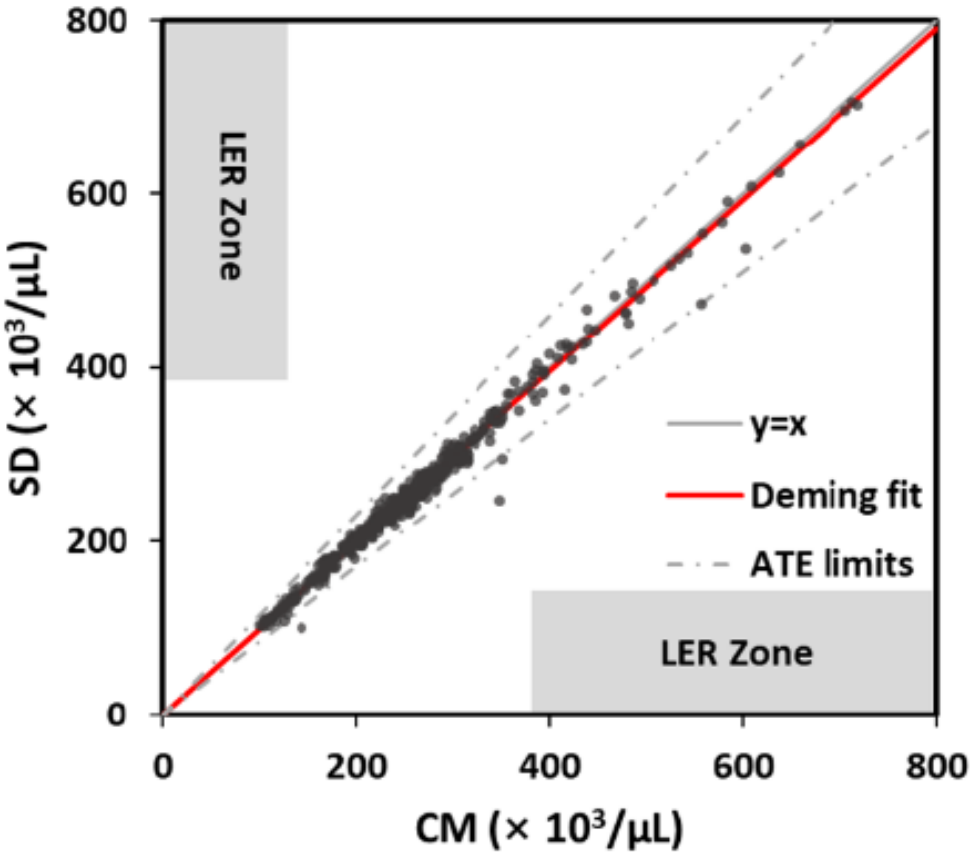
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±4%)
		2.5th Percentile	97.5th percentile	
[2.00, 4.24]	160	-2.7%	3.9%	97.5%
[4.24, 4.83]	157	-3.4%	2.3%	98.7%
[4.83, 8.25]	161	-3.7%	3.4%	98.1%
[2.00 to 8.25]	478	-3.4%	3.0%	98.1%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.01 (1.00, 1.02)	-0.05 (-0.09, -0.01)	4.0	-0.38% (-0.58%, -0.18%)	5.7	0.01% (-0.19%, 0.21%)

PLT (x 10^3/µL)



ATE = ± 15% Percent of samples inside of ATE	LER Percent of samples inside of LER
99.4% (468/471) 95%CI: (98.2%, 99.8%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

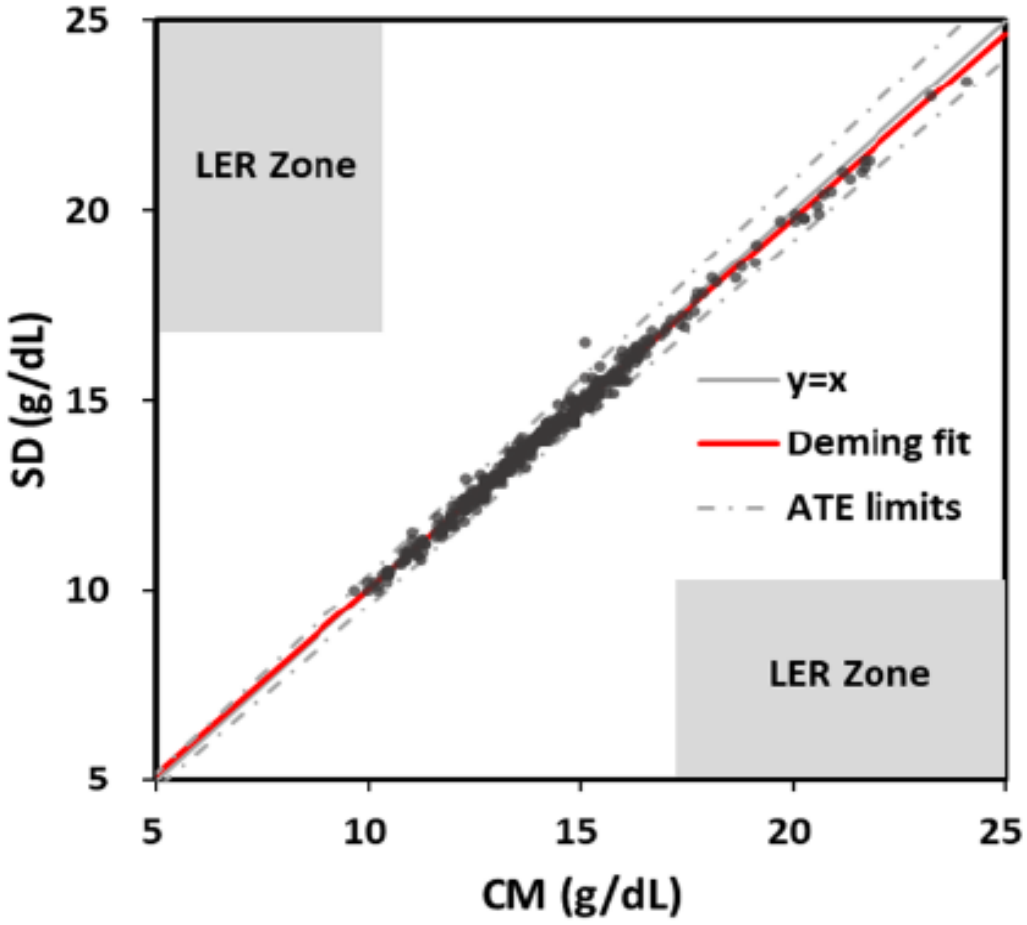
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±15%)
		2.5th Percentile	97.5th percentile	
[100, 217]	175	-9.0%	5.6%	99.4%
[217, 276]	144	-7.7%	6.1%	100.0%
[276, 750]	152	-10.6%	4.6%	98.7%
[100 to 750]	471	-7.8%	5.6%	99.4%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.99 (0.97, 1.00)	0.73 (-2.45, 3.90)	179	-0.80% (-1.55%, -0.04%)	413	-1.03% (-1.51%, -0.54%)

HGB (g/dL)



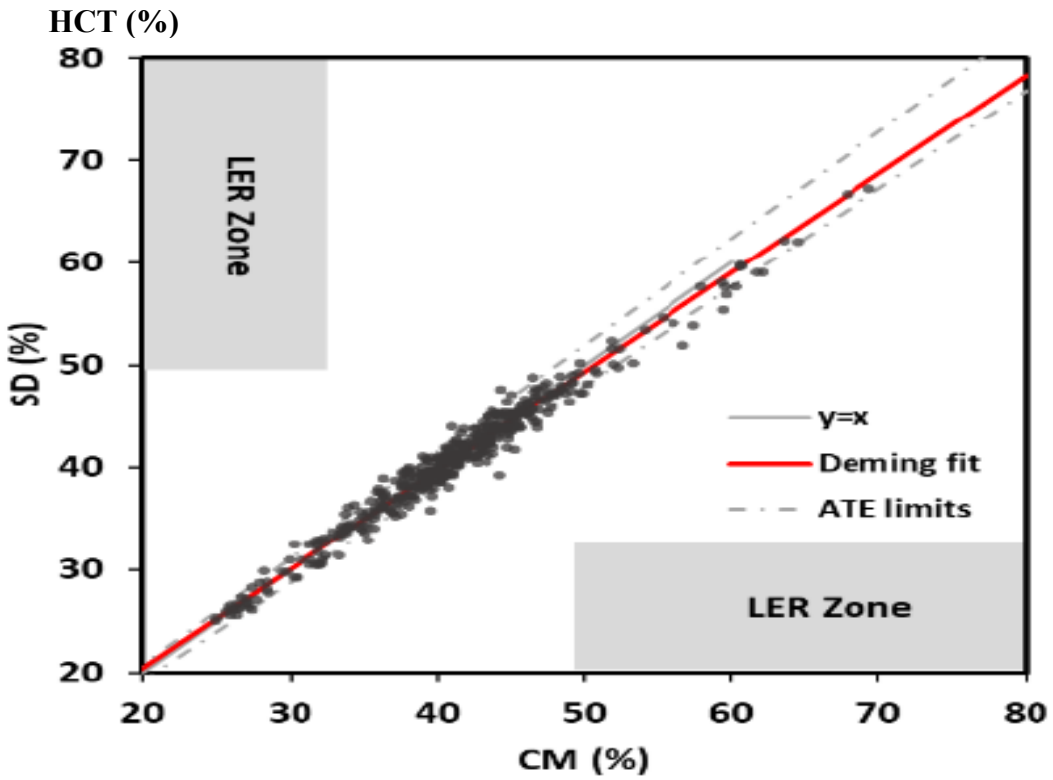
ATE = ± 4% Percent of samples inside of ATE	LER Percent of samples inside of LER
99.0% (473/478) 95%CI: (97.6%, 99.5%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±4%)
		2.5th Percentile	97.5th percentile	
[10.0, 13.2]	192	-2.5%	2.7%	99.0%
[13.2, 14.8]	147	-2.5%	2.5%	99.3%
[14.8, 24.0]	139	-3.4%	2.3%	98.6%
[10.0 to 24.0]	478	-3.0%	2.6%	99.0%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.97 (0.97, 0.98)	0.29 (0.17, 0.42)	11.1	0.10% (-0.14%, 0.34%)	16.8	-0.80% (-0.99%, -0.61%)



ATE = ± 5% Percent of samples inside of ATE	LER Percent of samples inside of LER
95.8% (435/454) 95%CI: (93.6%; 97.3%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

Total Error and ATE Analysis

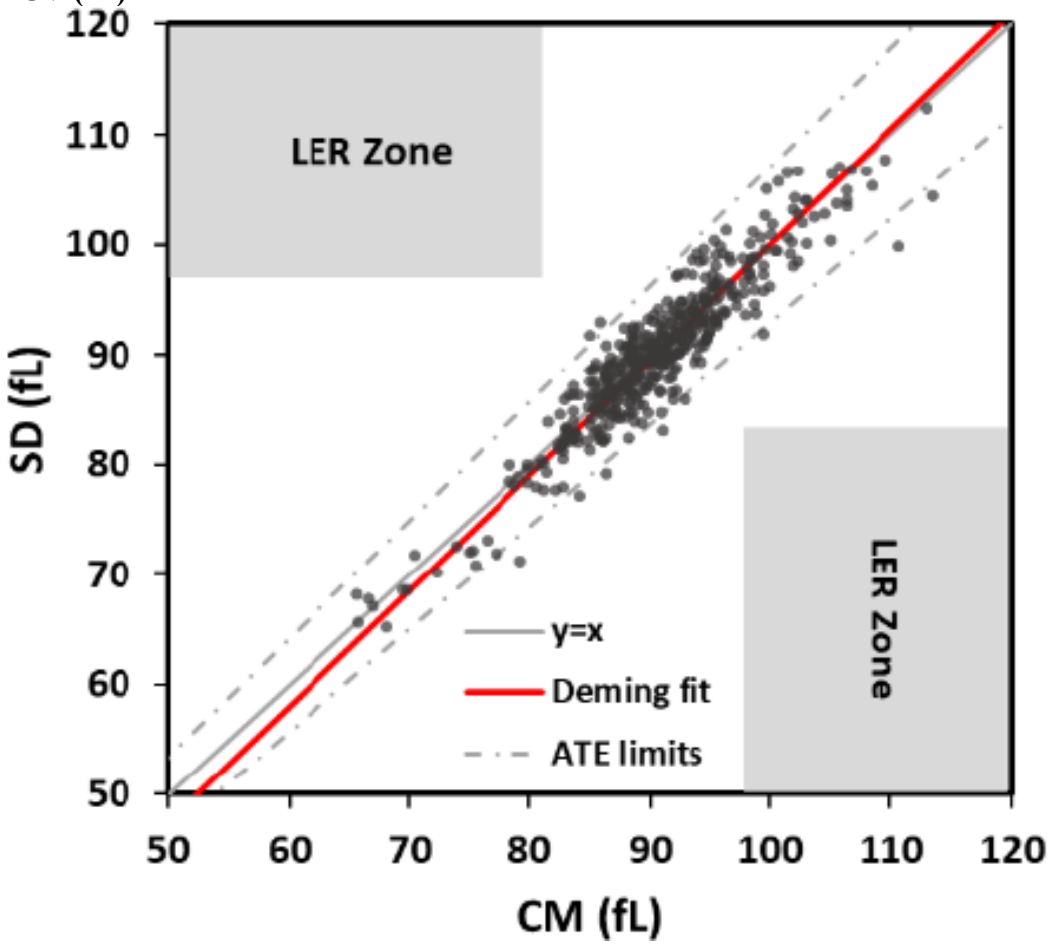
Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (± 5%)
		2.5th Percentile	97.5th percentile	
[25.0, 39.2]	155	-6.2%	5.8%	95.5%*
[39.2, 43.4]	147	-4.5%	3.6%	98.6%*
[43.4, 69.4]	152	-6.3%	3.7%	93.4%*
[25.0 to 69.4]	454	-6.2%	5.0%	95.8%*

*It was appropriately adjusted taking into account random measurement errors of the comparator (CLSI EP21).

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.96 (0.95, 0.98)	1.11 (0.56, 1.66)	35.5	-0.38% (-0.74%, -0.02%)	49.8	-1.28% (-1.62%, -0.93%)

MCV (fL)



ATE = ± 7% Percent of samples inside of ATE	LER Percent of samples inside of LER
97.9% (471/481) 95%CI: (96.2%, 98.9%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

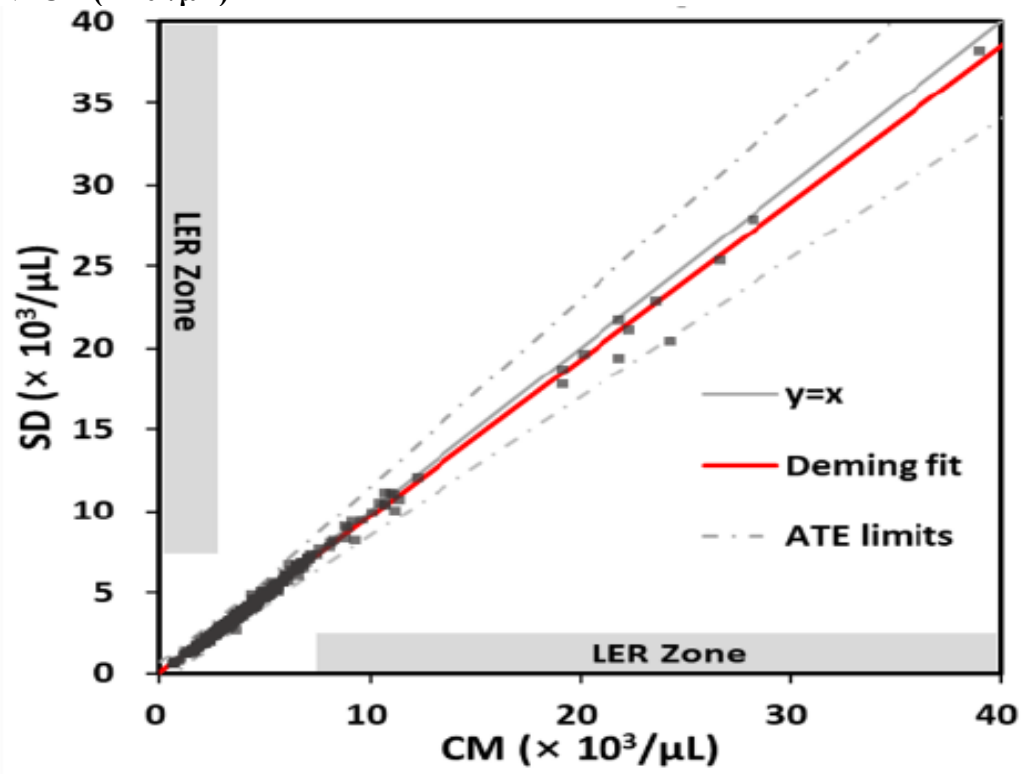
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (± 7%)
		2.5th Percentile	97.5th percentile	
[65.0, 88.3)	157	-6.7%	4.8%	96.8%
[88.3, 93]	169	-6.4%	4.3%	98.8%
(93, 113.5]	155	-5.2%	5.3%	98.1%
[65.7 to 115.0]	481	-6.4%	5.0%	97.9%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.05 (1.01, 1.09)	-4.91 (-8.77, -1.06)	82.4	-1.05% (-1.5%, -0.61%)	96.8	-0.17% (-0.49%, 0.15%)

NEUT (x 10^3/µL)



ATE = ± 0.7 (CM≤4.7); ± 15% (CM>4.7) Percent of samples inside of ATE	LER Percent of samples inside of LER
99.6% (441/443) 95%CI: (98.4%, 99.9%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

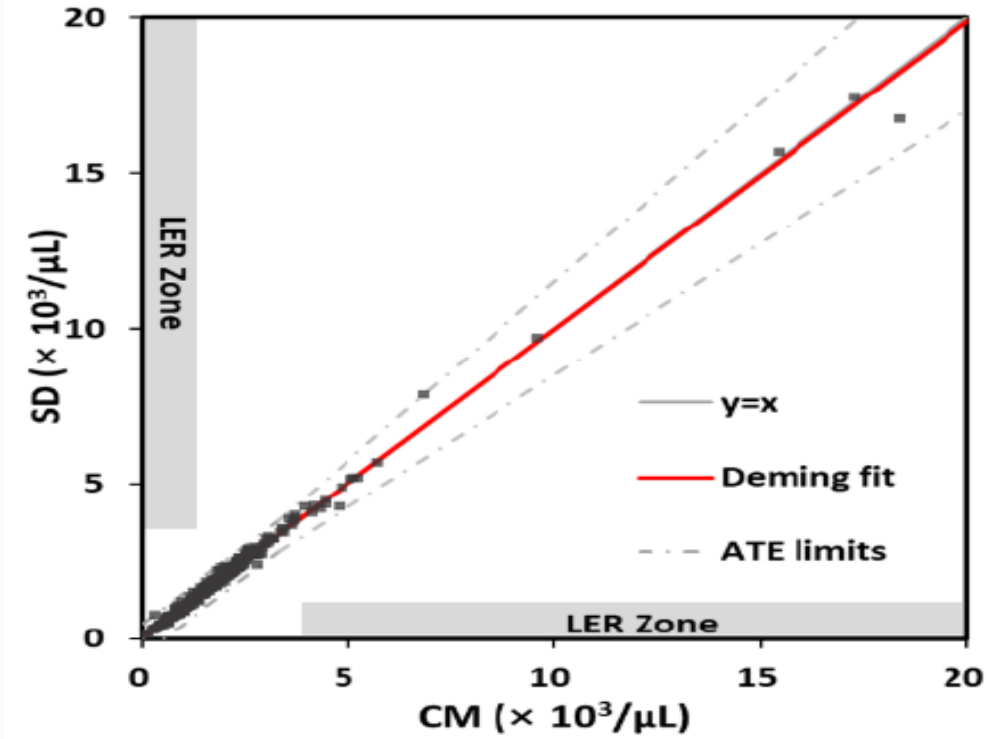
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±0.7 (CM≤4.7); ± 15% (CM>4.7))
		2.5th Percentile	97.5th percentile	
[0.63, 3.16]	156	-22.0%	13.0%	100.0%
[3.16, 4.7]	167	-36.0%	12.0%	99.4%
[4.7, 39.02]	120	-10.9%	5.1%	99.2%
[0.63 to 39.02]	443	-0.31 (CM≤4.7) -10.9% (CM > 4.7)	0.13 (CM≤4.7) 5.1% (CM > 4.7)	99.6%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.96 (0.94, 0.99)	0.06 (-0.03, 0.15)	1.65	0.00 (-0.03, 0.03)	6.75	-2.97% (-3.34%, -2.6%)

LYMPH (x 10^3/µL)



ATE = ± 0.5 (CM≤3.3); ± 15% (CM>3.3) Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (441/442) 95%CI: (98.8%, 100.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

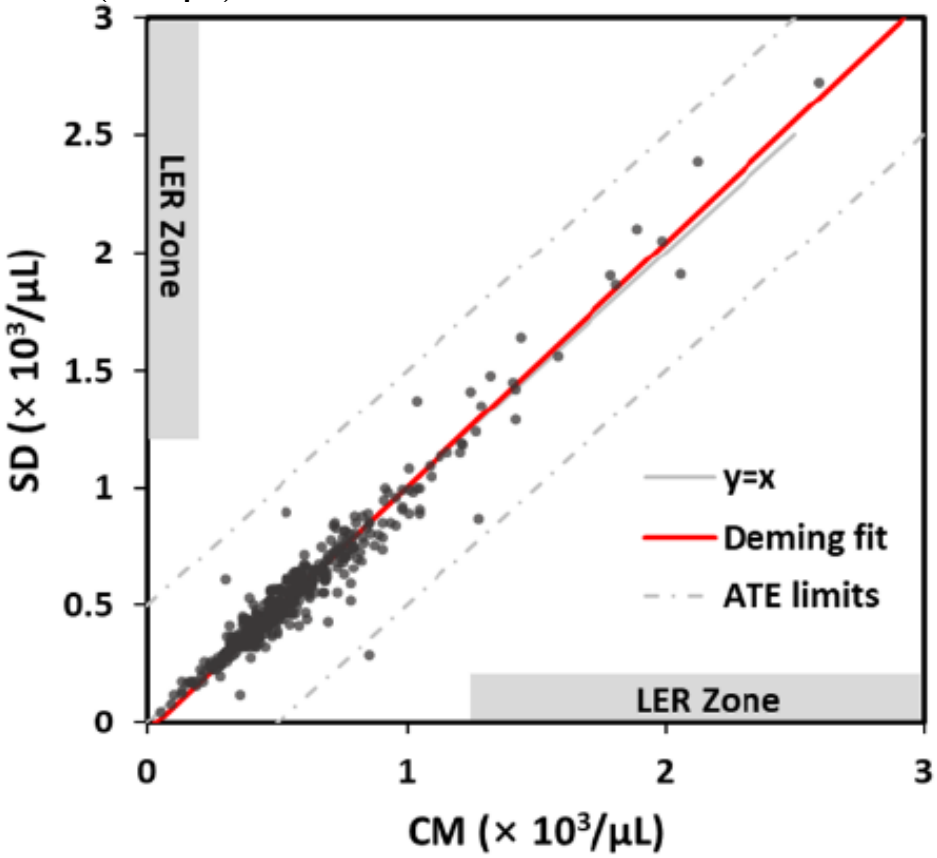
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±0.5 (CM≤3.3); ±15% (CM>3.3))
		2.5th Percentile	97.5th percentile	
[0.09, 1.56]	204	-0.1	0.3	100.0%
[1.56, 3.3]	212	-0.1	0.3	100.0%
[3.3, 18.36]	26	-10.5%	14.1%	96.2%
[0.09 to 18.36]	442	-0.1 (CM≤3.3) -10.5% (CM > 3.3)	0.3 (CM≤3.3) 14.1% (CM > 3.3)	99.8%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.99 (0.93, 1.05)	0.08 (-0.02, 0.18)	1.1	0.07 (0.05, 0.08)	3.5	1.12% (0.63%, 1.6%)

MONO (x 10^3/µL)



ATE = ± 0.5 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (441/442) 95%CI: (98.8%, 100.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

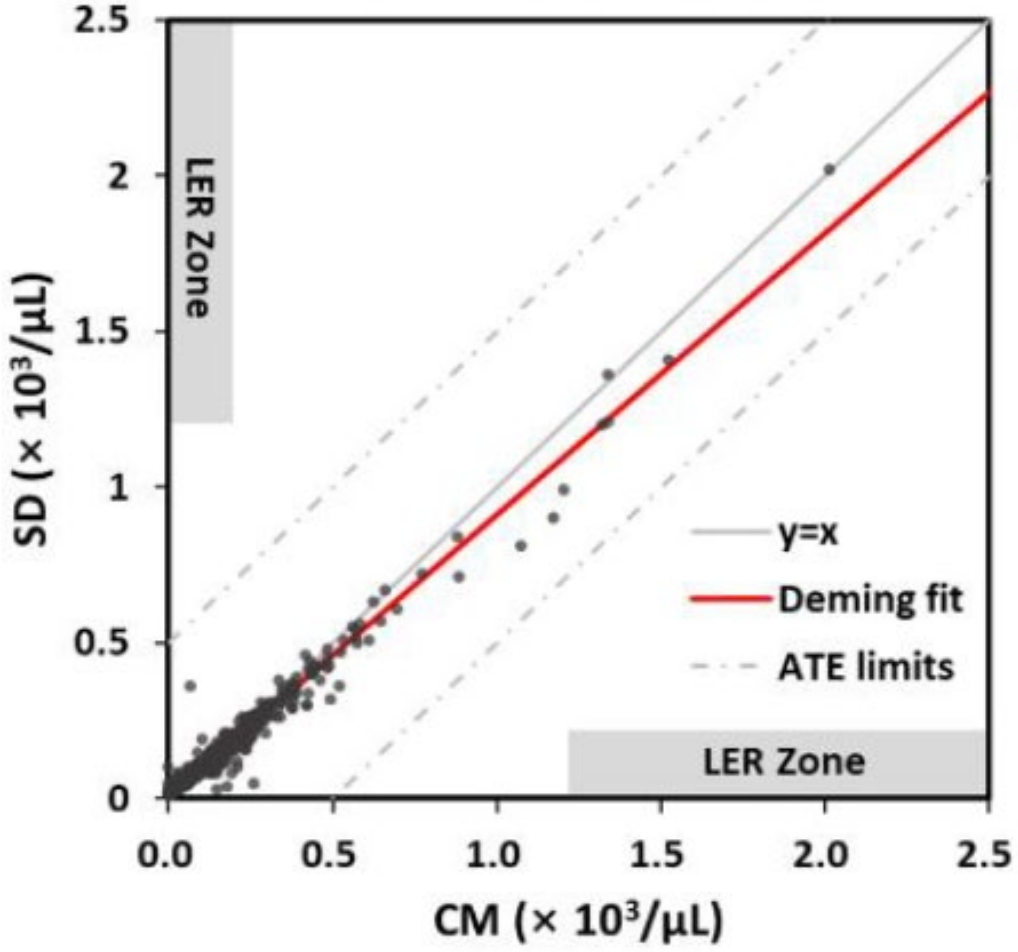
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±0.5)
		2.5th Percentile	97.5th percentile	
[0.06, 0.45]	147	-0.1	0.1	100.0%
[0.45, 0.61]	147	-0.1	0.1	100.0%
[0.61, 3.86]	148	-0.3	0.2	99.3%
[0.06 to 3.86]	442	-0.2	0.1	99.8%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.04 (1.01, 1.07)	-0.04 (-0.05, -0.02)	0.29	-0.02 (-0.04, -0.01)	1.00	0.00 (-0.01, 0.01)

EO (x 10^3/µL)



ATE = ± 0.5 Percent of samples inside of ATE	LER Percent of samples inside of LER
100% (463/463) 95%CI: (99.2%, 100.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

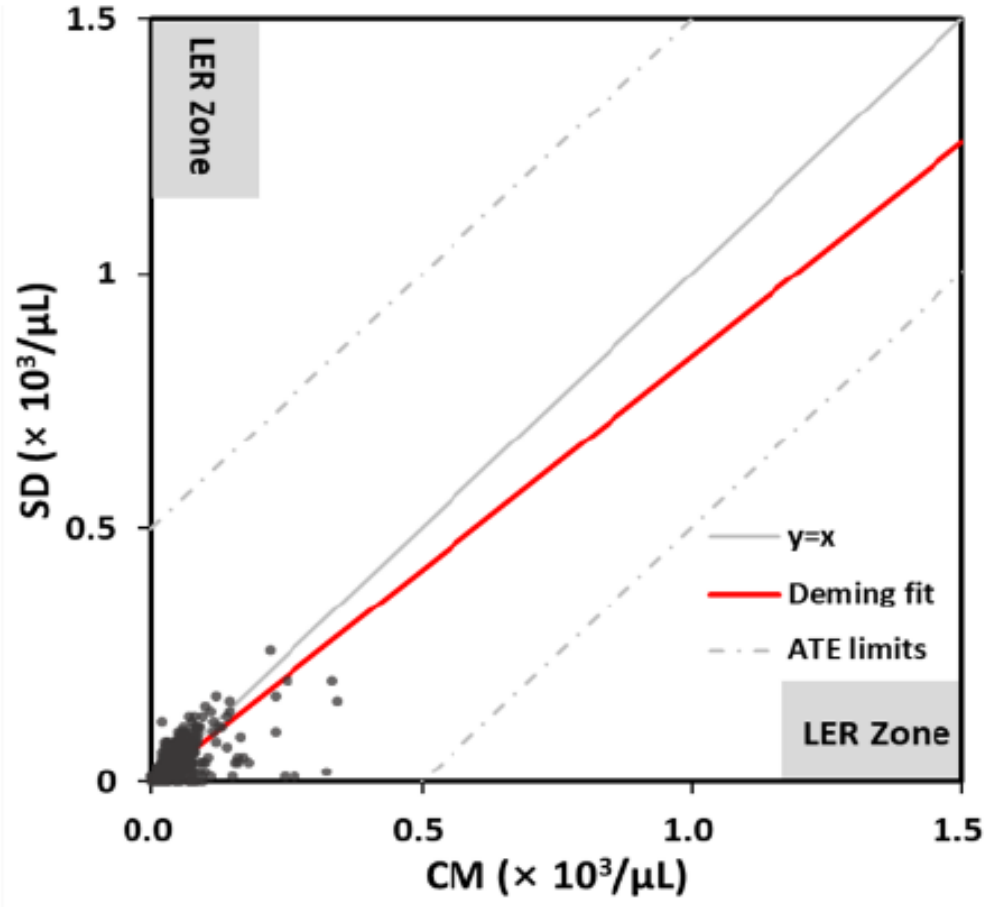
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±0.5)
		2.5th Percentile	97.5th percentile	
[0, 0.09]	148	0.0	0.1	100.0%
[0.09, 0.19]	169	-0.1	0.0	100.0%
[0.19, 2.02]	146	-0.2	0.0	100.0%
[0 to 2.02]	463	-0.1	0.1	100.0%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.90 (0.85, 0.96)	0.01 (0, 0.02)	0.04	0.00 (0, 0.01)	0.42	-0.03 (-0.04, -0.03)

BASO (x 10^3/µL)



ATE = ± 0.5 Percent of samples inside of ATE	LER Percent of samples inside of LER
100% (455/455) 95%CI: (99.2%, 100.0%)	0.0% (0/481) 95%CI: (0.0%; 0.8%)

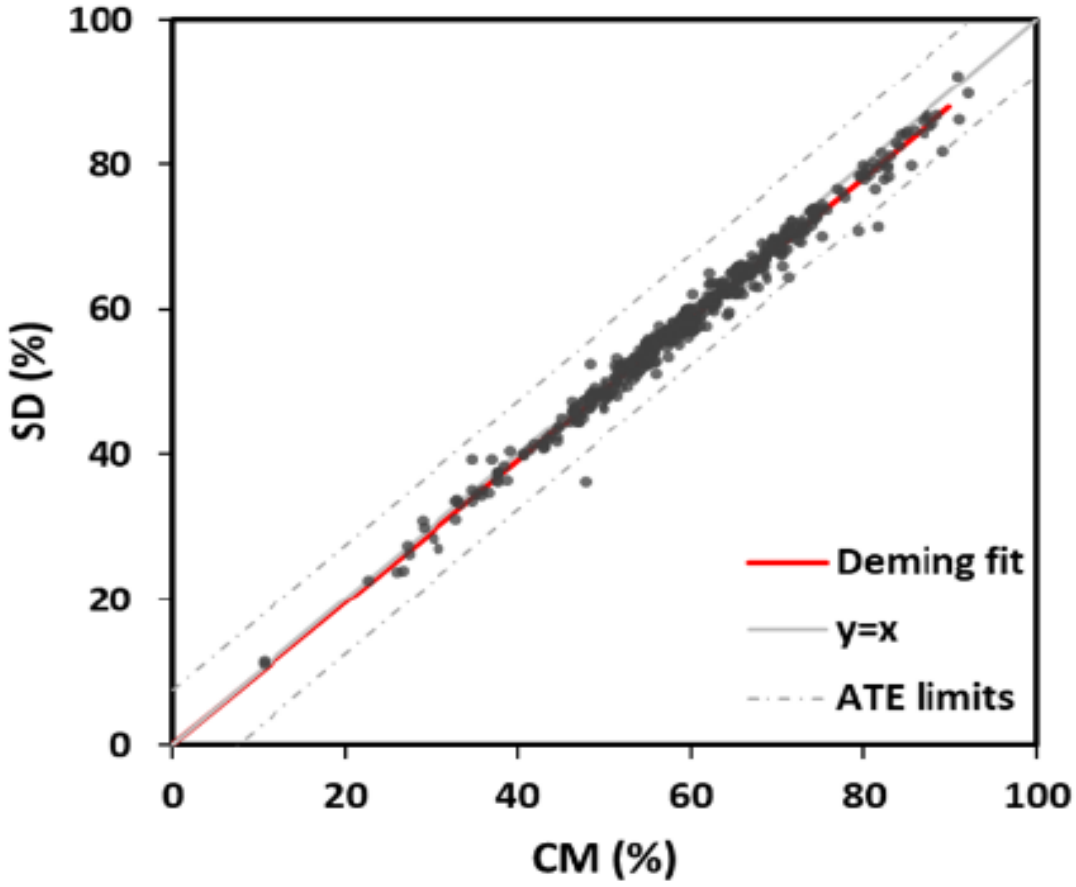
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±0.5)
		2.5th Percentile	97.5th percentile	
[0, 0.04]	190	0.0	0.0	100.0%
[0.04, 0.06]	153	-0.1	0.0	100.0%
[0.06, 0.35]	112	-0.2	0.1	100.0%
[0 to 0.35]	455	-0.1	0.1	100.0%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.84 (0.65, 1.03)	0.00 (-0.01, 0.01)	0.0	0.00 (-0.01, 0.01)	0.11	-0.02 (-0.02, -0.01)

NEUT(%)



ATE = ± 7.5 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.1% (439/443) 95%CI: (97.7%, 99.6%)	N/A

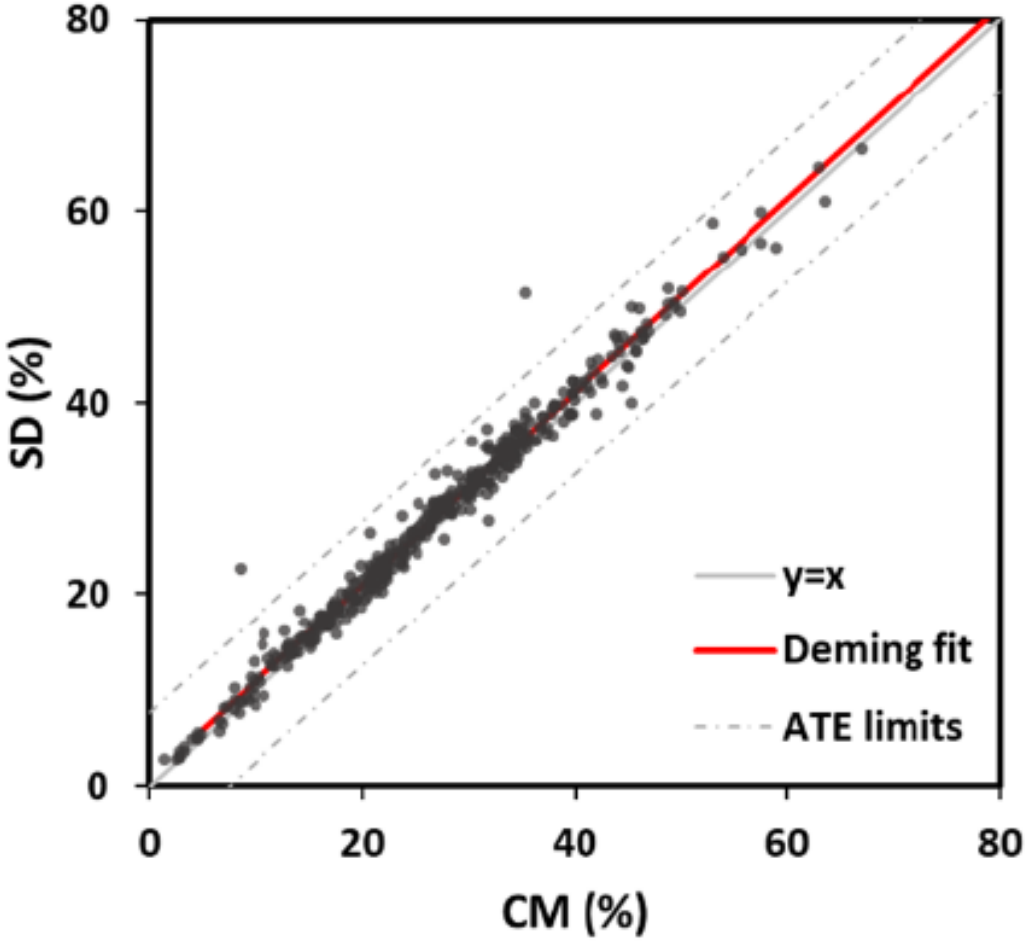
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±7.5)
		2.5th Percentile	97.5th percentile	
[22.8, 55.4]	148	-3.4	1.9	99.3%
[55.4, 65.4]	145	-4.0	1.2	100.0%
[65.4, 92.2]	150	-6.7	0.4	98.0%
[22.8 to 92.2]	443	-5.0	1.2	99.1%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.98 (0.96, 0.99)	0.06 (-0.71, 0.84)	37.3	-0.82 (-1.09, -0.54)	72.8	-1.65 (-1.86, -1.45)

LYMPH(%)



ATE = ± 7.5 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.6% (440/442) 95%CI: (98.4%, 99.9%)	N/A

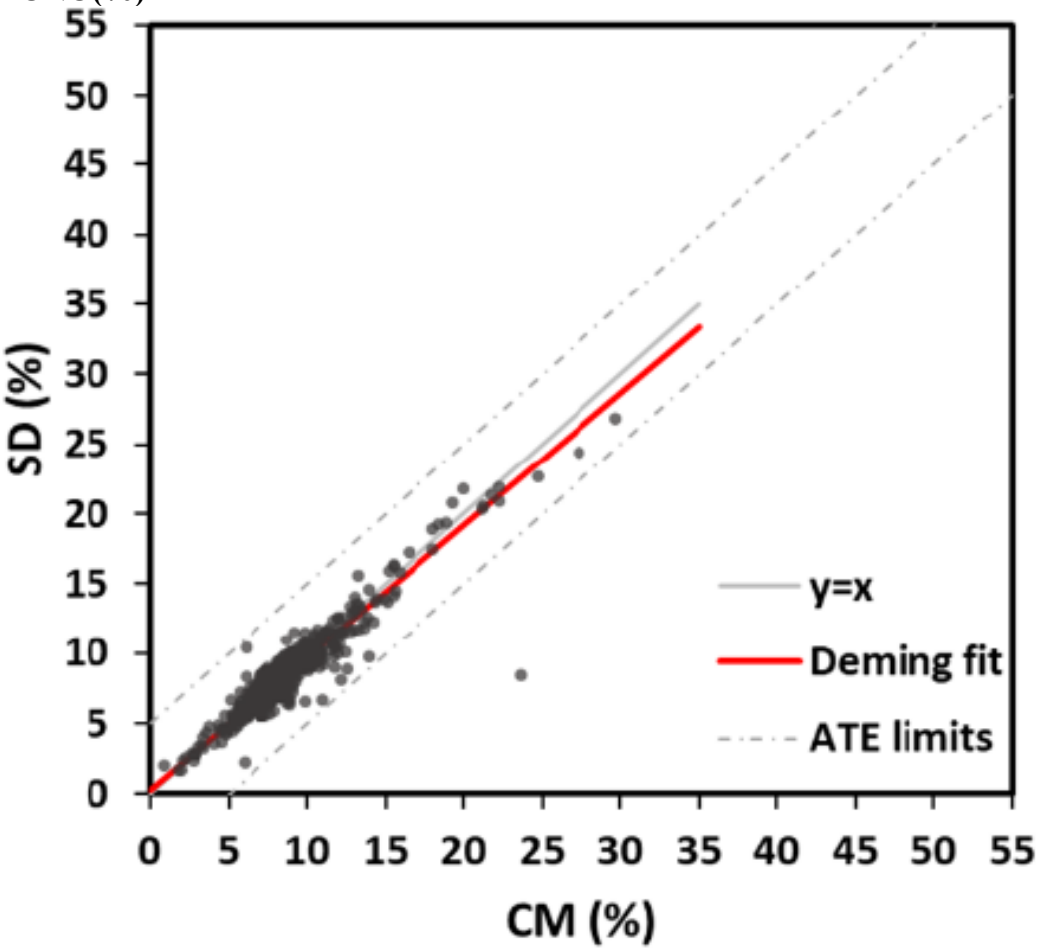
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±7.5)
		2.5th Percentile	97.5th percentile	
[1.4, 21.2]	146	-1.1	4.1	99.3%
[21.2, 31.8]	149	-1.4	4.6	100.0%
[31.8, 67]	147	-2.8	3.8	99.3%
[1.4 to 67]	442	-1.5	4.2	99.6%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.01 (0.99, 1.02)	0.79 (0.39, 1.2)	17.4	0.91 (0.71, 1.11)	49.1	1.13 (0.81, 1.45)

MONO(%)



ATE = ± 5.0 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (441/442) 95%CI: (98.8%, 100.0%)	N/A

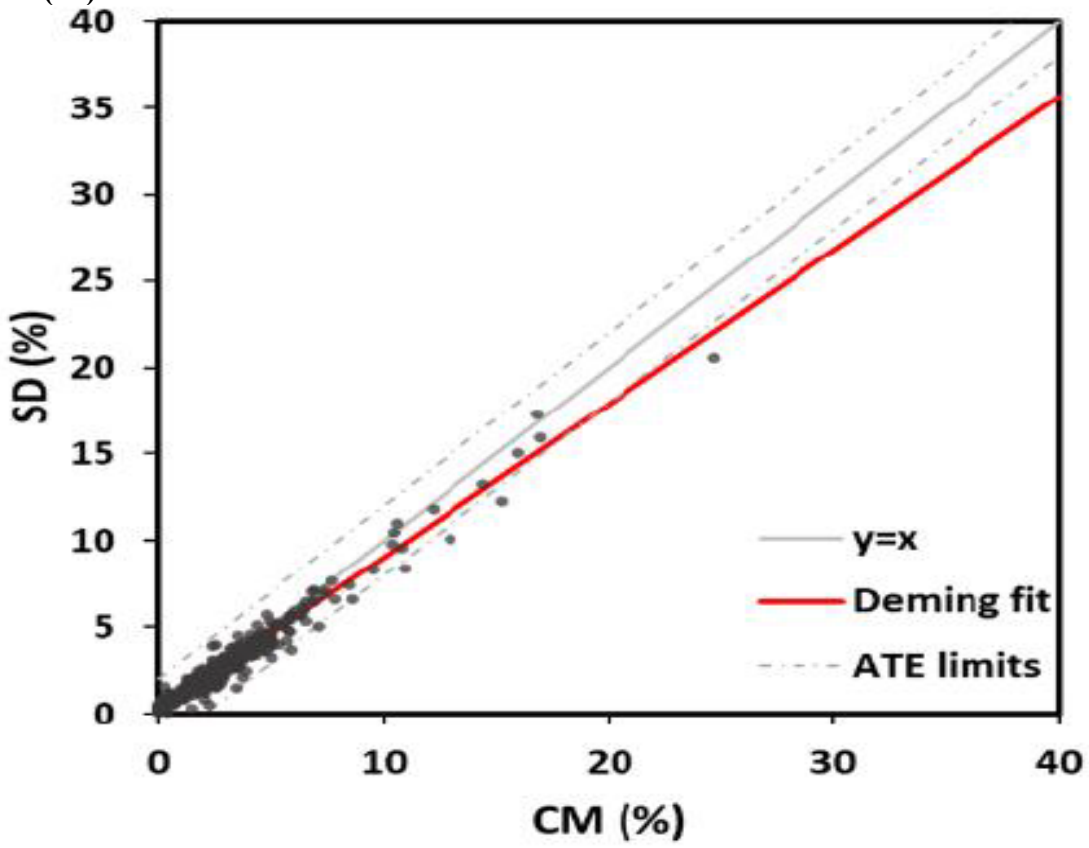
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±5.0)
		2.5th Percentile	97.5th percentile	
[1, 7.3]	147	-1.6	1.4	100.0%
[7.3, 9.2]	146	-2.1	1.3	100.0%
[9.2, 29.8]	149	-4.0	1.5	99.3%
[1 to 29.8]	442	-2.6	1.4	99.8%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.95 (0.89, 1)	0.21 (-0.19, 0.62)	4.9	-0.05 (-0.22, 0.12)	13.5	-0.52 (-0.69, -0.35)

EO (%)



ATE = ± 3.0 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (462/463) 95%CI: (98.8%, 100.0%)	N/A

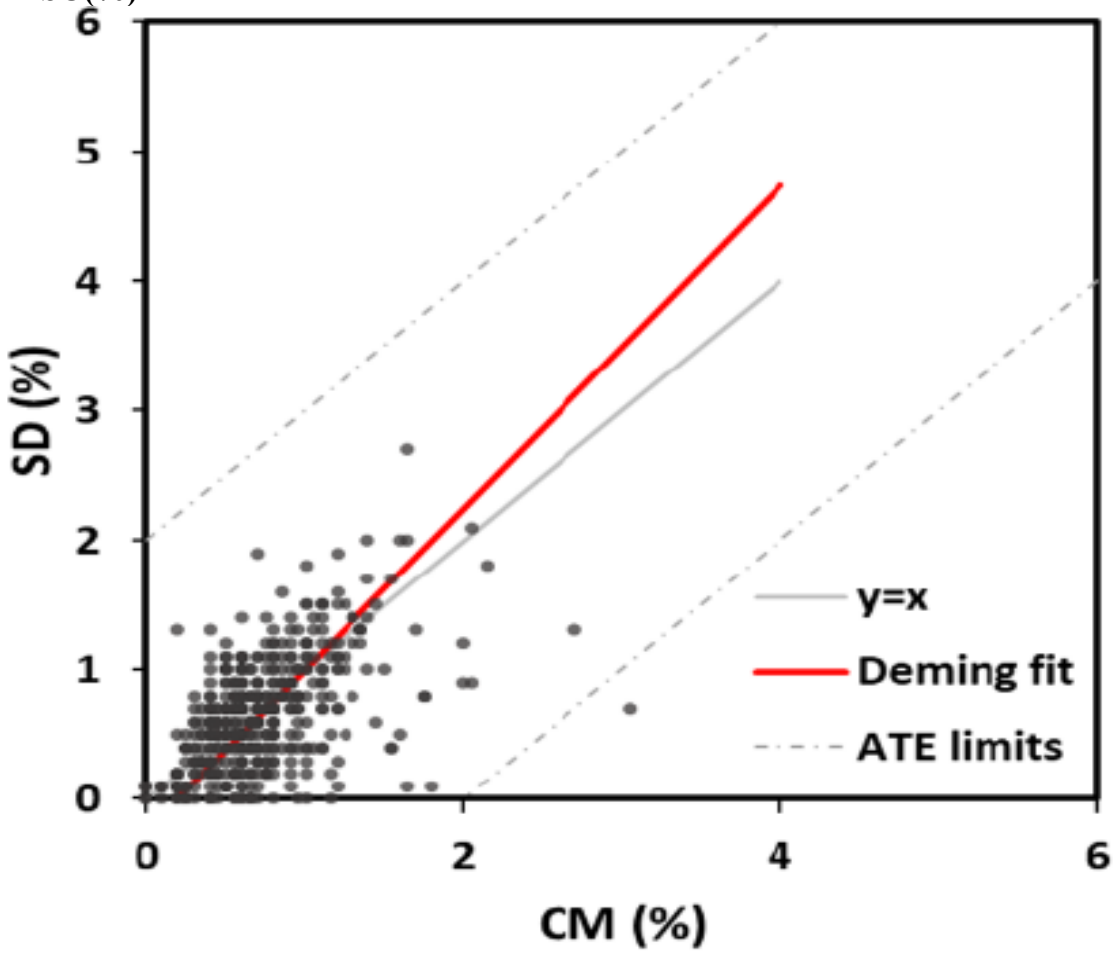
Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±3.0)
		2.5th Percentile	97.5th percentile	
[0, 1.5]	161	-0.3	0.7	100.0%
[1.5, 2.9]	150	-1.0	0.7	100.0%
[2.9, 24.7]	152	-2.5	0.6	99.3%
[0 to 24.7]	463	-1.5	0.7	99.8%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.89 (0.85, 0.93)	0.18 (0.09, 0.27)	0.6	0.11 (0.06, 0.17)	5.8	-0.48 (-0.54, -0.41)

BASO(%)



ATE = ± 2.0 Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (454/455) 95%CI: (98.8%, 100.0%)	N/A

Total Error and ATE Analysis

Range of CM Values (%)	N	Relative Differences		Percentage of observations inside ATE (±2.0)
		2.5th Percentile	97.5th percentile	
[0, 0.6]	166	-0.4	0.6	100.0%
[0.6, 0.8]	151	-0.7	0.5	100.0%
[0.8, 3.1]	138	-1.4	0.7	99.3%
[0 to 3.1]	455	-1.0	0.6	99.8%

%Biases Estimation by Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.24 (0.96, 1.53)	-0.25 (-0.43, -0.06)	0.1	-0.22 (-0.31, -0.15)	1.6	0.14 (0.04, 0.25)

Conclusion

The study results demonstrate that untrained users were able to perform the test accurately for all 16 hematology parameters using only the Quick Reference Guide and GUI of the Cito CBC System.

5. Questionnaire Results

Nine operators across the three CLIA waived sites were asked to complete a ten-question questionnaire that polled their opinions of the procedural steps to address ease of use, as well as delivered questions related to results interpretation (flags, positive/negative). The multiple-choice responses were presented as a 5-point Likert scale, where rankings ranged from "strongly agree" (5) to "strongly disagree" (1). Results from the questionnaire demonstrate that the Cito CBC System is simple to use for the operator.

D Labeling for Waived Devices

- The Quick Reference Guides (QRG) are written at no higher than a 7th grade reading level and pictures and diagrams have been provided, as appropriate.
- The package insert and QRG identify the test as CLIA waived, and contain a statement that a Certificate of Waiver is required to perform the test in a waived setting, and contain information on how users can obtain a certificate.
- The package insert and QRG contain a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test. 42 CFR 493.15(e)(1).

XI. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.