CLIA Waiver by Application

Approval Determination Decision Summary

A. Document Number

CW170012

B. Parent Document Number

K172604

C. Purpose of the Submission

This submission is a Dual 510(k) and CLIA Waiver by Application (Dual Submission) tracked as K172604 and CW170012. CW170012 was submitted for CLIA Waiver of the Sysmex XW-100 Automated Hematology Analyzer (XW-100).

The XW-100 device was cleared for point of care (POC) use under K143577 and CLIA categorized as moderately complex under CR140520. The XW-100 was modified for CLIA waived use and has a decreased number of reported parameters, simplified flagging, and a modified intended use. The waived version of the system was cleared under K172604 and contains a visible distinction so that the two versions (waived and POC) may be clearly distinguished in the marketplace.

D. Sample Type

Venous whole blood anticoagulated with K_2EDTA or K_3EDTA

E. Type of Test or Tests Performed

Complete blood count (WBC, RBC, HGB, HCT, MCV, PLT) and leukocyte 3-part differential (LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, NEUT#)

F. Applicant

Sysmex America, Inc.

G. Proprietary and Established Names

Sysmex XW-100 Automated Hematology Analyzer for CLIA Waived use

H. Test System Description

1. Overview

The Sysmex XW-100 is a quantitative automated hematology analyzer intended for *in vitro* diagnostic use to classify and enumerate the following parameters for venous whole blood anticoagulated with K_2 or K_3EDTA: WBC, RBC, HGB, HCT, MCV, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, and NEUT#.

The XW-100 is an electrical resistance blood cell counter. This technology may also be referred to as Direct Current (DC) or impedance. The analyzer uses a human whole blood specimen and produces results for 12 hematology parameters, including the basic CBC and three part WBC differential as described above.

2. Results Interpretation

The Sysmex XW-100 provides 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 analyzer instructs the operator to deliver the printout 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 XW-100 for CLIA waived use provides the following results for all specimens:

1) Normal result
2) Result with a high or low flag
3) Suppressed result

The XW-100 results algorithm 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, hemolysis, etc. When the condition is detected, the system generates a flag and the associated results are suppressed.
- Suppression of PLT when $<100 \times 10^3/\mu L$
- Suppression of HGB when <10.0 g/dL
- Suppression of HCT when <25.0 %
- Suppression of WBC when $<3.0 \times 10^3/\mu L$

Adult, adolescent, and pediatric reference ranges, Low and High sample flags, ALERT High and ALERT Low (suppressed) values are illustrated in the table below.

Adults (≥ 21 years of age)					
Parameter	**ALERT Low (not printed)**	**Low**	**Reference Range**	**High**	**ALERT High**
WBC ($x10^3/\mu L$)	< 3.0	3.0–3.8	3.9–10.4	10.5–50.0	> 50.0
RBC ($x10^6/\mu L$)		< 3.71	3.71–5.52	> 5.52	
HGB (g/dL)	< 10.0	10.0–10.8	10.9–16.7	16.8–24.0	> 24.0
HCT (%)	< 25.0	25.0–32.4	32.5–49.4	> 49.4	
PLT ($x10^3/\mu L$)	< 100	100–147	148–382	> 382	
Neut # ($x10^3/\mu L$)		< 2.2	2.2–7.1	> 7.1	
Neut (%)		< 46.4	46.4–76.9	> 76.9	
LYMPH # ($x10^3/\mu L$)		< 0.9	0.9–3.4	> 3.4	
LYMPH (%)		< 14.7	14.7–45.9	> 45.9	
Other WBC # ($x10^3/\mu L$)		< 0.2	0.2–1.2	> 1.2	
Other WBC (%)		< 3.2	3.2–16.9	> 16.9	
MCV (fL)		< 82.5	82.5–98.0	> 98.0	

Adolescents (≥ 12 to < 21 years of age)					
Parameter	**ALERT Low (not printed)**	**Low**	**Reference Range**	**High**	**ALERT High**
WBC ($x10^3/\mu L$)	< 3.0	3.0–4.7	4.8–10.8	10.9–50.0	> 50.0
RBC ($x10^6/\mu L$)		< 4.20	4.20–6.10	> 6.10	
HGB (g/dL)	< 10.0	10.0–11.9	12.0–18.0	18.1–24.0	> 24.0
HCT (%)	< 25.0	25.0–36.9	37.0–52.0	> 52.0	
PLT ($x10^3/\mu L$)	< 100	100–162	163–369	> 369	
Neut # ($x10^3/\mu L$)		< 1.9	1.9–8.6	> 8.6	
Neut (%)		< 40.0	40.0–80.0	> 80.0	
LYMPH # ($x10^3/\mu L$)		< 0.4	0.4–3.9	> 3.9	
LYMPH (%)		< 15.0	15.0–40.0	> 40.0	
Other WBC # ($x10^3/\mu L$)			0.0–2.0	> 2.0	
Other WBC (%)			0.0–19.0	> 19.0	
MCV (fL)		< 80.0	80.0–99.0	> 99.0	

Pediatrics (≥ 2 to 12 years of age)					
Parameter	**ALERT Low (not printed)**	**Low**	**Reference Range**	**High**	**ALERT High**
WBC ($x10^3/\mu L$)	< 3.0	3.0–4.7	4.8–13.5	13.6–50.0	> 50.0
RBC ($x10^6/\mu L$)		< 4.20	4.20–5.40	> 5.40	
HGB (g/dL)	< 10.0	10.0–10.4	10.5–16.0	16.1–24.0	> 24.0
HCT (%)	< 25.0	25.0–28.9	29.0–48.0	> 48.0	
PLT ($x10^3/\mu L$)	< 100	100–162	163–369	> 369	
Neut # ($x10^3/\mu L$)		< 1.9	1.9–8.6	> 8.6	
Neut (%)		< 35.0	35.0–76.0	> 76.0	
LYMPH # ($x10^3/\mu L$)		< 1.0	1.0–7.3	> 7.3	
LYMPH (%)		< 20.0	20.0–54.0	> 54.0	
Other WBC # ($x10^3/\mu L$)			0.0–2.3	> 2.3	
Other WBC (%)			0.0–19.0	> 19.0	
MCV (fL)		< 76.0	76.0–99.0	> 99.0	

3. Description of Changes

The primary difference between the Sysmex XW-100 for CLIA waived use and the XW-100 for POC is a software change. The software modification decreased the number of reported parameters and simplified the flagging (i.e. result suppression) for CLIA waived use, thereby necessitating a revised intended use/indications for use. Additionally, labeling excludes patients with primary or secondary chronic hematologic diseases/disorders.

I. Demonstrating "Simple"

The table below demonstrates how the Sysmex XW-100, Automated Hematology Analyzer is simple per the *Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Wavier Applications for Manufacturers of In Vitro Diagnostic Devices*, issued January 30, 2008.

Guidance Criteria	How Addressed on the XW-100 Analyzer
Is a fully automated instrument or a unitized or self-contained test.	The operator follows test processing on-screen prompts to enter required information, then inserts a sample tube of whole blood, and shuts the door.
Uses direct unprocessed specimens, such as capillary blood (finger stick), venous whole blood, nasal swabs, throat swabs, or urine.	The system uses venous whole blood from standard vacuum blood collection tubes with either K_2 or K_3 EDTA anticoagulant.

Guidance Criteria	How Addressed on the XW-100 Analyzer
Needs only basic, non-technique-dependent specimen manipulation, including any for decontamination.	On-screen prompts and pictographic representations guide the operator through the various steps of sample analysis, including collection tube verification (purple-top required), insertion of sample tube adapter, sample temperature verification (warm to the touch), sample mixing, and inserting the sample onto the analyzer.
Needs only basic, non-technique-dependent reagent manipulation, such as “mix reagent A and reagent B”.	All reagents and QC materials are stored at room temperature, are ready to use, and require no manipulation. The QC materials only require simple mixing by inversion prior to use. On-screen prompts instruct the user to mix the control by inversion.
Needs no operator intervention during the analysis steps.	Once the sample has been inserted into the analyzer, sample analysis begins and no additional operator intervention is required.
Needs no technical or specialized training with respect to troubleshooting or interpretation of multiple or complex error codes.	No technical or specialized training is required, as all error resolution troubleshooting is performed by the system automatically. The exceptions are simple power cycling and insertion of CELLCLEAN which is done by the operator when prompted by an on-screen message. An error code is only displayed when the operator is instructed to call Sysmex Technical Support as a means of documenting cause for service. The operator is never asked to remove a system cover or replace parts.
Needs no electronic or mechanical maintenance beyond simple tasks, e.g., changing a battery or power cord.	The only mechanical maintenance is weekly cleaning of the transducer and waste chamber which is automatically prompted and performed by the system. The operator is prompted to insert a tube of ready to use CELLCLEAN, allow the device to perform the maintenance, and the operator is instructed to open the sample door and remove and dispose of the used tube. The preventive maintenance takes less than 10 minutes and is required every 7 days. Maintenance is tracked automatically by the device.

Guidance Criteria	How Addressed on the XW-100 Analyzer
Produces results that require no operator calibration, interpretation, or calculation.	The operator never performs calibration or calculation. Results are printed with the associated reference range for the indicated age of the patient by the system with no operator involvement. The reference ranges 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.
Provides instructions in the package insert for obtaining and shipping specimens for confirmation testing in cases where such testing is clinically advisable.	The system requires only that the specimen be collected using correct phlebotomy technique. In the event that results generated are not consistent with other clinical findings or if flags are present, the clinician is advised to take further action.
Has test performance comparable to a traceable reference method as demonstrated by studies in which intended operators perform the test.	The XW-100 for POC (K143577) was determined to be substantially equivalent to the Sysmex pocH-100*i* run in the laboratory. In addition, data was provided comparing the XW-100 to manual microscopy.
Contains a quick reference instruction sheet that is written at no higher than a 7th grade reading level.	The Quick Reference Guides (QRGs) are easily understandable, with broad use of diagrams to convey the information. The QRGs were used in the CLIA waiver clinical study. Grade level was assessed using the Flesch-Kincaid program, and was assigned a 7th grade level.

In addition, "Simple" should <u>not</u> have the following characteristics:

Guidance Criteria	How Addressed on the XW-100 Analyzer
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 be collected using correct phlebotomy technique, be warmed if cold to the touch, and mixed following the on-screen prompts, pictures and timer.
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 challenges. In such cases, the potentially affected parameter results will not print.

J. Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-safe Mechanisms

1. Risk Assessment

   Sysmex designed and conducted CLIA waiver flex studies as a two-step process, as specified in the *Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Wavier Applications for Manufacturers of In Vitro Diagnostic Devices*, issued January 30, 2008. A risk analysis was developed focused on user skills and operational steps for the XW-100 in the CLIA waived environment to ensure the test system does not provide erroneous results. This assessment confirmed that most of the errors could not lead to an erroneous result because the fail-safe and failure alert mechanisms of the system software were successful in identifying the procedural error and reflexed to a lock-out function or error code.

2. Fail-safe and Failure Alert Mechanisms

   XW-100 system software fail-safe and failure alert mechanisms include enforcement of the following:

   - Use of reagents and quality control material within expiration dating
   - Use of quality control material within open container stability limits
   - Quality control within range every 8 hours
   - Quality control with a new lot of reagents
   - Patient testing lock-out if quality control out of range
   - Entry of patient date of birth (DOB)
   - No testing of patients less than two years of age based on DOB entry
   - Patient results not displayed on screen; results are printed
   - Weekly cleaning of the instrument with XW CELLCLEAN

Flex studies were designed and performed in order to establish the limits (band-width) of the errors and their impact on the results. Risks were categorized into three basic areas: (a) improper installation, (b) non-compliance with instructions for calibration, quality control (QC), and weekly care and (c) improper routine testing.

a) Risks associated with installation activities: two potential risks, reagent positioning and cap mismatch between diluent and waste containers, were evaluated within the flex studies.

b) Risks associated with non-compliance with calibration, QC, and weekly care: no flex studies were indicated.

c) Risks associated with improper routine testing: the risk assessment identified five potential areas where an operator error could lead to erroneous results. The areas spanned: sample tube types and sample volumes, adequate mixing of whole blood samples, inappropriate sample storage, the use of cold (refrigerated) blood samples,

and freeze/thawing of the reagents. These areas were evaluated within the flex studies.

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 either the XW QC CHECK controls or whole blood samples. For flex studies utilizing XW QC CHECK controls, control values (low, normal, high) were compared to lot specific acceptance ranges. For each study condition, the results for each parameter must fall within the acceptable QC ranges. Criteria for 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
WBC ($x10^3/\mu L$)	± 10%
RBC ($x10^6/\mu L$)	± 6%
HGB (g/dL)	± 7%
HCT (%)	± 6%
PLT ($x10^3/\mu L$)	± 15%

Flex Study 1: Reagent Positioning

To determine if reagent positioning affects analyzer performance, a study was conducted using three levels of XW QC CHECK controls (low, normal, and high), tested in singlet across 3 days, each day under different reagent positioning conditions. Reagent positions tested in this study included:

- Beside the system and at system level (control condition)
- Reagents placed on top of the system
- Reagents positioned below the system

Results

All controls passed and patient testing functionality was allowed when the reagent tray was positioned beside, on top, or below the system. Results from this study demonstrate that the function of the XW-100 is not impacted by reagent position.

Flex Study 2: Mismatching of Diluent and Waste Container Caps Study

A study was conducted to determine if a user error when switching the diluent and waste container caps could cause erroneous results. Three levels of XW QC CHECK controls (low, normal, and high) were tested in singlet. The QC lock-out status was challenged under three conditions:

- Correct setup of waste and diluent tubing (control condition)
- Diluent/waste line tubing mismatched with a full diluent bottle
- Diluent/waste line tubing mismatched with a partial diluent bottle

Results

Testing was only allowed for the control condition; all other testing resulted in a lock-out. Results from this study demonstrate that the instrument operational checks effectively detect if the diluent/waste container caps have been switched and provide a margin of safety if the user does not follow the color coding of the caps/connectors or adhere to instructions.

Flex Study 3: Inadequate Mixing- QC material and whole blood samples

To determine the effects of mixing on QC material and whole blood samples, a study was conducted using various collection tubes and storage at room temperature (18˚C to 25˚C) and refrigerated (2 ºC to 8 ºC). The study consisted of four parts:

Part 1–Inadequate Mixing of Quality Control Material

A study was conducted to determine if failure to follow the instructions for mixing the quality control material can cause erroneous results. Eight vials of the XW QC CHECK low control were used for this study. Three vials were mixed per the package insert (10 times) and assayed. The results were averaged and compared to the established control ranges. The remaining five control vials were mixed as follows (one vial per condition):

- no mixing
- inverted 5 times
- inverted 15 times
- mixed vigorously
- mixed using a mechanical rocker

Results

The results for the unmixed XW QC Check low control were all outside of the QC range. All other mixing conditions tested showed passing results. Results from this study demonstrate that failure to mix the quality control material will result in QC failures and the need to retest prior to proceeding to patient testing. All mixing methods tested showed passing results providing a margin of safety if the user does not adhere to mixing instructions.

Part 2−Inadequate Mixing of Whole Blood Samples

A study was conducted to determine if inadequate mixing of whole blood samples by the phlebotomist immediately post collection could cause erroneous results. Six standard K_2EDTA venipuncture tubes were collected by routine phlebotomy from 10 subjects. The phlebotomist mixed the samples after collection as indicated below:

- no mixing
- inverted 5 times
- inverted 10 times (control condition)
- inverted 15 times
- mixed vigorously
- mixed on a mechanical rocker

The samples were held at room temperature for a period of 20 minutes and then mixed per analyzer instructions prior to testing. The control condition of 10 inversions was tested in triplicate to establish baseline values, and all other conditions were tested once.

Results

For 9 of 10 donors, samples that were not mixed immediately post collection produced acceptable results. In addition, samples mixed by inversion 5 and 15 times, samples mixed vigorously by hand, and samples mixed on a mechanical rocker plate met acceptance criteria when compared to the baseline sample (mixed by inversion 10 times). Results from this study demonstrate that inadequate mixing of blood samples by the phlebotomist immediately post collection is unlikely to impact results. The flagging/suppression rules will lead to retesting the samples in the event of results outside of the normal range.

Part 3−Delay in Mixing/Testing after Sample Collection – Up to 30 Minutes

A study was conducted to determine if allowing a sample to settle for up to 30 minutes following collection without mixing prior to testing could cause erroneous results. For this study, six K_2EDTA venous samples were collected from each of five subjects for each temperature condition. The samples, tested immediately after the draw (control condition), were used to establish baseline values for analysis. All samples were allowed to settle at room temperature or refrigerated (2 ºC to 8 ºC) for 10, 15, 20, 25, and 30 minutes post collection, and all were then tested once. Samples were not mixed prior to analysis.

Results

Standard K_2EDTA venous samples stored refrigerated or at room temperature can be tested up to 10 minutes post draw without further mixing. Results from this study demonstrate that allowing venous samples to settle for more than 10 minutes post draw without mixing prior to testing affects the reported results. On-screen prompts remind the user to properly mix the sample prior to each analysis. The flagging/suppression rules will lead to retesting the samples in the event of results outside of the normal range.

Part 4−Delay in Mixing/Testing after Sample Collection – 2 hours

A study was conducted to determine if not properly mixing a sample after allowing the sample to settle for 2 hours following collection can cause erroneous results. For this study, eight K_2EDTA venous samples were collected from each of five subjects for each study condition and were stored at room temperature and refrigerated conditions. The samples tested immediately after the draw (control condition), were used to establish baseline values for analysis. All samples were allowed to settle for 2 hours prior to analysis, and were then re-suspended using the following number of inversions as variables: 0, 1, 3, 5, 10, and 15 inversions. All samples were tested once.

Results

Standard K_2EDTA venous samples stored at room temperature or refrigerated should be mixed as prompted on the screen prior to analysis. Results from this study demonstrate that testing of K_2EDTA tubes stored for 2 hours at recommended conditions, without proper mixing, will impact results. The on-screen prompt provides a reminder to mix the tube prior to testing. The flagging/suppression rules will lead to retesting the samples in the event of results outside of the normal range.

Flex Study 4: Tube Types and Sample Volumes

A study was conducted to evaluate the performance of the analyzer when using whole blood samples collected in the recommended anticoagulant tubes (i.e. K_2EDTA and K_3EDTA) as well as in various blood collection tubes with contraindicated anticoagulants. Additionally, the effects of under and overfilling the collection tubes during phlebotomy were evaluated.

Part 1−Tube Type Evaluation

To determine if the use of incorrect blood collection tubes can cause erroneous results, six whole blood samples per subject (10 subjects) were collected by venipuncture into tubes with the following anticoagulants: sodium citrate, sodium heparin, lithium heparin, K_2EDTA, K_3EDTA, and standard serum tubes (no anticoagulant). K_2EDTA and K_3EDTA blood collection tubes are the control conditions and are the only tube types indicated. The control conditions were tested in triplicate to establish baseline results.

Results

For serum tubes, all results were suppressed for 8 out of 10 samples. For sodium citrate tubes, all donors showed multiple results outside of the normal range; the flagging algorithm would instruct the user to retest the sample before printing results. For the retest, the on-screen prompt will again ask the user to confirm that the tube is a purple top tube. For the heparin tubes (sodium and lithium), some results were outside of the acceptance criteria for a few parameters, but no results exceeded the reference range. Results from this study demonstrate that the use of incorrect collection tube types (serum and sodium citrate) can impact results. On-screen prompts are provided with each sample

to guide the user through the steps to analyze a sample. The flagging/suppression rules will lead to retesting of samples in the event results are outside of the normal range.

Part 2–Sample Tube Fill Volume Evaluation

To determine if fill volume (under or over filled) in a blood sample collection tube can cause erroneous results, a study was conducted using one under filled and one overfilled standard blood tube prepared from K_2EDTA tubes from each donor in Part 1 of the study. Blood was transferred to venipuncture tubes without additive. Under filling was defined as less than 1 mL of blood in the venipuncture tube. Overfilling was defined as filling the venipuncture tube to the top without overflowing.

Results

The minimum fill volume for testing is 1 mL. When under and over filled tubes were tested from 10 donors, all under filled tubes (<1 mL) produced suppressed results and correct results were reported from all over filled tubes. Results from this study demonstrate that blood collection tubes with <1 mL fill volume produced suppressed results. Results were accurately reported for overfilled tubes. The flagging/suppression rules effectively prevent erroneous results and demonstrate a margin of safety if the user does not adhere to instructions.

Flex Study 5: Inappropriate Sample Storage

A study was conducted to determine the failure points for samples stored outside the recommended temperature conditions (e.g., heated and frozen). K_2EDTA whole blood samples were collected from five subjects for each study part. Samples were stored at room temperature (control condition) and at two temperature conditions outside the recommended storage conditions: frozen (-25˚C to -20˚C) and heated (30˚C to 37˚C). These samples were tested at 0, 1, 2, 4 and 6 hours. All testing was performed in triplicate and the results were averaged.

Results

Samples exposed to freezing conditions demonstrated a decreasing WBC count over time and resulted in WBC results flagged outside of the reference range beginning at 2 hours. RBC results also demonstrated a decreasing count over time, exceeding the acceptance criteria after 6 hours of exposure to freezing conditions. The HGB and HCT parameters were suppressed by 1 hour, following exposure to freezing conditions. For warmed samples, HGB and HCT parameters were suppressed for all samples by 2 hours. For PLT, all conditions gave normal results, with some exceeding the acceptance criteria, but none exceeded the reference range. Results from this study demonstrate that exposing samples to temperatures outside of the recommended storage conditions can affect samples results. The Operator’s Quick Guide provides appropriate guidance for sample handling. The flagging/suppression rules will lead to retesting the samples in the event of result outside of the normal range.

Flex Study 6: Reagent Freeze/Thaw

A study was conducted to determine if the XW-100 can detect compromised reagents due to freezing and lock out patient testing. Three levels of XW QC CHECK controls (low, normal, and high) were tested in singlet across 3 days, each day under different reagent storage conditions. The reagent conditions tested included:

- Reagents stored at room temperature (Condition 1; control condition)
- Pack D reagent stored at room temperature and Pack L reagent that had undergone a freeze/thaw cycle (Condition 2)
- Pack D reagent that had undergone a freeze/thaw cycle and Pack L reagent stored at room temperature (Condition 3)

Results

For Condition 2, two of the controls failed and the XW-100 analyzer displayed an error screen indicating that Sysmex should be contacted when the frozen XW pack L reagent was used to operate the instrument. For Condition 3, the low control failed on the two allowable attempts and the XW-100 analyzer displayed an error screen indicating that Sysmex should be contacted when the frozen XW pack D reagent was used to operate the instrument. Results from this study demonstrate that the use of frozen reagents that had undergone a freeze – thaw resulted in a QC error screen with a message instructing the user to contact Sysmex for assistance. Patient testing could not proceed.

Flex Study 7: Sample Handling – Room Temperature vs Refrigerated Whole Blood Sample

A study was conducted to determine the accuracy of results when samples were assayed cold (2˚C to 8˚C) versus the same sample assayed at room temperature (18˚C to 25˚C) (control condition). Four K_2EDTA venous samples were collected from five subjects. Each tube was tested in triplicate immediately after draw, and means were calculated to establish baselines for each parameter per sample. Specimens were then stored refrigerated for 1 hour. At the conclusion of the time period, the tube was removed, mixed as prompted, and tested one time without acclimation to room temperature.

Results

All samples that were refrigerated for 1 hour met the acceptance criteria for the five CBC parameters, WBC, RBC, HGB, HCT and PLT, when tested on the XW-100. A sample that has been stored refrigerated (2 ºC to 8ºC) for 1 hour may be tested without warming without impacting the results of the test. This provides a margin of safety if the operator does not warm the sample per the on-screen instructions.

Flex Study 8: Environmental Testing

In addition, risks related to the environment in CLIA waived settings, including the impact of tilt, vibration, and minor fluctuations in room temperature on the XW-100 were assessed. Samples were tested on the XW-100 while the analyzer was subjected to non-

level surfaces (tilt), vibration, or temperatures beyond recommended conditions to confirm that no erroneous results would be produced. Results from all environmental flex studies described below demonstrate that the analyzer design has a margin of safety if the recommended environmental conditions are not well controlled.

Tilt Testing

A study was conducted to determine if testing samples on the XW-100 on a non-level surface could cause erroneous results. Three levels of tilt from vertical were tested (5, 10 and 15 degrees) with the analyzer tested in four orientations, varying the low to high tilt each time (front to back, back to front, left to right and right to left). Samples representing a low, normal and abnormal (high) patient were analyzed in triplicate in each test position. Results were compared to the same sample tested in a level orientation.

Results

For the testing on the long axis of the analyzer (front to back and back to front), there were two instrument errors (related to waste sensor) that resulted in suppressed results for WBC. All other non-suppressed results were within the acceptance criteria and no erroneous results were produced. All remaining low and abnormal (high) samples flagged and/or suppressed as expected. The side to side (left and right) tilt at 15 degrees from level, resulted in the analyzer being unstable, as such no testing was completed. For all other combinations of tilt, all results for non-suppressed samples were within the acceptance criteria and no erroneous results were produced. All remaining low and abnormal (high) samples flagged and/or suppressed as expected.

Vibration Testing

A study was conducted to determine if testing samples on the XW-100 on a surface subject to environmental vibrations could cause erroneous results. The analyzer was subjected to three levels of vibration: 4.8 millimeters/second (mm/s), 10 mm/s, and 15 mm/s. An artificial sample was tested in triplicate at each vibration level. Results were compared to the same sample levels tested without vibration.

Results

All non-suppressed results were within the acceptance criteria and no erroneous results were produced. All low and abnormal (high) samples flagged and/or suppressed as expected.

Operating Temperature

A study was conducted to determine if operating the XW-100 outside of the recommended environmental temperature could cause erroneous results. Testing consisted of an initial baseline at nominal conditions (defined as between 15°C and 25°C) prior to moving the XW-100, the reagents, one set of the XW QC CHECK to the first setting of the temperature controlled chamber (33°C ± 2°C). As a control, an additional set of XW QC CHECK was maintained at nominal conditions outside the temperature

controlled chamber. Once the XW-100 and reagents equilibrated to the new temperature in the chamber (a 4-hour adjustment period was allowed), testing the artificial samples was conducted once on the same day. Testing of the artificial samples continued twice a day for four additional days. This testing was repeated with the temperature controlled chamber set at 12°C ± 2°C.

Results

For the high temperature portion (33° ± 2°) of the study, all non-suppressed results were within the acceptance criteria and no erroneous results were produced. All remaining low and abnormal (high) samples flagged and/or suppressed as expected. For the low temperature portion (12° ± 2°) of the study, all non-suppressed results were within the acceptance criteria and no erroneous results were produced. All remaining low and abnormal (high) samples were flagged and/or suppressed as expected.

Flex Study 9: Sample Challenge Study

A sample challenge study was conducted to determine if the XW-100 will flag and/or suppress results for samples with abnormal findings that could lead to the reporting of erroneous results in the CLIA waived setting. Residual K_2/K_3 EDTA venous whole blood samples (n=229) were utilized for testing in this protocol. Samples were tested on the XW-100 and on the pocH-100*i*. The majority of the XW-100 results from this study consisted of suppressed values rather than numerical outputs. Acceptance criterion was the XW-100 not reporting erroneous results when compared to results from the pocH-100*i*.

For all 229 samples, the XW-100 results were appropriately suppressed per the suppression rules and the presence of potentially interfering substances did not result in the reporting of erroneous results when compared to the pocH-100*i*. The number of samples and potential sources of sample error are shown below. Some samples displayed multiple potential sources of error.

Potential Source of Error	Samples Tested
Cold Agglutinins	5
Fragmented RBC's	6
High Lipids	12
High WBC Count	42
Hyperglycemia	11
Hypernatremia	1
Hypochromic Anemia	21
Hyponatremia	1
Immunoglobulin	4
Immunosuppressive Drugs	3
In vivo Hemolysis	2
Large and Giant Platelets	30

Potential Source of Error	Samples Tested
Microcytes	25
Microorganisms (bacterial aggregates, parasites, fungi)	3
Nucleated RBCs	5
Platelet Agglutination	4
Platelet Aggregates	4
Sample Coagulation	2
Warm Agglutinins	1
Other (primarily High MCV, Immature Granulocytes Present, Atypical Lymphocytes)	141

Conclusion

Sample challenge data demonstrate that the XW-100 appropriately suppressed results and avoided the reporting of erroneous results.

K. Demonstrating "Insignificant Risk of an Erroneous Result" (Accuracy)

1. Clinical Study Design

A clinical study was conducted to evaluate the performance of the XW-100 in the hands of the intended users when performed in a CLIA waived setting.

Clinical Study Sites
Testing was performed at six CLIA waived testing sites. Sites had a diverse population of patients and covered a wide range of specialties including family practice, internal medicine, pediatrics, diabetes practice, and a phase I study unit.

Operators
Fourteen untrained operators participated in the clinical study. Operators had no laboratory training or prior knowledge of the system operation and included medical assistants, nurses, 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 college. The operators performed the testing using the Quick Reference Guides; no additional training was provided to the operators.

Subjects (patients)
Patients receiving routine blood draws in the CLIA waived setting were eligible for the study. Five hundred eighty two (582) patients (304 males and 278 females) ranging in age from 2 to 92 years were included in the study. One venous whole blood sample (K_2EDTA or K_3EDTA) was collected from each subject. Each specimen was tested on the XW-100 waived method (WM) at the CLIA waived testing sites by an untrained operator. Twenty nine (29) samples had suppressed results attributed to standard instrument flags for sample issues (e.g. incomplete lysis, unreliable result).

2. Comparative Method

The comparative method (CM), the pocH-100i, is a traceable calibration method. Testing was performed on the pocH-100i in triplicate in moderately/highly complex 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 ($x10^3/\mu L$)	±10%
RBC ($x10^6/\mu L$)	±6%
HGB (g/dL)	±7%
HCT(%)	±6%
PLT ($x10^3/\mu L$)	±15%
NEUT# ($x10^3/\mu L$)	±15% if CM>4.7 ±0.7 if CM≤4.7
LYM# ($x10^3/\mu L$)	±15% if CM>3.3 ±0.5 if CM≤3.3
OTHER WBC# ($x10^3/\mu L$)	±0.5
MCV (fL)	±7%

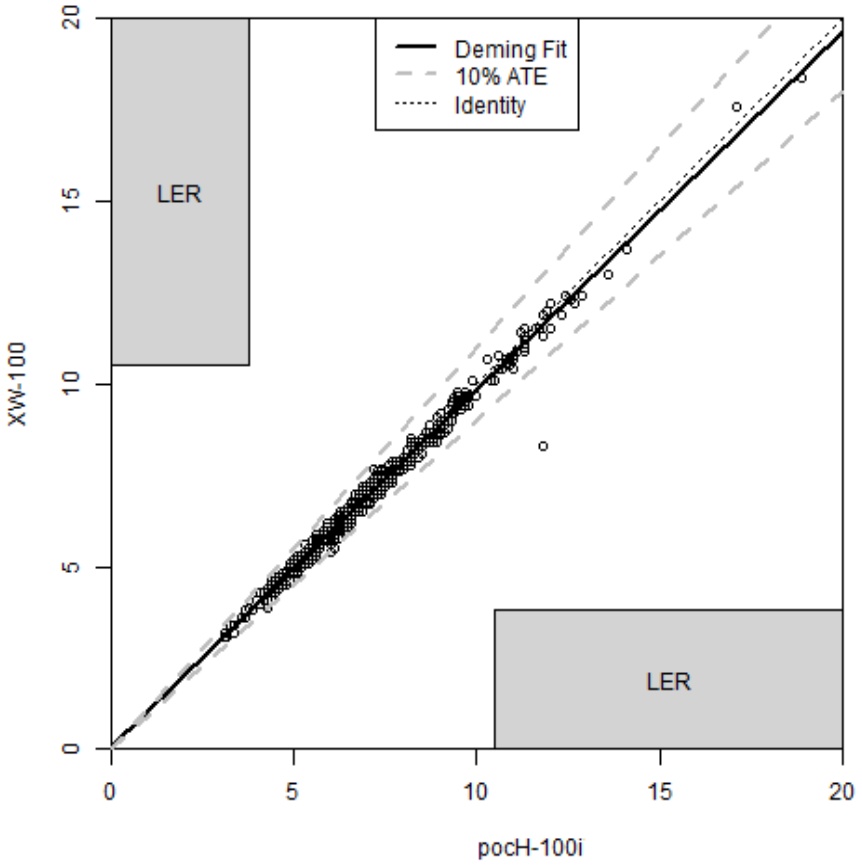
Systematic differences between the XW-100 results and the CM were calculated at the lower and upper limits of the reference interval for adults (≥21 years old) for each hematology parameter. Limit of erroneous results (LER) for each hematology parameter was set by two regions described as (CM=Low and WM=High) and (CM=High and WM=Low) where Low and High are related to the reference interval for adults (≥21 years old).

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 XW-100 results within ATE and LER, along with 95% confidence intervals were calculated
- Total error (an interval for the 95% differences or relative differences between the Sysmex XW-100 result and CM result (an average of 3 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
- ATE and regression analyses were performed by site and for all sites combined

WBC (x 10^3/µL)



ATE = ± 10% Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (552/553) 95% CI: (99.0%; 100.0%)	0.0% (0/553) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM values (10^3/µL)	N	Relative Differences	
		2.5th percentile	97.5th Percentile
[3.1; 5.9]	191	-5.9%	4.8%
[6.0; 7.9]	221	-6.2%	4.0%
[8.0; 18.9]	141	-4.9%	2.9%
[3.1; 18.9]	553	-5.9%	4.1%

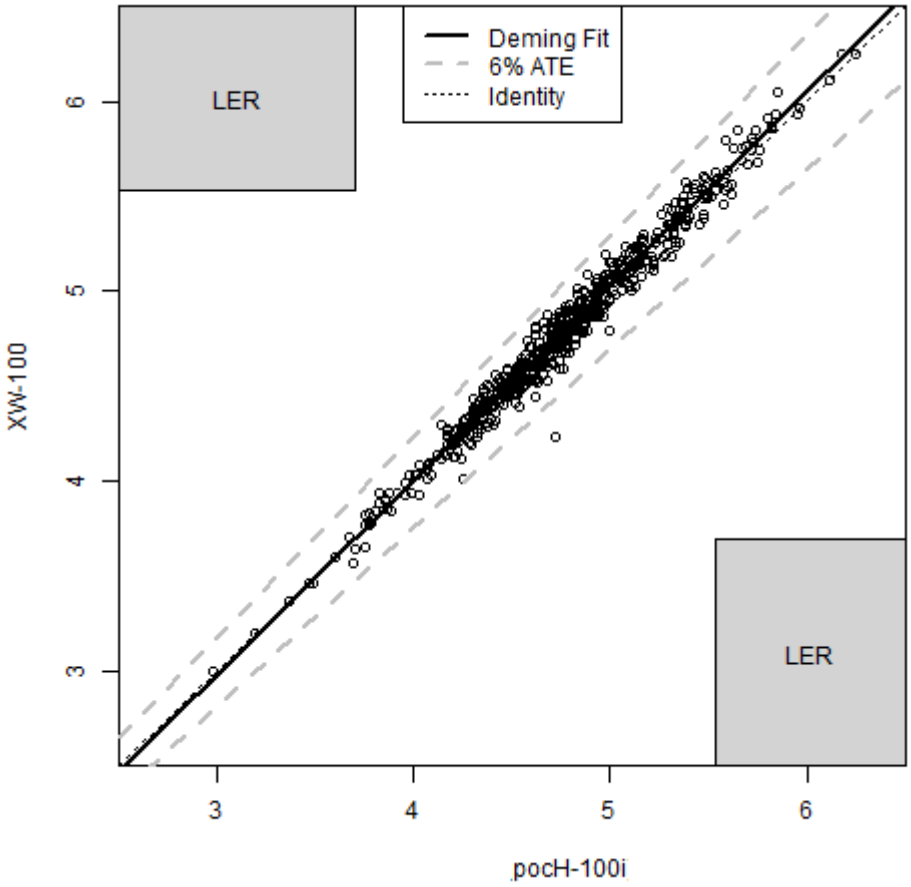
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.979 (0.968; 0.989)	0.063 (-0.000; 0.126)	3.9	-0.5% (-1.2%; 0.1%)	10.4	-1.5% (-2.0%; -1.1%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE Zone	Deming Regression		%Bias at 3.9 (95% CI)	%Bias at 10.4 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	99.1% (106/107) (94.9%; 100.0%)	0.967 (0.927; 1.007)	0.052 (-0.202; 0.307)	-2.0% (-4.6%; 0.6%)	-2.8% (-4.4%; -1.2%)
2	100.0% (110/110) (96.6%; 100.0%)	0.994 (0.976; 1.013)	-0.118 (-0.253; 0.016)	-3.6% (-5.2%; -2.0%)	-1.7% (-2.4%; -1.1%)
3	100.0% (24/24) (86.2%; 100.0%)	1.014 (0.989; 1.040)	0.036 (-0.124; 0.195)	2.4% (0.6%; 4.1%)	1.8% (0.6%; 2.9%)
4	100.0% (83/83) (95.6%; 100.0%)	1.009 (0.992; 1.027)	-0.063 (-0.172; 0.045)	-0.7% (-1.8%; 0.4%)	0.3% (-0.5%; 1.1%)
5	100.0% (116/116) (96.8%; 100.0%)	0.977 (0.963; 0.990)	0.003 (-0.090; 0.097)	-2.2% (-3.4%; -1.1%)	-2.3% (-2.8%; -1.8%)
6	100.0% (113/113) (96.7%; 100.0%)	1.013 (0.999; 1.027)	-0.018 (-0.101; 0.064)	0.9% (0.0%; 1.7%)	1.1% (0.5%; 1.8%)

RBC (10^6/µL)



ATE = ± 6% Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (577/578) 95% CI: (99.0%; 100.0%)	0.0% (0/578) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM Values (10^6/µL)	N	Relative Differences	
		2.5th percentile	97.5th Percentile
[2.98; 4.49]	158	-2.6%	3.1%
[4.50; 4.99]	259	-2.5%	3.9%
[5.00; 6.63]	161	-2.0%	3.3%
[2.98; 6.63]	578	-2.4%	3.2%

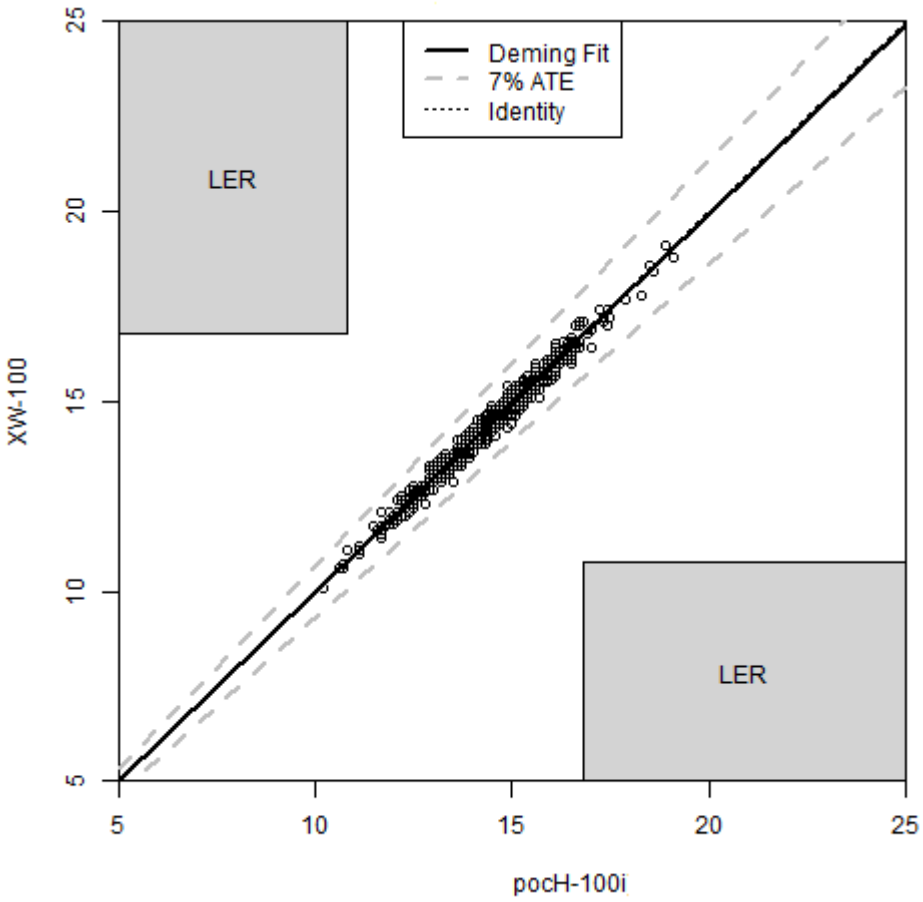
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	% Bias (95% CI)	UL of RI	% Bias (95% CI)
1.024 (1.013; 1.035)	-0.09 (-0.142; -0.039)	3.71	-0.0% (-0.4%; 0.3%)	5.52	0.8% (0.6%; 1.0%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE Zone	Deming Regression		% Bias at 3.71 (95% CI)	% Bias at 5.52 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	99.2% (118/119) (95.4%; 100.0%)	1.032 (1.014; 1.049)	-0.116 (-0.197; -0.035)	0.1% (-0.5%; 0.6%)	1.1% (0.7%; 1.5%)
2	100.0% (113/113) (96.7%; 100.0%)	1.028 (1.004; 1.052)	-0.130 (-0.244; -0.016)	-0.7% (-1.5%; 0.0%)	0.4% (0.1%; 0.8%)
3	100.0% (25/25) (86.7%; 100.0%)	1.000 (0.943; 1.056)	-0.058 (-0.335; 0.220)	-1.6% (-3.3%; 0.2%)	-1.1% (-1.8%; -0.4%)
4	100.0% (85/85) (95.7%; 100.0%)	0.988 (0.963; 1.013)	0.013 (-0.102; 0.128)	-0.8% (-1.5%; -0.2%)	-0.9% (-1.4%; -0.5%)
5	100.0% (119/119) (96.9%; 100.0%)	0.999 (0.983; 1.015)	0.037 (-0.038; 0.111)	0.9% (0.5%; 1.4%)	0.6% (0.3%; 0.9%)
6	100.0% (117/117) (96.8%; 100.0%)	1.037 (1.017; 1.056)	-0.090 (-0.184; 0.003)	1.2% (0.6%; 1.8%)	2.0% (1.7%; 2.4%)

HGB (g/dL)



ATE = ± 7% Percent of samples inside of ATE	LER Percent of samples inside of LER
100.0% (484/484) 95% CI: (99.2%; 100.0%)	0.0% (0/484) 95% CI: (0.0%; 0.8%)

Total Error

Range of CM Values (g/dL)	N	Relative Differences	
		2.5th percentile	97.5th percentile
[10.2; 13.4]	130	-2.4%	2.6%
[13.5; 14.9]	187	-2.9%	2.7%
[15.0; 19.1]	167	-3.1%	2.1%
[10.2; 19.1]	484	-2.8%	2.4%

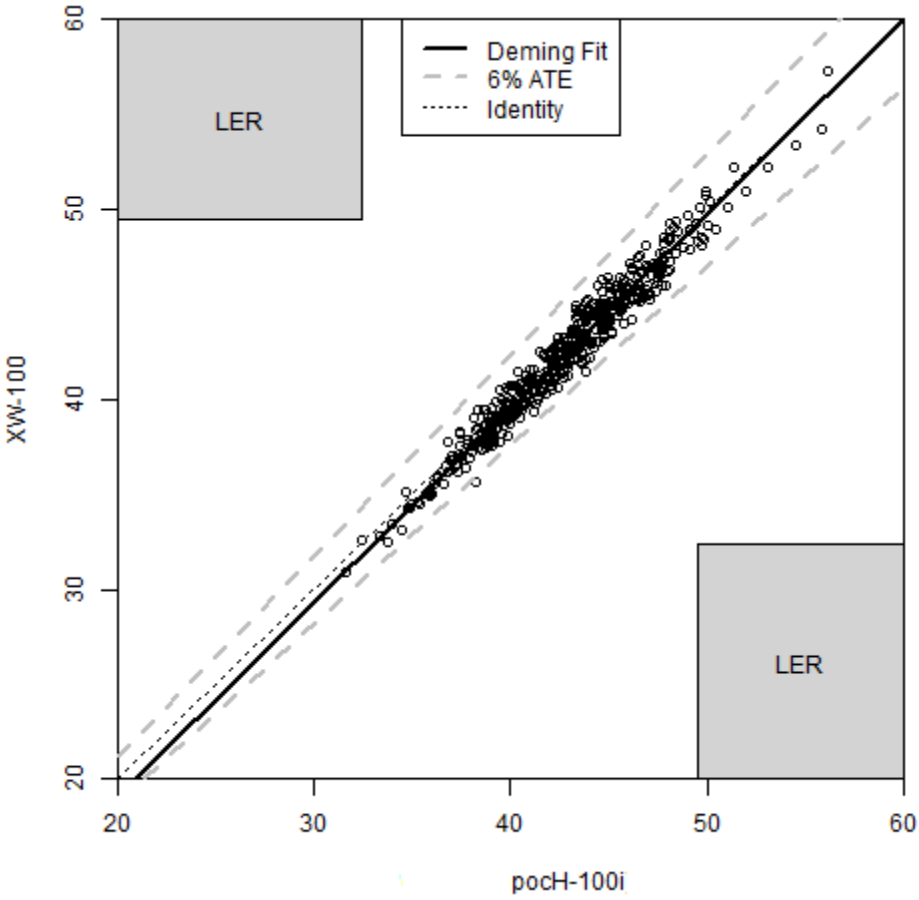
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.992 (0.980; 1.004)	0.08 (-0.092; 0.252)	10.9	-0.0% (-0.4%; 0.3%)	16.7	-0.3% (-0.5%; -0.1%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE Zone	Deming Regression		% Bias at 10.9 (95% CI)	% Bias at 16.7 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	100.0% (53/53) (93.2%; 100.0%)	0.984 (0.958; 1.010)	0.004 (-0.366; 0.374)	-1.6% (-2.3%; -0.8%)	-1.6% (-2.0%; -1.1%)
2	100.0% (104/104) (96.4%; 100.0%)	0.997 (0.982; 1.012)	-0.058 (-0.271; 0.156)	-0.8% (-1.3%; -0.4%)	-0.6% (-1.0%; -0.3%)
3	100.0% (25/25) (86.7%; 100.0%)	0.975 (0.935; 1.015)	0.263 (-0.260; 0.786)	-0.1% (-0.9%; 0.7%)	-0.9% (-1.8%; -0.0%)
4	100.0% (82/82) (95.5%; 100.0%)	0.996 (0.967; 1.024)	0.244 (-0.150; 0.638)	1.8% (1.1%; 2.6%)	1.0% (0.5%; 1.6%)
5	100.0% (104/104) (96.4%; 100.0%)	0.962 (0.942; 0.982)	0.413 (0.132; 0.693)	-0.1% (-0.7%; 0.6%)	-1.4% (-1.7%; -1.0%)
6	100.0% (116/116) (96.8%; 100.0%)	1.012 (0.991; 1.033)	-0.111 (-0.422; 0.200)	0.2% (-0.6%; 1.0%)	0.5% (0.2%; 0.8%)

HCT (%)



ATE = ± 6% Percent of samples inside of ATE	LER Percent of samples inside of LER
99.8% (483/484) 95% CI: (98.8%; 100.0%)	0.0% (0/484) 95% CI: (0.0%; 0.8%)

Total Error

Range of CM Values (%)	N	Relative Differences	
		2.5th percentile	97.5th percentile
[31.6; 39.9]	108	-4.3%	2.5%
[40.0; 44.9]	244	-3.8%	2.9%
[45.0; 56.1]	132	-3.8%	2.5%
[31.6; 56.1]	484	-3.9%	2.6%

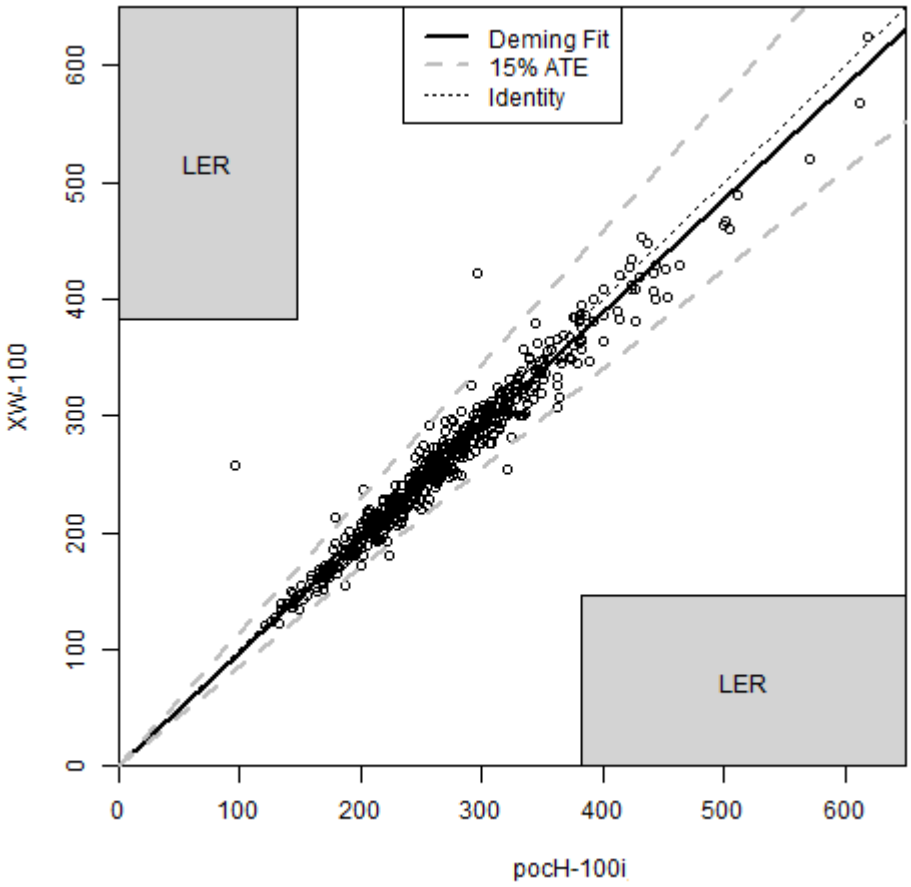
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1.026 (1.008; 1.043)	-1.461 (-2.192; -0.730)	32.5	-1.9% (-2.5%; -1.4%)	49.4	-0.4% (-0.7%; -0.1%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE Zone	Deming Regression		%Bias at 32.5 (95% CI)	%Bias at 49.4 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	100.0% (53/53) (93.2%; 100.0%)	1.011 (0.977; 1.045)	0.141 (-1.276; 1.558)	1.5% (0.5%; 2.5%)	1.4% (0.8%; 2.0%)
2	99.0% (103/104) (94.8%; 100.0%)	0.986 (0.959; 1.013)	-0.311 (-1.465; 0.843)	-2.4% (-3.2%; -1.5%)	-2.0% (-2.5%; -1.6%)
3	100.0% (25/25) (86.7%; 100.0%)	0.980 (0.928; 1.033)	-0.220 (-2.415; 1.976)	-2.6% (-4.1%; -1.2%)	-2.4% (-3.3%; -1.6%)
4	100.0% (82/82) (95.5%; 100.0%)	0.991 (0.964; 1.019)	-0.211 (-1.341; 0.920)	-1.5% (-2.3%; -0.7%)	-1.3% (-1.8%; -0.8%)
5	100.0% (104/104) (96.4%; 100.0%)	0.962 (0.941; 0.984)	0.828 (-0.051; 1.708)	-1.2% (-1.8%; -0.6%)	-2.1% (-2.4%; -1.7%)
6	100.0% (116/116) (96.8%; 100.0%)	1.024 (0.995; 1.053)	-0.741 (-2.016; 0.533)	0.1% (-0.9%; 1.2%)	0.9% (0.6%; 1.3%)

PLT (10^3/µL)



ATE = ± 15% Percent of samples inside of ATE	LER Percent of samples inside of LER
98.8% (566/573) 95% CI: (97.5%; 99.4%)	0.0% (0/573) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM values (10^3/µL)	N	Relative Differences	
		2.5th percentile	97.5th percentile
[96; 224]	156	-12.3%	6.7%
[225; 299]	246	-10.7%	8.3%
[300; 619]	171	-11.6%	4.0%
[96; 619]	573	-11.0%	6.9%

Regression Analysis*

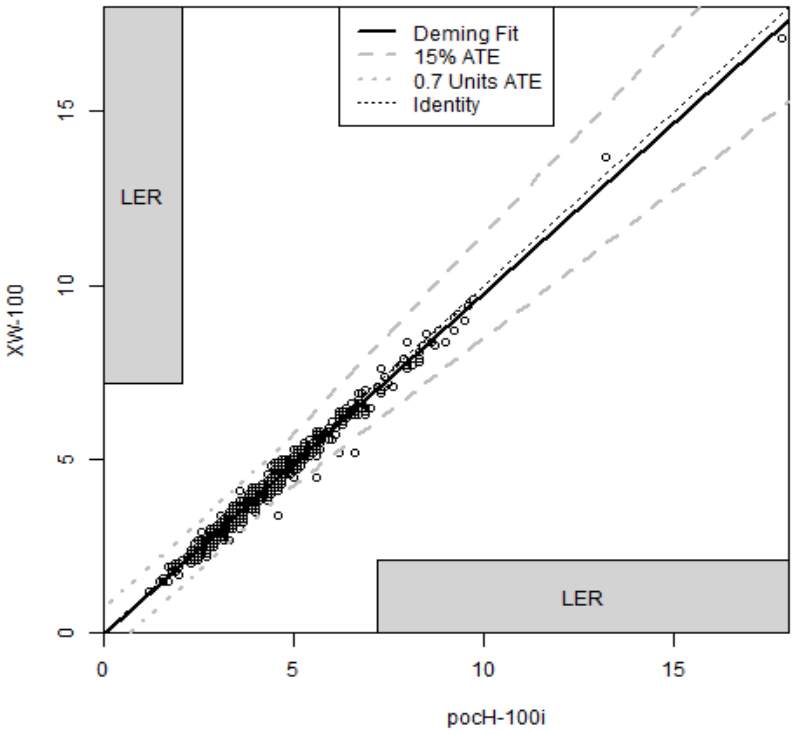
Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
0.971 (0.956; 0.986)	0.497 (-3.083; 4.077)	148	-2.5% (-3.6%; -1.5%)	382	-2.7% (-3.4%; -2.1%)

ATE and Regression Analyses by Site*

Site	Percent of Samples within ATE Zone	Deming Regression		%Bias at 148 (95% CI)	%Bias at 382 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	98.3% (117/119) (94.1%; 99.5%)	1.007 (0.966; 1.047)	-0.490 (-9.696; 8.717)	0.3% (-2.1%; 2.7%)	0.5% (-1.2%; 2.3%)
2	98.2% (111/113) (93.8%; 99.5%)	0.947 (0.907; 0.988)	6.969 (-4.116; 18.053)	-0.6% (-4.2%; 3.0%)	-3.4% (-4.8%; -2.1%)
3	100.0% (25/25) (86.7%; 100.0%)	0.952 (0.913; 0.992)	9.455 (-0.079; 18.989)	1.6% (-1.2%; 4.4%)	-2.3% (-4.0%; -0.6%)
4	100.0% (85/85) (95.7%; 100.0%)	1.019 (0.988; 1.050)	-7.484 (-14.821; -0.146)	-3.2% (-5.2%; -1.1%)	-0.1% (-1.4%; 1.2%)
5	98.3% (115/117) (94.0%; 99.5%)	0.928 (0.904; 0.953)	1.914 (-4.493; 8.322)	-5.9% (-8.0%; -3.8%)	-6.7% (-7.6%; -5.7%)
6	99.1% (113/114) (95.2%; 100.0%)	0.955 (0.924; 0.986)	2.287 (-4.355; 8.929)	-3.0% (-4.6%; -1.4%)	-3.9% (-5.4%; -2.4%)

*At site 1, there was 1 out of 119 (0.8%) points not included in regression analysis (XW-100 result=258 and pocH-100i result=96).

NEUT # (10^3/µL)



ATE = ± 15% or 0.7 Units Percent of samples inside of ATE	LER Percent of samples inside of LER
99.3% (546/550) 95% CI: (98.1%; 99.7%)	0.0% (0/550) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM values (10^3/µL)	N	Absolute or Relative Differences	
		2.5th percentile	97.5th percentile
[1.2; 3.4]	178	Absolute Differences	
		-0.4	0.2
[3.5; 4.7]	155	Absolute Differences	
		-0.5	0.3
[4.8; 17.8]	217	Absolute Differences	
		-0.6	0.2
		Relative Differences	
		-9.0%	-3.9%
[1.2; 17.8]	550	Absolute Differences	
		-0.5	0.3

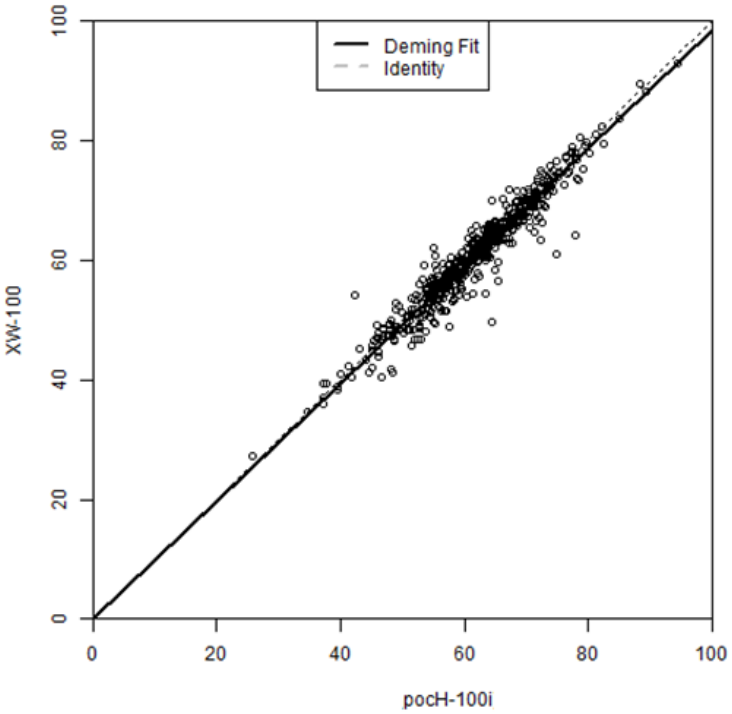
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	%Bias (95% CI)
0.980 (0.966; 0.995)	-0.023 (-0.084; 0.038)	2.2	-0.07 (-0.10; -0.04)	7.1	-2.3% (-3.0%; -1.6%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE Zone	Deming Regression		Bias at 2.2 (95% CI)	%Bias at 7.1 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	99.1% (106/107) (94.9%; 100.0%)	0.960 (0.936; 0.985)	0.046 (-0.062; 0.153)	-0.04 (-0.10; 0.02)	-3.3% (-4.4%; -2.2%)
2	99.1% (108/109) (95.0%; 100.0%)	0.990 (0.961; 1.018)	-0.096 (-0.220; 0.029)	-0.12 (-0.18; -0.05)	-2.4% (-3.7%; -1.1%)
3	100.0% (24/24) (86.2%; 100.0%)	1.020 (0.910; 1.130)	-0.002 (-0.406; 0.402)	0.04 (-0.12; 0.21)	1.9% (-3.3%; 7.1%)
4	100.0% (82/82) (95.5%; 100.0%)	1.014 (0.987; 1.042)	-0.106 (-0.212; 0.001)	-0.07 (-0.13; -0.02)	-0.0% (-1.4%; 1.3%)
5	99.1% (115/116) (95.3%; 100.0%)	0.976 (0.956; 0.996)	-0.079 (-0.173; 0.016)	-0.13 (-0.19; -0.08)	-3.5% (-4.4%; -2.6%)
6	99.1% (111/112) (95.1%; 100.0%)	0.995 (0.961; 1.029)	-0.025 (-0.147; 0.097)	-0.04 (-0.09; 0.02)	-0.9% (-2.7%; 0.9%)

NEUT %



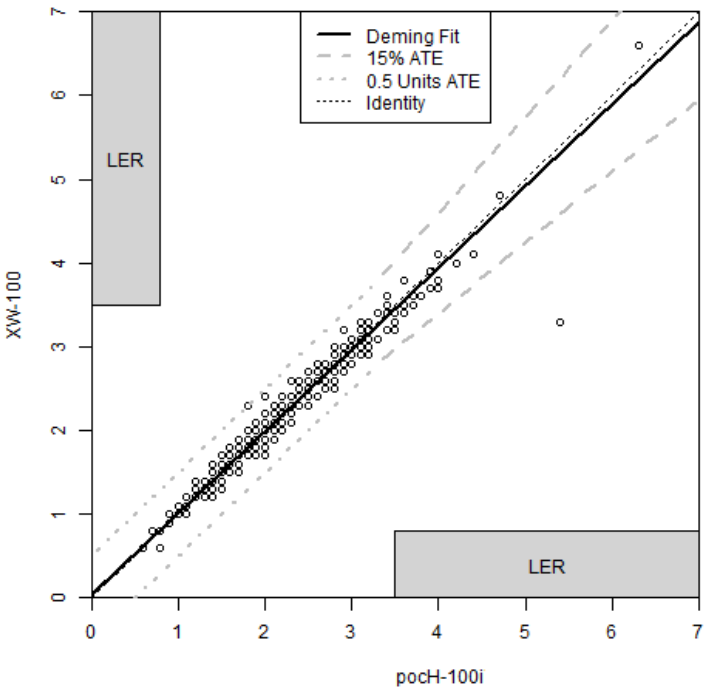
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	Bias (95% CI)
0.983 (0.960; 1.007)	0.201 (-1.254; 1.656)	46.4	-0.57 (-0.99; -0.15)	76.9	-1.08 (-1.47; -0.68)

Regression Analyses by Site

Site	Deming Regression		Bias at 46.4 (95% CI)	Bias at 76.9 (95% CI)
	Slope (95% CI)	Intercept (95% CI)		
1	0.945 (0.877; 1.014)	3.164 (-1.193; 7.520)	0.63 (-0.60; 1.87)	-1.03 (-2.07; 0.00)
2	0.985 (0.931; 1.039)	0.197 (-3.140; 3.533)	-0.48 (-1.39; 0.43)	-0.93 (-1.88; 0.03)
3	0.942 (0.872; 1.012)	3.368 (-0.479; 7.214)	0.69 (-0.14; 1.51)	-1.08 (-2.75; 0.58)
4	1.018 (0.961; 1.075)	-1.748 (-5.296; 1.801)	-0.90 (-1.86; 0.06)	-0.34 (-1.28; 0.60)
5	1.054 (1.011; 1.097)	-4.617 (-7.489; -1.746)	-2.11 (-3.06; -1.17)	-0.47 (-1.05; 0.12)
6	0.953 (0.898; 1.008)	1.527 (-1.813; 4.868)	-0.66 (-1.54; 0.21)	-2.10 (-3.11; -1.09)

LYMPH # (10^3/µL)



ATE = ± 15% or 0.5 Units Percent of Samples inside of ATE	LER Percent of Samples inside of LER
99.8% (552/553) 95% CI: (99.0%; 100.0%)	0.0% (0/553) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM values (10^3/µL)	N	Absolute or Relative Differences	
		2.5th percentile	97.5th percentile
[0.6; 1.5]	132	Absolute Differences	
		-0.2	0.2
[1.6; 2.5]	300	Absolute Differences	
		-0.2	0.2
[2.6; 6.3]	121	Absolute Differences	
		-0.3	0.2
		Relative Differences	
		-8.6%	7.7%
[0.6; 6.3]	553	Absolute Differences	
		-0.2	0.2

Regression Analysis*

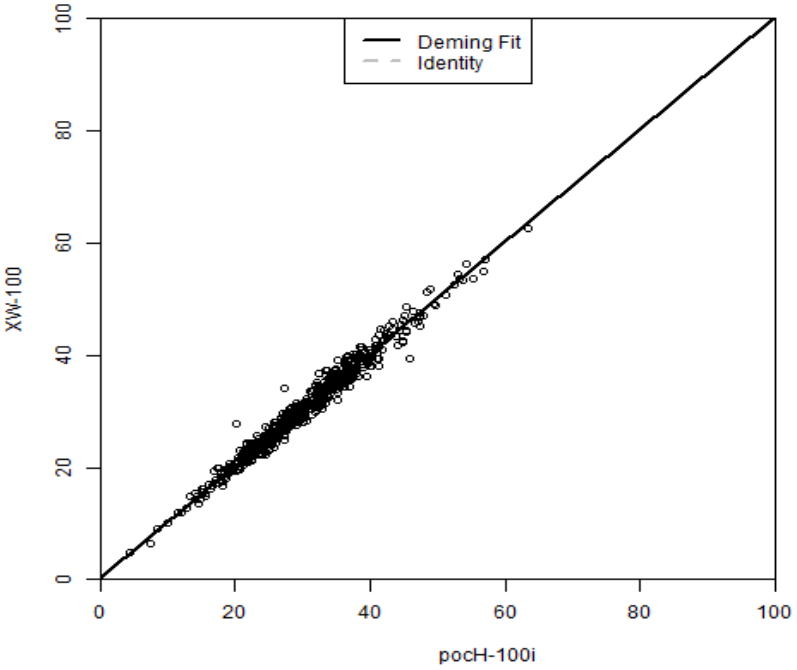
Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	%Bias (95% CI)
0.977 (0.957; 0.998)	0.045 (0.005; 0.084)	0.9	0.02 (0.00; 0.05)	3.4	-1.0% (-1.9%; -0.0%)

ATE and Regression Analyses by Site*

Site	Percent of Samples within ATE Zone	Deming Regression		Bias at 0.9 (95% CI)	%Bias at 3.4 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	99.1% (106/107) (94.9%; 100.0%)	0.945 (0.908; 0.981)	0.075 (-0.003; 0.154)	0.03 (-0.02; 0.07)	-3.3% (-4.8%; -1.8%)
2	100.0% (110/110) (96.6%; 100.0%)	0.967 (0.937; 0.997)	0.027 (-0.040; 0.095)	-0.00 (-0.04; 0.04)	-2.5% (-3.8%; -1.2%)
3	100.0% (24/24) (86.2%; 100.0%)	1.045 (1.008; 1.082)	-0.048 (-0.147; 0.050)	-0.01 (-0.07; 0.06)	3.1% (1.6%; 4.6%)
4	100.0% (83/83) (95.6%; 100.0%)	1.028 (0.989; 1.067)	-0.026 (-0.100; 0.048)	-0.00 (-0.04; 0.04)	2.0% (0.2%; 3.9%)
5	100.0% (116/116) (96.8%; 100.0%)	0.977 (0.940; 1.013)	0.047 (-0.024; 0.118)	0.03 (-0.01; 0.07)	-0.9% (-2.6%; 0.8%)
6	100.0% (113/113) (96.7%; 100.0%)	1.001 (0.968; 1.034)	0.041 (-0.012; 0.095)	0.04 (0.02; 0.07)	1.3% (-0.5%; 3.2%)

*At site 1, there was 1 out of 107 (0.9%) points not included in regression analysis (XW-100 result=3.3 and pocH-100i result=5.4).

LYMPH (%)



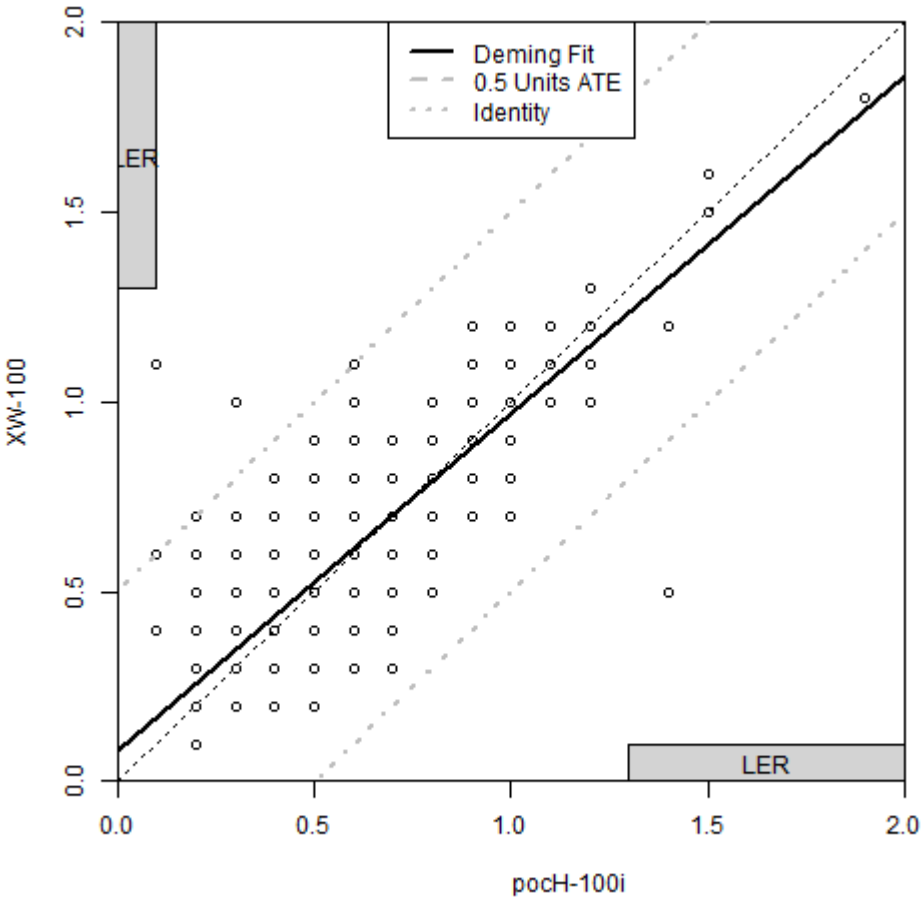
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	Bias (95% CI)
0.998 (0.984; 1.012)	0.406 (-0.006; 0.818)	14.7	0.38 (0.16; 0.60)	45.9	0.32 (0.05; 0.59)

Regression Analyses by Site

Site	Deming Regression		Bias at 14.7 (95% CI)	%Bias at 45.9 (95% CI)
	Slope (95% CI)	Intercept (95% CI)		
1	0.943 (0.907; 0.979)	1.735 (0.620; 2.851)	0.90 (0.28; 1.51)	-0.88 (-1.49; -0.27)
2	1.006 (0.974; 1.039)	-0.100 (-1.138; 0.938)	-0.01 (-0.59; 0.57)	0.19 (-0.34; 0.73)
3	0.979 (0.943;1.015)	0.670 (-0.490; 1.830)	0.36 (-0.34; 1.06)	-0.30 (-1.08; 0.48)
4	1.042 (1.005;1.078)	-0.851 (-2.018; 0.316)	-0.24 (-0.88; 0.40)	1.06 (0.44; 1.67)
5	1.036 (1.004;1.067)	-0.296 (-1.176; 0.583)	0.23 (-0.21; 0.67)	1.35 (0.71; 1.98)
6	0.995 (0.967;1.023)	0.641 (-0.134; 1.417)	0.57 (0.18; 0.95)	0.41 (-0.17; 0.99)

OTHER WBC # (10^3/µL)



ATE = ± 0.5 Units Percent of samples inside of ATE	LER Percent of samples inside of LER
99.3% (542/546) 95% CI: (98.1%; 99.7%)	0.0% (0/546) 95% CI: (0.0%; 0.7%)

Total Error

Range of CM Values (10^3/µL)	N	Absolute Differences	
		2.5th percentile	97.5th percentile
[0.1; 0.4]	203	-0.1	0.4
[0.5; 0.6]	204	-0.2	0.3
[0.7; 1.9]	139	-0.3	0.2
[0.1; 1.9]	546	-0.2	0.3

Regression Analysis*

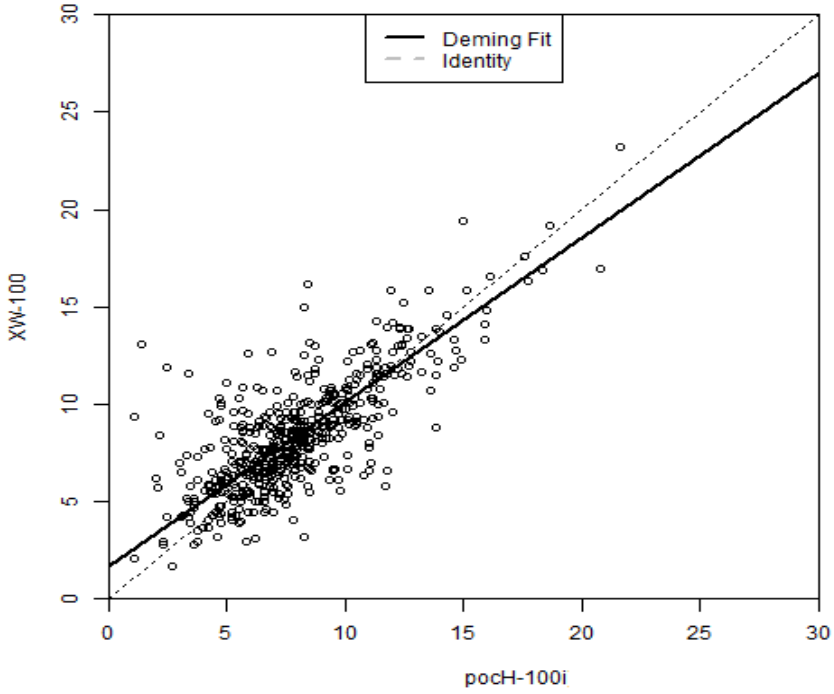
Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	Bias (95% CI)
0.889 (0.837; 0.941)	0.083 (0.053; 0.113)	0.2	0.06 (0.04; 0.08)	1.2	-0.05 (-0.09; -0.01)

ATE and Regression Analyses by Site*

Site	Percent of Samples within ATE zone	Deming Regression		Bias at 0.2 (95% CI)	Bias at 1.2 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	99.1% (105/106) (94.8%; 100.0%)	0.913 (0.787; 1.038)	0.054 (-0.020; 0.127)	0.04 (-0.01; 0.09)	-0.05 (-0.13; 0.03)
2	99.1% (108/109) (95.0%; 100.0%)	0.880 (0.733; 1.026)	0.089 (0.004; 0.173)	0.06 (0.01; 0.12)	-0.06 (-0.15; 0.04)
3	100.0% (24/24) (86.2%; 100.0%)	0.947 (0.800; 1.094)	0.052 (-0.054; 0.157)	0.04 (-0.04; 0.12)	-0.01 (-0.10; 0.08)
4	100.0% (80/80) (95.4%; 100.0%)	0.890 (0.755; 1.025)	0.070 (0.001; 0.138)	0.05 (0.00; 0.09)	-0.06 (-0.16; 0.04)
5	99.1% (115/116) (95.3%; 100.0%)	0.962 (0.837; 1.086)	0.040 (-0.031; 0.112)	0.03 (-0.02; 0.08)	-0.01 (-0.09; 0.08)
6	99.1% (110/111) (95.1%; 100.0%)	0.775 (0.637; 0.914)	0.167 (0.091; 0.243)	0.12 (0.07; 0.17)	-0.10 (-0.20; -0.01)

*At site 1, there was 1 out of 106 (0.9%) points not included in regression analysis (XW-100 result=0.5 and pocH-100i result=1.4) and at site 6, there was 1 out of 111 (0.9%) points not included in regression analysis (XW-100 result=1.1 and pocH-100i result=0.1).

OTHER WBC (%)



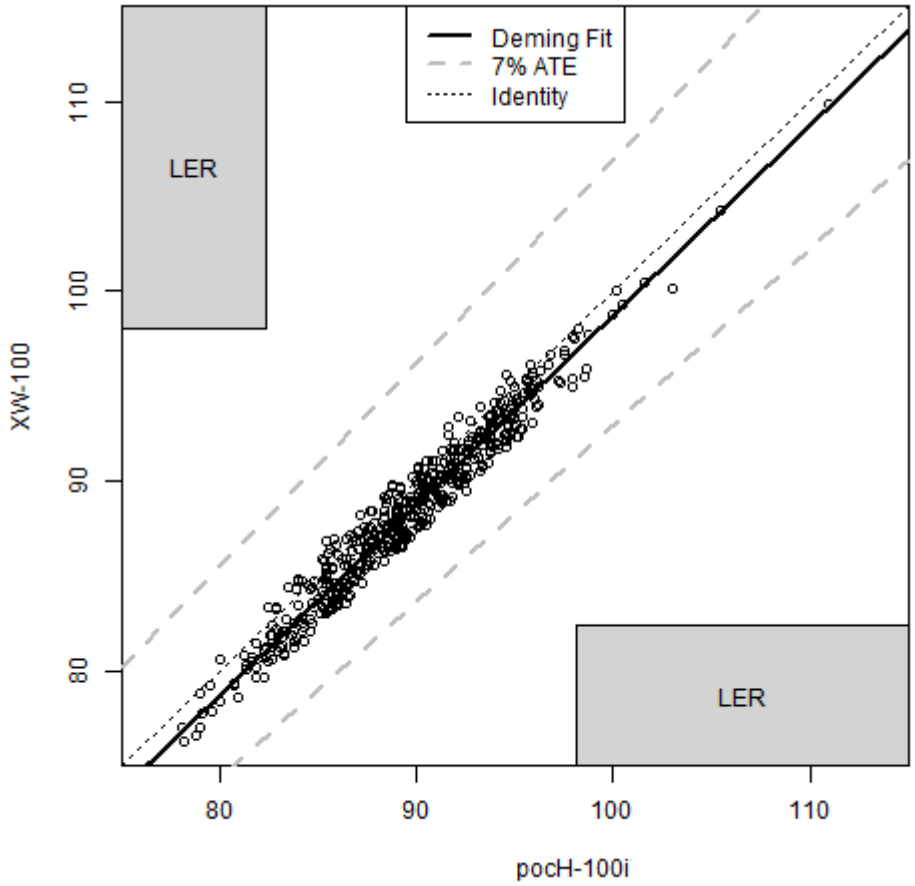
Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	Bias (95% CI)	UL of RI	Bias (95% CI)
0.846 (0.777;0.915)	1.673 (1.094;2.251)	3.2	1.18 (0.81;1.55)	16.9	-0.93 (-1.55;-0.30)

Regression Analyses by Site

Site	Deming Regression		Bias at 3.2 (95% CI)	Bias at 16.9 (95% CI)
	Slope (95% CI)	Intercept (95% CI)		
1	0.910 (0.783; 1.036)	0.880 (-0.072; 1.831)	0.59 (0.02; 1.17)	-0.64 (-1.90; 0.62)
2	0.853 (0.691; 1.015)	1.740 (0.459; 3.021)	1.27 (0.48; 2.06)	-0.74 (-2.28; 0.80)
3	0.995 (0.692; 1.299)	0.008 (-2.928; 2.945)	-0.00 (-1.90; 1.89)	-0.07 (-2.30; 2.15)
4	0.820 (0.662;0.978)	1.601 (0.352;2.850)	1.03 (0.26;1.79)	-1.44 (-2.93;0.06)
5	0.979 (0.815; 1.144)	0.592 (-0.751; 1.935)	0.53 (-0.31; 1.36)	0.24 (-1.26; 1.75)
6	0.643 (0.465; 0.820)	3.895 (2.251; 5.538)	2.75 (1.67; 3.84)	-2.14 (-3.58; -0.71)

MCV (fL)



ATE = ± 7% Percent of samples inside of ATE	LER Percent of samples inside of LER
100.0% (484/484) 95% CI: (99.2%; 100.0%)	0.0% (0/484) 95% CI: (0.0%; 0.8%)

Total Error

Range of CM Values (fL)	N	Relative Differences	
		2.5th percentile	97.5th percentile
[78.1; 86.9]	140	-3.0%	1.1%
[87.0; 91.9]	197	-2.9%	1.0%
[92.0; 110.9]	147	-3.0%	0.5%
[78.1; 110.9]	484	-3.0%	1.0%

Regression Analysis

Slope (95% CI)	Intercept (95% CI)	LL of RI	%Bias (95% CI)	UL of RI	%Bias (95% CI)
1 (0.982; 1.018)	-1.179 (-2.806; 0.449)	82.5	-1.4% (-1.6%; -1.2%)	98	-1.2% (-1.4%; -1.0%)

ATE and Regression Analyses by Site

Site	Percent of Samples within ATE zone	Deming Regression		%Bias at 82.5 (95% CI)	%Bias at 98.0 (95% CI)
		Slope (95% CI)	Intercept (95% CI)		
1	100.0% (53/53) (93.2%; 100.0%)	0.984 (0.960; 1.008)	2.003 (-0.075; 4.081)	0.8% (0.7%; 1.0%)	0.4% (0.1%; 0.7%)
2	100.0% (104/104) (96.4%; 100.0%)	0.968 (0.948; 0.987)	0.930 (-0.810; 2.670)	-2.1% (-2.3%; -1.9%)	-2.3% (-2.5%; -2.1%)
3	100.0% (25/25) (86.7%; 100.0%)	1.009 (0.968; 1.050)	-1.868 (-5.326; 1.590)	-1.3% (-1.5%; -1.2%)	-1.0% (-1.6%; -0.4%)
4	100.0% (82/82) (95.5%; 100.0%)	0.973 (0.956; 0.990)	2.024 (0.497; 3.551)	-0.3% (-0.5%; -0.1%)	-0.7% (-0.8%; -0.5%)
5	100.0% (104/104) (96.4%; 100.0%)	0.962 (0.946; 0.979)	1.136 (-0.377; 2.649)	-2.4% (-2.5%; -2.2%)	-2.6% (-2.8%; -2.4%)
6	100.0% (116/116) (96.8%; 100.0%)	1.020 (1.004; 1.036)	-2.808 (-4.262; -1.353)	-1.4% (-1.6%; -1.2%)	-0.8% (-1.0%; -0.7%)

Conclusion

The study results demonstrate that untrained users were able to perform the test accurately for all 12 hematology parameters using only the Quick Reference Guides of the Sysmex XW-100.

5. Questionnaire Results

Operators

Fourteen operators across the six CLIA waived sites were asked to complete a 6-question questionnaire that polled their opinions of the procedural steps to address ease of use. The multiple-choice responses were presented as a 5-point Likert scale, where rankings ranged from “strongly agree” (5) to “strongly disagree” (1).

Clinicians
The six clinicians (site investigators) at the CLIA waived sites were asked to complete a 5-question questionnaire that polled their opinions of ease of result interpretation. The responses were either “yes” (scored as 1), or “no” (scored as 0).

Results from the two questionnaires demonstrate that the Sysmex XW-100 is simple to use for the operator and provides results that are easy to interpret for the clinician.

L. 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).

M. Conclusion:

The submitted information in this CLIA waiver application is complete and supports a CLIA Waiver approval decision.