510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K172604

B. Purpose for Submission:

This submission is a Dual 510(k) and CLIA Waiver by Application (Dual Submission) tracked as K172604 and CW170012. K172604 was submitted for clearance of a new device. The new device is a modification of the device previously cleared for point of care (POC) use under K143577 and CLIA categorized as moderately complex under CR140520.

C. Manufacturer and Instrument Name:

Sysmex America Inc., XW-100 Automated Hematology Analyzer for CLIA Waived Use

D. 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#).

E. System Descriptions:

1. Device Description:

   The XW-100 Automated Hematology Analyzer (XW-100) is an electrical resistance blood cell counter. This technology may also be referred to as Direct Current (DC) or impedance. The XW-100 analyzes human whole blood specimens anticoagulated with K_2EDTA or K_3EDTA and reports results for 12 hematology parameters, including the basic complete blood count (CBC), 3-part white blood cell (WBC) differential.

2. Principles of Operation:

   The XW-100 uses direct current with hydrodynamic focusing for all parameters except hemoglobin, which is measured photometrically. The patient sample is aspirated, measured, diluted with diluent (and lysed for WBC measurement), then directed into a transducer chamber by a hydrodynamic focusing nozzle. The transducer chamber has a minute hole, or aperture. Electrodes are mounted on both sides of the aperture chamber, through which the direct current flows. Blood cells suspended in the diluted sample are injected through the aperture by the hydrodynamic focusing nozzle. The hydrodynamic focusing nozzle is positioned in front of the aperture and in line with the aperture's center. All blood cells are separated from each other and pass through the aperture in one direction, one cell at a time. When a cell passes through the aperture, it causes a change in the direct current resistance, which is proportional to the cell's size. These resistance

changes are captured as electric pulses. The various blood cell counts are calculated by counting the pulses that occur in each cell size category. The analyzer then determines blood cell volume and identifies cells by creating and analyzing histograms of the various cell populations using their respective pulse heights. Hemoglobin is measured photometrically using a non-cyanide method.

3. Modes of Operation:

   The XW-100 operates by automated whole blood analysis.

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ____X____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes ____X____ or No _____

4. Specimen Identification:

   Specimen identification input is manual (by operator).

5. Specimen Sampling and Handling:

   The XW-100 processes anticoagulated venous whole blood collected in K_2EDTA or K_3EDTA collection tubes. Samples are manually mixed by inversion and loaded into an onboard sample adapter one at a time.

6. Calibration:

   The XW-100 is factory calibrated.

7. Quality Control:

   The XW-100 system performance is evaluated using XW QC CHECK, a stabilized whole blood matrix quality control material designed for statistical process control of the analyzer. Assayed parameters include: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, LYM%, OTHER WBC%, NEUT%, LYM#, OTHER WBC#, NEUT#, RDW-SD, RDW-CV and MPV.

8. Software:

   The XW-100 POC software was modified to serve a CLIA waived setting. These changes included consolidating flags and messages for simplicity. No new cybersecurity risks

were identified with respect to these updated software changes. Refer to submission K143577 for additional software information.

FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

Yes____X____ or No_____

F. Regulatory Information:

1. Regulation section:

   21 CFR § 864.5220, Automated differential cell counter

2. Classification:

   Class II

3 Product code:

   GKZ, Counter, Differential Cell

4. Panel:

   Hematology (81)

G. Intended Use:

1. Indication(s) for Use:

   The XW-100 Automated Hematology Analyzer (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/K_3 EDTA: WBC, RBC, HGB, HCT, MCV, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, NEUT#. It is not for use in diagnosing or monitoring patients with primary or secondary chronic hematologic diseases/disorders, oncology patients, critically ill patients, or children under the age of 2.

2. Special Conditions for Use Statement(s):

   The XW-100 is intended to be used by operators with a minimum of an earned high school diploma or equivalent.

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:

Sysmex XW-100 Automated Hematology Analyzer (K143577)

2. Comparison with Predicate Device:

Similarities		
Item	**Device**	**Predicate (K143577)**
Intended Use	The XW-100 Automated Hematology Analyzer (XW-100) is a quantitative automated hematology analyzer intended for in vitro diagnostic CLIA waived use to classify and enumerate the following parameters for venous whole blood anticoagulated with K2/K3 EDTA: WBC, RBC, HGB, HCT, MCV, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, and NEUT#. It is not for use in diagnosing or monitoring patients with primary or secondary chronic hematologic diseases/disorders, oncology patients, critically ill patients, or children under the age of 2.	The Sysmex XW-100™ is a quantitative automated hematology analyzer intended for *in vitro* diagnostic point-of- care use to classify and enumerate the following parameters for venous whole blood anticoagulated with K2/K3 EDTA: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, NEUT#, RDW-SD, RDW-CV, and MPV. It is not for use in diagnosing or monitoring oncology patients, children under the age of 2, or for chronically or critically ill patients.
Test Principle	Impedance technology (direct current detection) with hydrodynamic focusing for all parameters except hemoglobin, which is measured photometrically.	Same
Measuring Channel	Single hydrodynamic focused impedance chamber	Same
Sample Type	Anticoagulated (K_2EDTA or K_3EDTA) venous whole blood	Same
Sample aspiration volume	15 µL	Same
Reagents	XW Pack L (lyse) XW Pack D (diluent)	Same
System Throughput	20 cycles per hour	Same
Test System Dimensions	Width: 7 inches Height: 14 inches Depth: 18 inches	Same
Mode of Operation	Whole blood mode	Same
Calibration and Quality Control	XW QC CHECK (K143577) SCS™-1000 calibrator (K943268)	Same

There is no difference between the XW-100 for CLIA waived use and the XW-100 cleared for POC settings (predicate), aside from the Intended Use population and the software modifications which produce a decreased number of reported parameters and simplified flagging.

I. Special Control/Guidance Document Referenced (if applicable):

CLSI EP05-A3. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline* –Third Edition, 2014

CLSI EP09-A3. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline* – Third Edition, 2013

CLSI EP21-A2. *Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures*. 2nd ed., 2016

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

J. Performance Characteristics*:*

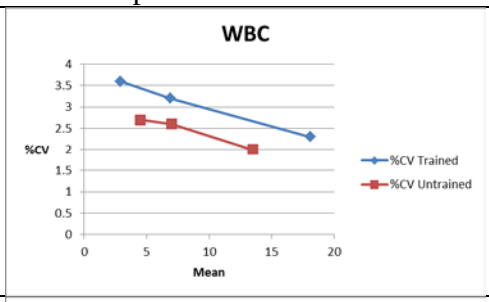
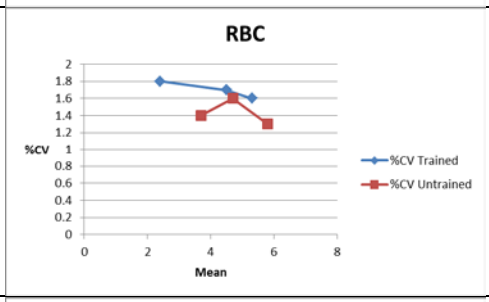
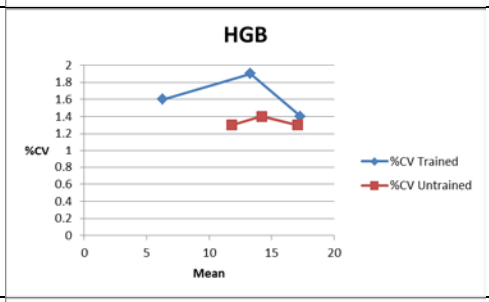
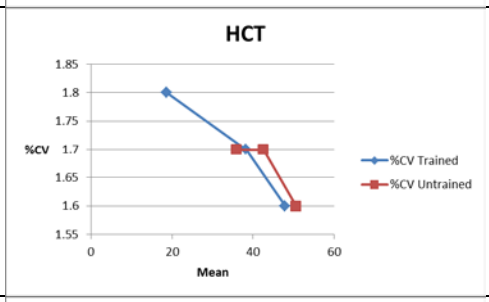
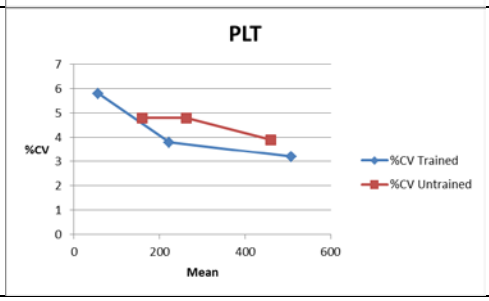
1. Analytical Performance:

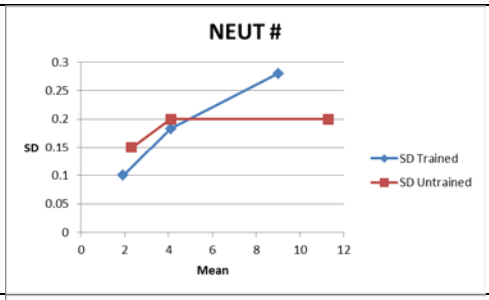
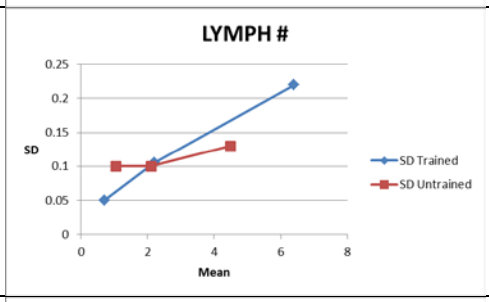
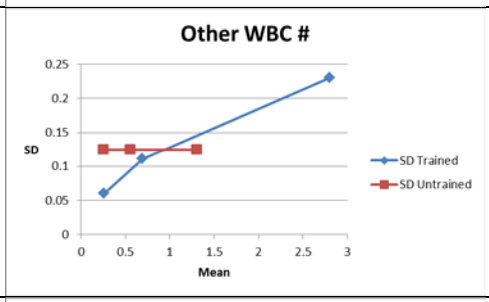
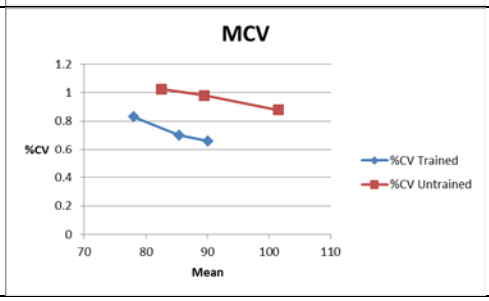
   a. Accuracy:

   A clinical comparison study was conducted to evaluate the performance of the XW-100 in the hands of the intended users (untrained operators) when performed in a CLIA waived setting. Reference submission CW170012 for the details of this study.

   b. Precision/Reproducibility:

   For each hematology parameter, information about total error of the XW-100 in the hands of untrained operators for three sub-ranges (Low, Medium and High) were compared to the total imprecision in the reproducibility study of the XW-100 in the hands of trained operators using precision profiles. Reference submission CW170012 for details regarding total error. For details regarding the reproducibility study, refer to the Decision Summary for K143577. Analysis of the precision profiles described in the table below demonstrate that the XW-100 device in the hands of untrained and trained operators have similar imprecision. The imprecsion estimates include repeatability, different runs, different days, and different sites.

Measurand	Precision profiles
WBC	
RBC	
HGB	
HCT	
PLT	

NEUT #	
LYMP #	
Other WBC #	
MCV	

c. *Linearity*:

Measuring ranges of the new device were narrower than those of the XW-100 in the hands of trained operators, therefore, linearity data of the XW-100 were applicable to the new device. Refer to submission K143577 for the details of the linearity study.

d. *Carryover*:

Carryover of the XW-100 was evaluated during the clearance of the device for the POC setting. Refer to submission K143577 for the details of this study.

e. *Interfering Substances*:

An interference study was conducted to determine the interference level with the

hematology results generated by the XW-100 for the following interfering substances: Bilirubin F, Bilirubin C, hemolytic hemoglobin, chyle, and lipids (Intralipid). Refer to submission K143577 for the details of this study.

2. Other Supportive Instrument Performance Data Not Covered Above:

In 2008 and 2009, the Hematology and Pathology Devices Panel of the Medical Devices Advisory Committee met to provide advice and recommendations to the FDA regarding the CLIA waiver application for an automated WBC analyzer. The panel expressed several key concerns during the meeting leading to a recommendation that the WBC analyzer not be granted waived status. Below is a list of panel concerns and the solutions implemented by Sysmex to mitigate these concerns.

Panel Questions/Concerns	Solution
Do clinically important but undetected interferences, such as NRBC or abnormal WBC, affect the system's status as a simple test?	A sample challenge study was conducted to verify that the XW-100 will appropriately flag and/or suppress results for samples with abnormal findings, such as Nucleated Red Blood Cells (NRBC's), that could lead to the reporting of erroneous results in the CLIA waived setting. For all 229 samples tested, with a variety of potential sources of error, the XW-100 results were appropriately suppressed and the presence of potentially interfering substances did not result in the reporting of erroneous results.
Reflex testing in moderately complex laboratories, triggered by abnormal WBC results, can enable diagnosis of clinically serious diseases. Does the absence of such reflex testing increase the potential for an erroneous clinical impression in a waived setting?	For results that are outside the reference range, the XW-100 prompts the user to repeat testing before results are printed by the device. Once the printout is received, the clinician will then make the decision of how to proceed based on the results and within the context of the patient's clinical presentation.
Is this ATE zone consistent with what is needed for adequate clinical performance across all WBC levels and clinical contexts?	The Allowable Total Error (ATE) utilizing the CLIA'88 42 CFR 493.941 ranges was defined. The CLIA '88 regulations were not appropriate for performance validation requirements and more stringent ATE limits for reportable parameters on the XW-100 in the CLIA waived setting were developed. Reference submission CW170012 for ATE values for all reported parameters.

Panel Questions/Concerns	Solution
The intent of Congress when CLIA ’88 was passed was that all tests should be the same and patients should expect the same level of accuracy from a lab test performed by their personal physician as they do from a lab test conducted in a large hospital or a commercial lab.	The accuracy of the XW-100 was previously demonstrated in the point-of-care setting (K143577). In addition, the data generated from the clinical field study for the XW-100 in the CLIA waived setting in conjunction with the flex studies demonstrates the XW-100 is simple to use and does not generate erroneous results.
Quality control should be required.	The XW-100 requires quality control be run every 8 hours and have acceptable results. The acceptability of QC results is interpreted by the instrument software and not the operator in the waived setting. If QC does not pass, the operator is locked out and patient testing is prevented.
What do the error codes signify and how many error codes are there?	All error resolution is performed by the system automatically. The exceptions are simple power cycling and insertion of XW CELLCLEAN which is done by the operator when prompted by an on-screen message. There are no error codes an operator has to interpret.
If operator training is necessary, is the device really simple? Can any of the setup features be locked so that an operator cannot skip the correct setup?	The XW-100 does not require operator training. On-screen prompts and Quick Guides are available to direct the operator through instrument setup and testing. The device software does not allow the operator to skip steps in the device setup or in running patient samples.
What would happen if an EDTA sample is inadequately mixed?	A flex study was conducted to assess the use of a sample that is inadequately mixed by the phlebotomist post venipuncture as well as inadequate mixing prior to testing the sample. Results from this study demonstrate that inadequate mixing of blood samples by the phlebotomist immediately post collection is unlikely to impact results. Results also revealed that testing samples that have been allowed to settle for more than 10 minutes without proper mixing prior to testing 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 when results are outside of the normal range.

Panel Questions/Concerns	Solution
Current cell counters are complicated. They require substantial maintenance and regular calibration.	The only maintenance required for the XW-100 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 XW CELLCLEAN. Once the XW CELLCLEAN is inserted, the device performs weekly cleaning. After completion of weekly cleaning, the device prompts the operator to open the sample door and remove and dispose of the used tube. The weekly cleaning takes less than 10 minutes and is required every 7 days. Weekly cleaning is tracked automatically by the device. The operator never performs calibration. The XW-100 is calibrated prior to shipping to customers. Quality control (QC) is required every 8 hours to ensure the system is functioning properly. If QC fails twice in a row, the user is instructed to call Sysmex Technical Assistance Center (TAC). A replacement instrument is sent to the customer and the current instrument will be returned for service and/or recalibration.
Since these systems report many components of the complete blood count, understanding of all the results often requires interpretation by a medical technologist or a physician.	The operator is not required to interpret results. Results are printed with the reference range comparatives for the indicated age of the patient by the system with no operator involvement. For any parameter results outside of the normal range, the operator will be prompted by the software to repeat testing. If the results from the second run confirm the results from the first run, the results will print. If the results from the second run do not confirm the results from the first run, the results are suppressed on the printout. The instrument instructs the operator to deliver the printout to the ordering clinician. Once the printout is received, the clinician will then make the decision of how to proceed based on the results and within the context of the patient's clinical presentation.

Panel Questions/Concerns	Solution
The CLIA waived study was not performed in the U.S. Is there sufficient data to show that the test can be performed with a reasonable degree of accuracy that would not invalidate its medical usefulness when used by CLIA waived operators in CLIA waived settings?	The XW-100 clinical study was conducted at six CLIA waived testing sites in the U.S. at locations with diverse patient and operator demographics. The sites covered a wide range of specialties, including family practice, internal medicine, diabetes practice, and pediatrics.
Has the performance of the device been adequately studied in the leukopenic population. For example, cancer patients undergoing chemotherapy or many African-Americans with benign leukopenia.	The XW-100 is contraindicated for use in diagnosing or monitoring patients with primary or secondary chronic hematologic diseases/disorders, oncology patients, or children under the age of 2.
Another criterion for a simple test is that instruction for confirmatory testing should be provided where advisable. Clear criteria for confirmatory testing of abnormal or inconsistent test results should be established.	When the XW-100 detects a specimen abnormality, the instrument printout contains a message for the clinician that reads "RECOMMEND FURTHER TESTING." This message alerts clinicians that further testing is recommended. Sending these samples to the moderately/highly complex lab for further testing is in line with current standard of care and will not cause a delay in patient diagnosis.
The number one patient safety issue, is patient identification. Is there some ability to enter or store that information to ensure accurate results are matched with the right patient?	The instrument produces a printout with the patient ID, date of birth, results, and any flags. Results are not displayed on the screen of the device. This reduces the risk of an operator providing results of an incorrect patient to the clinician or making a transcription error when documenting results in a medical record. The instrument instructs the operator to deliver the printout to the clinician. The operator has no other responsibility in this process.
When you have normal versus abnormal, how much judgment is required? Can results be printed, saved, or retrieved so there is a record of the results.	Results are printed with the reference range comparatives for the indicated age of the patient by the system with no operator involvement. For results that are outside the reference range, the XW-100 will print one of the following: 1) numeric result plus a "High" or "Low" flag 2) "****" (suppressed result) plus an "ALERT L" or "ALERT H" flag. A results printout is always produced by the instrument when testing is fully completed.

K. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

L. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.