CLIA Waiver by Application Approval Determination

Decision Summary

A. Document Number

CW210002

B. Parent Document Number

K210346

C. CLIA Waiver Type:

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

D. Applicant

Sysmex America, Inc.

E. Proprietary and Established Names

Sysmex XW-100 Automated Hematology Analyzer for CLIA Waived use

F. Measurand (analyte)

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

G. Sample Type(s)

Venous whole blood anticoagulated with K2EDTA or K3EDTA

H. Type of Test

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

I. 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 K2 or K3EDTA: 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.

This device was previously cleared (K143577) for point-of-care use to classify and enumerate the following parameters for venous whole blood anticoagulated with K2/K3EDTA: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, NEUT#, RDW-SD, RDW-CV, and MPV. The device was cleared and CLIA waiver granted (K172604/CW170012) for the XW-100 with a software modification that reduced the parameters reported (WBC, RBC, HGB, HCT, MCV, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, and NEUT#) and simplified the flagging (i.e. result suppression). Labeling for the CLIA Waived device excludes the use in patients with primary or secondary chronic hematologic diseases/disorders.

2. Test System Components

XW-100 Analyzer for CLIA Waived Use

- XW pack D (2 x 2 L) is a proprietary reagent which is used to blank the system, dilute the whole blood sample prior to analysis and rinse the analyzed sample out of the system post analysis.
- XW pack L (2 x 250 mL) is a proprietary reagent which is used to lyse RBCs during the testing process to determine WBC and Hemoglobin parameters.
- XW CELL CLEAN (20 single use tubes/box) is a proprietary single use weekly care fluid which keeps the aspiration pipette, sample path, and rinse cup clean and operational.
- XW QC CHECK (2 vials of each level per package) is a proprietary 3 level control which is performed to verify correct system performance.

3. 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 × 10^3/µL
- Suppression of HGB when <10.0 g/dL
- Suppression of HCT when <25.0 %
- Suppression of WBC when <3.0 × 10^3/µL

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/µL)	< 3.0	3.0–3.8	3.9–10.4	10.5–50.0	> 50.0
RBC (x10^6/µL)		< 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/µL)	< 100	100–147	148–382	> 382	
Neut # (x10^3/µL)		< 2.2	2.2–7.1	> 7.1	
Neut (%)		< 46.4	46.4–76.9	> 76.9	
LYMPH # (x10^3/µL)		< 0.9	0.9–3.4	> 3.4	
LYMPH (%)		< 14.7	14.7–45.9	> 45.9	
Other WBC # (x10^3/µL)		< 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/µL)	< 3.0	3.0–4.7	4.8–10.8	10.9–50.0	> 50.0
RBC (x10^6/µL)		< 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	

4. Description of Changes
   This submission supports the new version of the CLIA Waiver software, version 1.14 from the previously cleared version, 1.03.

J. Demonstrating "Simple"

Refer to CW170012

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

1. Risk Analysis

   Refer to CW170012

2. Fail-Safe and Failure Alert Mechanisms

   Refer to CW170012

3. Flex Studies

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

   The following flex studies were conducted to support CW170012:

   1. Reagent Positioning
   2. Mismatching of Diluent and Waste Container Caps Study
   3. Inadequate Mixing – QC Material and Whole Blood Samples
   4. Tube Types and Sample Volumes
   5. Inappropriate Sample Storage
   6. Reagent Freeze/Thaw
   7. Sample Handling – Room Temperature vs Refrigerated Whole Blood Sample
   8. Environmental Testing (tilt, vibration, operating temperature)
   9. Sample Challenge Study

   Refer to CW170012 for more information regarding these studies and study results.

   The new version of the software was determined to have no impact on the environmental studies (tilt, vibration and environmental temperature).

   The software fail-safe and fail alert mechanisms are not impacted with the new version of software. A review of the existing risk control measures from the flex studies identified three areas from the improper routine testing that could be impacted by the changes to the software for v1.14 and were therefore reassessed using the original acceptance criteria (that the result falls within established Allowable Total Error (ATE) ranges, as indicated 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%

The areas of retrospective evaluation included:
1. Sample tube volume and tube type
2. Inadequate mixing (whole blood specimens)
3. Sample storage temperature

These areas are intended to confirm that flagging and/or suppression of specimen results with incorrect tube volume or type, inadequate mixing, or incorrect sample storage temperature prevents reporting of erroneous results with the new software version. The retrospective evaluation of the original Flex Study data from these studies demonstrated that the v1.14 software continues to suppress potential erroneous results appropriately.

A new Sample Challenge Study, originally conducted and described in CW170012, was performed to confirm the appropriate suppression of results for samples associated with interferences, artifacts, or associated conditions for which parameter results should be suppressed in a CLIA Waived environment. In this study, 173 pre-selected, de-identified leftover K2EDTA venous whole blood (normal and abnormal) samples were tested on XW-100 CLIA Waived analyzers using software versions v1.03 (K172604 clearance), v1.13 (on-market), or v1.14 (candidate device) by trained operators. The samples were also run on the Sysmex XN-10 analyzer (K112605). Blood smear analysis and WBC differential counts were performed on all samples as a confirmatory method by qualified examiners in accordance with CLSI H20-A2 – *Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard – Second Edition.*
Samples with interfering substances, rare cells, pathologies, or morphologies with emphasis on samples with known conditions to affect RBC indices were specifically targeted for challenge samples. Samples with parameter flags (Alert High and Alert Low) were also evaluated in the study. A list of abnormalities targeted for challenge samples is provided below.

Challenge Samples
Cold Agglutinins
Fragmented RBC's
High Lipids
High WBC Count
Hyperglycemia
Hypernatremia
Hypochromic Anemia
Hyponatremia
Immunoglobulin
Immunosuppressive Drugs
In Vivo Hemolysis

Challenge Samples
Large and Giant Platelets
Microcytes
Microorganisms (bacterial aggregates, parasites, fungi)
Nucleated RBCs
Platelet Agglutination
Platelet Aggregates
Warm Agglutinins
Other (primarily High MCV, Immature Granulocytes, Atypical Lymphocytes)

Deming linear regression analysis was performed on all unsuppressed results for all reported parameters. The results of this study demonstrated that appropriate and expected suppression of results occurred for the XW-100 CLIA Waived analyzer with v1.14 software for challenge samples, as confirmed by blood smear analysis with WBC differential counts and results from the XN-10 analyzer. Regression analysis indicated that the v1.14 software performed similar to the previously cleared software (v1.03, K172604 and CW170012) and software currently on the market (v1.13).

Conclusion: The software change does not impact the appropriate suppression of results for challenging samples and unaffected parameters maintain similar performance to the previously cleared XW-100 CLIA Waived analyzer.

L. Demonstrating "Insignificant Risk of an Erroneous Result" –Accuracy

1. Comparision Study

   Refer to CW170012

2. Operator Questionnaire

   Refer to CW170012

M. Labeling for Waived Devices

The labeling consists of:

1. Sysmex XW-100 Instructions for Use Manual
2. Clinician's Quick Guide
3. Operator's Quick Guide

4. Shutdown Quick Guide
5. Start-Up Quick Guide
6. Technical Specifications

2. The following elements are appropriately present:

- 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 QRGs identify the test as CLIA waived, and the Clinician's QRG contains a statement that a Certificate of Waiver is required to perform the test in a waived setting.
- The package insert and Clinician's 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).
- The User's Manual and Quick Reference Guide provide instructions for conducting quality control procedures.
- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

N. Conclusion:

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