

**10(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

K071652

B. Purpose for Submission:

New Device

C. Measurand:

White Blood Cells (WBC)

D. Type of Test:

Quantitative

E. Applicant:

HemoCue, Inc.

F. Proprietary and Established Names:

HemoCue WBC System

G. Regulatory Information:

1. Regulation section:

21 CFR 864.5200, Automated Cell Counter or Semi-Automated Cell Counter

2. Classification:

Class II

3. Product code:

GKL

4. Panel:

81 (Hematology)

H. Intended Use:

1. Intended use(s):

The HemoCue WBC system is indicated for use for quantitative determination of white blood cells (WBC) count in capillary or venous whole blood. The HemoCue WBC system is for In Vitro Diagnostic use only. The HemoCue Analyzer is only to be used with HemoCue WBC Microcuvettes. The HemoCue system is indicated for use in clinical laboratories and for point of care settings

2. Indication(s) for use:

The HemoCue WBC system is indicated for use for quantitative determination of white blood cells (WBC) count in capillary or venous whole blood. The HemoCue WBC system is for In Vitro Diagnostic use only. The HemoCue Analyzer is only to be used with HemoCue WBC Microcuvettes. The HemoCue system is indicated for use in clinical laboratories and for point of care settings

3. Special conditions for use statement(s):

Not applicable.

4. Special instrument requirements:

Not applicable.

I. Device Description:

The HemoCue WBC System is composed of the following parts:

- The HemoCue WBC Analyzer (a portable analyzer): The main parts are cuvette holder, cuvette moving arm, magnifying optic unit, camera, image processing software, display, and power adapter. Also included with the analyzer are the Operating Manual, Quick Reference guide, and Instruction CD.
- The HemoCue WBC Microcuvettes (disposable microcuvettes): Made of polystyrene plastic and contains the hemolyzing agent, stain, and nonactive agents. A package insert is also included.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Sysmex XS-1000i, Automated Haematology analyzer

Manual light microscopic WBC method (Class I exempt)

2. Predicate 510(k) number(s):

K060656

3. Comparison with predicate:

Similarities			
<i>Item</i>	<i>HemoCue WBC System</i>	<i>Sysmex XS-1000i</i>	<i>Manual light microscope WBC method</i>
Intended Use	The HemoCue WBC system is indicated for use for quantitative determination of white blood cells (WBC) count in capillary or venous whole blood. The HemoCue WBC system is for In Vitro Diagnostic use only. The HemoCue Analyzer is only to be used with HemoCue WBC Microcuvettes. The HemoCue system is indicated for use in clinical laboratories and for point of care settings.	The Sysmex XS is an automated hematology analyzer for in-vitro diagnostic use in clinical laboratories.	Manual method for white blood cell location and counting. For in-vitro diagnostic use.
Intended use sites	Point of care, Clinical laboratory	Clinical laboratory	Clinical laboratory
Specimen	Whole blood (capillary and venous)	Whole blood (capillary and venous)	Whole blood (capillary and venous)

Differences			
Item	HemoCue WBC System	Sysmex XS-1000i	Manual light microscope WBC method
Method for WBC count	A hemolysing agent lyses the red cells in the microcuvette and a staining agent colors the white cells. An image is taken of the stained white cells and the number of cells is counted by image analysis.	The XS performs hematology analyses using the following methods: Sheath Flow DC Detection Method, Flow Cytometry Methods using a semiconductor Laser and SLS-hemoglobin method.	Dilute aliquot of blood in diluents, which lyses the red cells and stains the nuclei of the whole blood cells. White blood cells are counted (Bürker chamber) microscopically (Light microscope x40 magnification grade) in a haemocytometer with chambers of known volume
Sample volume	10 µL	20 µL	20 µL
Measurement Range	0.3 – 30.0 x 10 ⁹ /L (=0.3 x10 ³ /µL)	WBC: 0.00 – 999.99 x10 ³ /µL	Not specified.
Calibration	Factory calibrated, no further calibration	Automatic and manual calibration using fresh normal blood	N/A
Interferences	Nucleated RBCs may interfere (falsely high)	Where the following are present, the WBC count may be reported falsely high: Red blood cells resistant to hemolysis, Cold agglutinins, Platelet aggregation, Nucleated RBCs, Cryoglobulin	Platelet aggregation, Reticulocytes (immature red blood cells)

K. Standard/Guidance Document Referenced (if applicable):

EP6-A *Evaluation of the Linearity of Quantitative Measurement Procedures*, Approved Guideline, CLSI

EP5A *Evaluation of Precision Performance of Clinical Chemistry Device* Approved Guideline, CLSI

EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples*, Approved Standard-Second Edition, CLSI

EP7-P *Interference Testing in Clinical Chemistry*, CLSI

L. Test Principle:

The HemoCue WBC System consists of the HemoCue WBC Analyzer together with specially designed microcuvettes, HemoCue WBC Microcuvettes. The microcuvette (single-use only) serves both as a sample container and a reaction chamber. A blood sample of approximately 10 µL is drawn into the cavity by capillary action. A hemolysing agent lyses the red cells in the microcuvette and a staining agent colors the white blood cells. An image is taken of the stained white blood cells and the number of cells is counted by image analysis. The result is presented within 3 minutes on the analyzer's display.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-Run and Total precision was determined using four HemoCue WBC Microcuvette batches and five HemoCue Analyzers. Commercially available controls at three different levels were used. The WBC count concentration was measured in duplicate twice a day, during 20 consecutive days. Additionally, a study was performed using fresh blood samples. The study was performed on venous whole blood samples run in duplicate. The results are as follows:

Precision study with control material:

<i>Evaluated levels</i>	<i>n</i>	<i>Within – run</i>	<i>Total</i>
$2.5 \times 10^9/\text{L}$	400	4.1 %	5.4 %
$7.2 \times 10^9/\text{L}$	400	2.9 %	3.5 %
$19 \times 10^9/\text{L}$	400	1.6 %	1.9 %

Precision study with patient sample material:

<i>Evaluated levels</i>	<i>n</i>	<i>Total</i>
$0.3\text{-}1.0 \times 10^9/\text{L}$	12	10.4 %
$1.1\text{-}3.5 \times 10^9/\text{L}$	52	4.1 %
$3.6\text{-}10 \times 10^9/\text{L}$	209	3.5 %
$10.1\text{-}20 \times 10^9/\text{L}$	88	2.5 %
$20.1\text{-}30 \times 10^9/\text{L}$	35	2.2 %
Total	396	3.2

b. *Linearity/assay reportable range:*

Nine different WBC levels were prepared from a whole blood sample and a buffy coat. All levels were analyzed with five replicates on five HemoCue WBC systems. The evaluation of seven levels determined that the HemoCue WBC system is linear between $0.3 - 30.0 \times 10^9/\text{L}$ ($=0.3 \times 10^3/\mu\text{L}$)

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Microcuvette Stability (Open Vial): Stability testing was performed using whole blood samples with a WBC concentration of $4\text{-}10 \times 10^9/\text{L}$ on three batches. The vials were opened ten times during the testing period. Four microcuvettes per storage condition were taken out and analyzed on three different analyzers. The open vial stability has been verified for three months when stored at $15 - 35^\circ\text{C}$ ($59\text{-}95^\circ\text{F}$), $<90\%$ condensing humidity.

Whole Blood: Stability testing was performed on six different venous blood samples with low ($3\text{-}4 \times 10^9/\text{L}$), normal ($5\text{-}10 \times 10^9/\text{L}$) and high WBC levels ($>13 \times 10^9/\text{L}$). The

samples were analyzed initially, after 24 hours and after 48 hours. The samples were stored in room temperature and refrigerator, respectively. The results confirmed that specimens are stable 48 hours, both in refrigerator and room temperature.

d. Detection limit:

Functional Sensitivity (FS) is estimated as the mean concentration for a spiked sample whose CV is 20%. The FS has been determined to be $0.3 \times 10^9/L$

e. Analytical specificity:

Not applicable.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

396 venous specimens were analyzed in duplicate at four sites for the HemoCue System and Sysmex 1000i. Total mean difference was 0.5% and the correlation between methods was $r^2 = 0.992$.

111 venous specimens were collected from two sites and analyzed on both the HemoCue WBC system and the manual light microscope WBC method. The HemoCue WBC fulfilled the accuracy, precision and outlier acceptance criteria. The correlation was between the methods was $r^2 = 0.992$.

b. Matrix comparison:

Capillary whole blood was collected in EDTA Microtainer tube from 68 donors. Venous whole blood was collected in EDTA Vacutainer tubes from 28 of the same 68 donors. The capillary whole blood was analyzed in parallel on HemoCue WBC system and Sysmex XS-1000i. The venous whole blood was analyzed in parallel on The HemoCue WBC system and Sysmex XS-1000i. It was concluded that there is no statistical difference between the systems when analyzing venous and capillary samples.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected values stated below are expected normal ranges for WBC count for individuals within each group.

Adults: $4 - 10 \times 10^9/L$

Children 1 year: $6.0 - 16.0 \times 10^9/L$

Children 2-6 years: $5.0-15.0 \times 10^9/L$

Children 6-12 years: $5.0-13.0 \times 10^9/L$

Infants 1 month: $5.0-19.0 \times 10^9/L$

Infants 2 months: $5.0-15.0 \times 10^9/L$

Infants 3-6 months: $6.0-18.0 \times 10^9/L$

N. Instrument Name:

HemoCue WBC Analyzer

O. System Descriptions:

1. Modes of Operation:

Random access: The microcuvettes serve as sample container and a reaction chamber.

2. Software:

The HemoCue WBC Analyzer performs the WBC count by taking an image of the stained cells, and then counting them using a specially designed algorithm. The results are presented for the user on a display. Additionally, the user may attach a printer. The software application embedded in the analyzer provides the full functionality of the device. This software handles and controls the following: User Interface, Measuring hardware, Measuring algorithm, Communication via a RS232 interface (i.e. printer).

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

Yes X or No

3. Specimen Identification:

Manual recording of specimen identification is required.

4. Specimen Sampling and Handling:

Capillary Blood sampling is performed by a fingertip puncture and applied directly to the HemoCue WBC Microcuvette.

Venous Blood should be sampled at room temperature (15-35°C). If refrigerated (2-8°C, can be stored for 48 hours) allow to warm to room temperature. Sample tubes should be mixed thoroughly on a mechanical mixer for at least 2 minutes or inverted 8-10 times by hand. A drop of blood should be placed on a hydrophobic plastic or glass slide using a pipette or other suitable transfer device. The HemoCue WBC Microcuvette should be filled in on continuous process from this drop of blood.

5. Calibration:

The system was designed and developed to establish agreement with manual light microscopy method for WBC count. The system is factory calibrated and needs no further calibration.

6. Quality Control:

The HemoCue WBC Analyzer has an internal quality control, the "self-test." Every time the analyzer is turned on, it will automatically verify the measurement performance. If additional quality control is required for regulatory reason, it is recommended to contact HemoCue, Inc. or the local distributor for current recommendations of suitable control material.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Interference studies were performed taking sample abnormalities, drugs, metabolites, sample additives and dietary substances into consideration. A list of substances were tested and found not to interfere. This list is included in the labeling (with highest concentration or percentages tested). Nucleated RBCs was the only condition that may interfere to cause the results to be falsely high.

Q. Proposed Labeling:

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

R. Conclusion:

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

