# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
INSTRUMENT ONLY

## I Background Information:

### A 510(k) Number

K201301

### B Applicant

Scopio Labs LTD.

### C Proprietary and Established Names

X100 with Full Field Peripheral Blood Smear (PBS) Application

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| JOY | Class II | 21 CFR 864.5260 - Automated Cell-Locating Device | HE - Hematology |

## II Submission/Device Overview:

### A Purpose for Submission:

Clearance of a new device

### B Type of Test:

White blood cell (WBC) differential, red blood cell (RBC) morphology evaluation and platelet estimation

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

**B Indication(s) for Use:**

The X100 with Full Field Peripheral Blood Smear Application is intended to locate and display images of white cells, red cells, and platelets acquired from fixed and stained peripheral blood smears and assists a qualified technologist in conducting a WBC differential, RBC morphology evaluation, and platelet estimate using those images. For in vitro diagnostic use only. For professional use only.

**C Special Conditions for Use Statement(s):**

Rx - For Prescription Use Only

## IV Device/System Characteristics:

**A Device Description:**

X100 with Full Field Peripheral Blood Smear (PBS) Application automatically locates and presents images of blood cells on peripheral smears. The user browses through the imaged smear to gain high-level general impression. The user reviews the suggested classification of each white cell according to type and may manually change the suggested classification of any cell. The user can also characterize red cell morphology on observed images. In addition, the system suggests the location of platelets. The user reviews each detected platelet and the suggested platelet estimation and may manually change the detections or the estimation. The Full Field PBS is intended to be used by skilled users, trained in the use of the device and in the identification of blood cells.

The Full Field PBS consists of two major components: 1) The X100 Microscope, an optic scanning unit where sample slides are inserted to the digital microscope for imaging, and 2) The X100 Scopiobox, an operating and analyzing computer which controls the X100 microscope and serves the Full Field PBS application.

To acquire a high-resolution image, the sample slide is moved by the X100 microscope positioning stage under its main optic tube, which has a microscope objective with a tube lens and high-resolution camera. The X100 microscope captures multiple images of the sample under a plurality of illumination conditions (different durations, different illumination angles, different illumination patterns, different wavelengths), without the need for immersion oil. Using a physical model and the captured images, the X100 Scopiobox reconstructs high-resolution images of the sample.

**B Instrument Description Information:**

1. Instrument Name:

   X100 with Full Field Peripheral Blood Smear Application

2. Specimen Identification:

The slide's barcode is captured automatically and assigned to each case. The device also supports typing the barcode manually.

3. Specimen Sampling and Handling:

   A peripheral blood sample collected in $K_2$EDTA or $K_3$EDTA tubes is mixed manually or automatically. A thin blood film is wedged on a clean dry glass slide (a blood smear) and stained with Romanowsky stain. After the staining process is completed, the slide is covered using any standard cover slipping method.

4. Calibration:

   The Full Field PBS system requires initial calibration for its mechanical and optical performances. An initial calibration process is performed on a standard blood smear slide as part of the manufacturing process of the device. The calibration is verified after installation by a technician or a qualified operator. Calibration can also be performed if a problem arises in the daily QC testing.

5. Quality Control:

   Quality Control (QC) testing is performed on a daily basis ("daily QC"). The daily QC involves testing a standard blood smear slide prepared on the same day. During the daily QC the user reviews the images received from the Full Field PBS and verifies that at least 95% of the WBCs in the scanned image were identified and located correctly by the system. The Full Field PBS application maintains a digital QC log, enabling the user to review and to track the history of QC testing performed by the Full Field PBS.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

Easy Cell Locator
Light, Microscope

### B Predicate 510(k) Number(s):

K092116

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | K201301 | K092116 |
|---|---|---|
| Device Trade Name | X100 with Full Field Peripheral Blood Smear Application | EasyCell Cell Locator |

| **General Device Characteristic Similarities** | | |
|---|---|---|
| Intended Use / Indications for Use | The X100 with Full Field Peripheral Blood Smear Application is intended to locate and display images of white cells, red cells, and platelets acquired from fixed and stained peripheral blood smears and assists a qualified technologist in conducting a WBC differential, RBC morphology evaluation, and platelet estimate using those images. For in vitro diagnostic use only. For professional use only. | The EasyCell is intended to locate and display images of white cells, red cells, and platelets acquired from fixed and stained peripheral blood smears and assists a qualified technologist in conducting a WBC differential, RBC morphology evaluation, and platelet estimate using those images. For in vitro diagnostic use only. For professional use only. |
| Sample Type | Stained blood film glass slides of peripheral whole blood | Same |
| Sample Preparation | Romanowsky stain | Same |
| Analysis Technique: White Blood Cells | WBC are located/counted by moving according to the battlement pattern (ensuring that each cell is counted only once). Cell images are analyzed using standard mathematical methods, including deterministic artificial neural networks (ANN's) trained to distinguish between classes of white blood cells. The cell images are pre-classified, and the user reviews the suggested classification, and accepts or reclassifies the images. | Same |
| Analysis Technique: Red Blood Cells | Red blood cells: The device presents an overview image. The examiners characterize red blood cell morphology from the image. | Same |

| | | |
|---|---|---|
| Daily QC | The QC procedure controls for slide preparation (both smearing and staining) and device performance. If the QC procedure does not pass, the operator must resolve the problem and rerun the QC before processing samples. | Same |
| **General Device Characteristic Differences** | | |
| Analysis Technique: Platelets | Platelets are automatically located/counted by moving according to the battlement pattern (ensuring that each cell is counted only once).<br>The user reviews the suggested estimate of the platelet concentration, and accepts or modifies the result. | The device presents a series of images. The reviewers manually count and estimate the platelet concentration from the images according to a procedure in the User's Manual. |
| Pre-classified WBC | Cell images are grouped into eighteen (18) categories: Band Neutrophils; Segmented Neutrophils; Lymphocytes; Atypical Lymphocytes; Large Granular Lymphocytes; Aberrant Lymphocytes; Monocytes; Eosinophils; Basophils; Promyelocyte; Metamyelocytes; Myelocytes; Blasts; Plasma Cells; Nucleated Red Blood Cells; Unclassified; Smudge cells; Dirt | Cell images are grouped into eight (8) categories:<br>Neutrophils (Band or Segmented; Lymphocytes; Monocytes; Eosinophils; Basophils; Nucleated Red Blood Cells; Smudge cells; Other (which is intended to hold morphologically abnormal cells.) |
| High-Resolution Image Acquisition | Fully automated scan and image acquisition. Captures multiple images under plurality of illumination conditions and reconstructs a 100X magnification image of the viewed area, without the need for immersion oil. | Fully automated scan and image acquisition. Captures images at 10X resolution to locate certain cells and then capture images of those cells using a 100X magnification lens and immersion oil. |

## VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
CLSI EP12-A2: User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition
CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition
CLSI H20-A2: Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard - Second Edition
IEC 62471 First edition 2006-07: Photobiological safety of lamps and lamp systems

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

**Repeatability**

The repeatability study was performed according to the CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition.

A 20x2x2 repeatability study for the analyses of white blood cells differential and platelet estimation was conducted using a single instrument at a single site with 15 selected test samples. Over the course of 20 testing days, 2 daily runs were performed using 2 replicas. The selected samples represented different clinical conditions, to include all automatically located and pre-classified cell types. In total, 1,200 scans were analyzed.

As a high-level summary, the following tables capture, for each variance component, the maximum measurement received for the upper bound of the 95% CI of the standard deviation. All repeatability study results met acceptance criteria.

| Maximum SD upper bound values of 95% CI | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Cell Type | Variance Components | | | | | | | |
| | Repeatability | | Between-Run | | Between-Day | | Within-Laboratory Precision | |
| | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI |
| **Segmented & Band Neutrophil** | 53.3 % | 1.8 % | 83.4% | 1.3 % | 66.4 % | 1.9 % | 75.2 % | 2.2 % |
| **Lymphocyte** | 48.6 % | 1.6 % | 48.6% | 0.8 % | 18.2 % | 1.9 % | 18.2 % | 2.1 % |
| **Variant Forms Lymphocyte** | 6 % | 1.3 % | 6 % | 0.4 % | 2.8 % | 0.7 % | 6 % | 1.3 % |
| **Monocyte** | 9.7 % | 1.6 % | 3.7 % | 0.5 % | 5.9 % | 0.8 % | 9.7 % | 1.6 % |
| **Eosinophil** | 6.3 % | 0.6 % | 2.6 % | 0.3 % | 3.3 % | 0.8 % | 3.3 % | 0.8 % |
| **Basophil** | 0.5 % | 0.4 % | 0.5 % | 0.3 % | 0.5 % | 0.6 % | 0.5 % | 0.7 % |
| **Plasma cell** | 0.6 % | 0.4 % | 0.6 % | 0.2 % | 0.5 % | 0.1 % | 0.5 % | 0.4 % |

| Maximum SD upper bound values of 95% CI | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Cell Type | Variance Components | | | | | | | |
| | Repeatability | | Between-Run | | Between-Day | | Within-Laboratory Precision | |
| | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI | Mean | SD upper bound of 95% CI |
| **Immature Granulocyte** | 0.8 % | 0.5 % | 0.7 % | 0.3 % | 0.7 % | 0.7 % | 0.7 % | 0.7 % |
| **Blast** | 3 % | 1.2 % | 3 % | 0.4 % | 0 % | 0 % | 3 % | 1.1% |
| **NRBC** | 5.8 % | 0.6 % | 3.5 % | 0.2 % | 3.5 % | 0.4 % | 5.8 % | 0.6 % |

| Maximum SD upper bound values of 95% CI | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Cell Type | Variance Components | | | | | | | |
| | Repeatability | | Between-Run | | Between-Day | | Within-Laboratory Precision | |
| | Mean | SD upper bound values of 95% CI | Mean | SD upper bound values of 95% CI | Mean | SD upper bound values of 95% CI | Mean | SD upper bound values of 95% CI |
| **Platelet Estimation** | 305.5 | 31.7 | 155.3 | 18.1 | 153.1 | 23.8 | 213.9 | 34.4 |

## Reproducibility

The reproducibility study was performed according to the CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition.

A 3x5x5 reproducibility study for the analyses of white blood cells differential and platelet estimation was performed across 3 different sites. The study was conducted at each site, with 10 test samples, for 5 testing days, using 5 replicas scanned with the local device. The selected samples represented different clinical conditions, to include all automatically located and pre- classified cell types. In total, 750 scans were analyzed.

As a high-level summary, the following tables capture, for each variance component, the maximum measurement received for the standard deviation. Reproducibility study results passed pre-defined acceptance criteria.

| Maximum SD Values | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Cell Type | Variance Components | | | | | | | | | |
| | Repeatability | | Between-Day | | Within-Laboratory Precision | | Between-Site | | Reproducibility | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| **Segmented & Band Neutrophil** | 52.9 % | 1.7 % | 50.6 % | 1.1 % | 52.9 % | 1.7 % | 50.6 % | 3.9 % | 50.6 % | 4.2 % |
| **Lymphocyte** | 23.4 % | 1.4 % | 26.5 % | 2 % | 26.5 % | 2.2 % | 17.2 % | 2.8 % | 26.5 % | 3.1 % |
| **Variant Forms Lymphocyte** | 9.9 % | 1.1 % | 5.2 % | 1.3 % | 5.2 % | 1.5 % | 5.2 % | 1.1 % | 5.2 % | 1.9 % |
| **Monocyte** | 6.5 % | 1.2 % | 6.5 % | 0.6 % | 6.5 % | 1.3 % | 8.2 % | 1.2 % | 8.2 % | 1.5 % |
| **Eosinophil** | 2.7 % | 0.4 % | 2.7 % | 0.3 % | 2.7 % | 0.5 % | 2.7 % | 0.4 % | 2.7 % | 0.7 % |
| **Basophil** | 0.5 % | 0.3 % | 0.8 % | 0.1 % | 0.5 % | 0.3 % | 0.6 % | 0.3 % | 0.8 % | 0.4 % |
| **Plasma cell** | 0.6 % | 0.2 % | 0.6 % | 0.1 % | 0.6 % | 0.3 % | 0.6 % | 0.4 % | 0.6 % | 0.5 % |
| **Immature Granulocyte** | 1.8 % | 0.5 % | 1.8 % | 0.4 % | 1.8 % | 0.6 % | 1.8 % | 1 % | 1.8 % | 1.2 % |
| **Blast** | 4.3 % | 0.8 % | 4.3 % | 0.1 % | 4.3 % | 0.8 % | 4.3 % | 1.1 % | 4.3 % | 1.4 % |
| **NRBC** | 6.7 % | 0.5 % | 6.7 % | 0.1 % | 6.7 % | 0.6 % | 6.7 % | 0.9 % | 6.7 % | 1.1 % |

| Maximum SD Values | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Cell Type | Variance Components | | | | | | | | | |
| | Repeatability | | Between-Day | | Within-Laboratory Precision | | Between-Site | | Reproducibility | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| **Platelet Estimation** | 217.2 | 22.0 | 217.2 | 17.8 | 217.2 | 28.3 | 217.2 | 29.7 | 217.2 | 41.0 |

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Accuracy (Instrument):

   **Method Comparison**

   A Method Comparison study was conducted to compare the results achieved by trained examiners using the X100 with Full Field Peripheral Blood Smear Application (the Test Method) to the results achieved by using a manual light microscope. The study was performed according to the CLSI H20-A2: Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard— Second Edition.

   A total of 645 specimens were collected and analyzed at three sites. 335 specimens were from normal (healthy) subjects and 310 were from subjects with specific disease conditions. Slides were prepared from each specimen. The slides were randomly selected, blinded and evaluated by two examiners at each site.

   White Blood Cells

   Following analysis at each site, a pooled analysis of the multi-center results was conducted. The following table summarizes the results of the Deming regression comparison method for the multi-center study. All 95% CI of slope and intercept and Pearson correlation coefficient met the acceptance criteria for accuracy measured by Deming regression for WBC differential.

**WBC correlation between reference method and test method (Multi-center Deming Regression for 200 WBC Differential)**

| Cell Type | Intercept (95% CI) | Slope (95% CI) | Pearson correlation coefficient (r) |
|---|---|---|---|
| Neutrophil (%) | **0.39** (-0.44 to 1.21) | **1.00** (0.99 to 1.01) | **98%** |

| Cell Type | Intercept (95% CI) | Slope (95% CI) | Pearson correlation coefficient (r) |
|---|---|---|---|
| Lymphocyte (%) | **-0.51** (-1.02 to 0.00) | **0.99** (0.96 to 1.02) | **96%** |
| Monocyte (%) | **-0.15** (-0.60 to 0.31) | **0.94** (0.86 to 1.02) | **95%** |
| Eosinophil (%) | **0.00** (-0.17 to 0.16) | **0.89** (0.82 to 0.96) | **98%** |

Overall WBC differential efficiency (agreement), sensitivity and specificity were measured, as well as for distributional WBC (Band and Segmented Neutrophil, Monocyte, Lymphocyte and Eosinophil) and morphological WBC (Immature Granulocyte, Variant Forms Lymphocyte, Blast, NRBC and Plasma cell) between subject device and manual microscope.

**WBC Differential Efficiency, Sensitivity and Specificity**

| | Morphological Abnormality | Distributional Abnormality | Overall |
|---|---|---|---|
| Efficiency | **96.82%** (96.12% to 97.43%) | **95.75%** (94.95% to 96.46%) | **96.29%** (95.77% to 96.76%) |
| Sensitivity | **85.46%** (80.19% to 89.78%) | **88.83%** (85.94% to 91.31%) | **87.86%** (85.38% to 90.06%) |
| Specificity | **97.79%** (97.16% to 98.31%) | **97.43%** (96.70% to 98.03%) | **97.62%** (97.16% to 98.02%) |

Predicted bias analysis (Bland-Altman) of WBC differential is summarized below. The mean differences and 95% limits of agreements per cell type were measured.

Red Blood Cells

Results of overall agreement for RBC morphology evaluation are shown below. Results passed pre-defined acceptance criteria.

**Red blood cells overall agreement**

| RBC | Overall Agreement with 95% CI |
|---|---|
| Overall | **99.77%** (99.71% to 99.83%) |

| RBC Morphology Group | Overall Agreement with 95% CI |
|---|---|
| Color | **99.49%** (99.14% to 99.73%) |
| Shape | **99.77%** (99.68% to 99.84%) |
| Size | **99.61%** (99.36% to 99.78%) |
| Inclusions | **100.00%** (99.93% to 100.00%) |

| RBC Morphology Group | Overall Agreement with 95% CI |
|---|---|
| Arrangement | **96.65%** (95.52% to 97.57%) |

Platelet Estimation

Platelet estimation efficiency, sensitivity and specificity measurements between subject device and manual microscope are as follows. Results passed pre-defined acceptance criteria.

**Platelet Estimation Efficiency, Sensitivity and Specificity**

| Platelet Estimation | |
|---|---|
| Efficiency | **94.89%** (92.78% to 96.53%) |
| Sensitivity | **90.00%** (83.51% to 94.57%) |
| Specificity | **96.28%** (94.11% to 97.82%) |

**Method Comparison Study of 100 to 200 WBC Differential and 5 to 10 FOV Platelet Estimation**

All slides from the Method Comparison study were also analyzed by Full Field PBS device using 100 WBC differential and 5 FOV platelet estimation. The results were compared to the 200 WBC differential and 10 FOV platelet estimation of the manual light microscope. Accuracy (Deming Regression), efficiency, sensitivity and specificity were measured.

White Blood Cells

**100 WBC correlation between reference method and 200 WBC test method**

| Cell Type | Intercept (95% CI) | Slope (95% CI) | Pearson correlation coefficient (r) |
|---|---|---|---|
| Neutrophil (%) | **0.87** (0.00 to 1.75) | **0.99** (0.98 to 1.01) | **98%** |
| Lymphocyte (%) | **-0.50** (-1.01 to 0.00) | **0.99** (0.96 to 1.01) | **96%** |
| Monocyte (%) | **-0.13** (-0.57 to 0.31) | **0.93** (0.86 to 1.01) | **94%** |
| Eosinophil (%) | **0.01** (-0.20 to 0.22) | **0.88** (0.80 to 0.97) | **97%** |

**100 WBC Efficiency, Sensitivity and Specificity**

| | Morphological Abnormality | Distributional Abnormality | Overall |
|---|---|---|---|
| Efficiency | **96.48%** (95.74% to 97.12%) | **95.06%** (94.21% to 95.82%) | **95.77%** (95.22% to 96.27%) |

| | | | |
|---|---|---|---|
| Sensitivity | **81.06%** (75.34% to 85.94%) | **86.35%** (83.23% to 89.07%) | **84.83%** (82.14% to 87.26%) |
| Specificity | **97.79%** (97.16% to 98.31%) | **97.17%** (96.41% to 97.80%) | **97.50%** (97.03% to 97.91%) |

Platelets

**5 FOV Platelet Estimation Efficiency, Sensitivity and Specificity**

| Platelet Estimation | |
|---|---|
| Efficiency | **94.55%** (92.39% to 96.24%) |
| Sensitivity | **90.00%** (83.51% to 94.57%) |
| Specificity | **95.84%** (93.58% to 97.48%) |

5. Carry-Over:

Not applicable.

**B Other Supportive Instrument Performance Characteristics Data:**

Not Applicable.

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

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