510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY

I Background Information:

A 510(k) Number

K243144

B Applicant

Scopio Labs Ltd.

C Proprietary and Established Names

X100 with Full Field Peripheral Blood Smear (PBS) Application
X100HT 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:

This submission is for the addition of a Decision Support System (DSS) to support the user's review of red blood cell (RBC) morphology and platelet clumps.

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/X100HT 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:

The X100/X100HT with Full Field Peripheral Blood Smear (PBS) Application ("Full Field PBS") automatically locates and presents images of blood cells on peripheral blood smears. The user browses through the imaged smear to gain a 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 reviews and may manually change the suggested platelet estimation as well. In this modified version, a decision support system (DSS) has been added to support the user's review of red blood cell (RBC) morphology and platelet clumps. The DSS's recommendations are presented to the user by means of a dotted line around the grade or parameter suggested by the DSS. The user is instructed to review the DSS's suggestions and must actively mark the appropriate selection.

The device consists of two main hardware components: the digital scanner (X100/X100HT) and the processing unit.

The RBC analysis starts from the center of the monolayer, detecting non-overlapping RBCs at a single region at a time, moving outward in a spiral to analyze additional regions. The analysis process includes two steps – the first step keeps analyzing regions until 10,000 non-overlapping RBCs are detected. These cells are then assigned morphological labels. The final grading is set by converting the morphology percentages of the analyzed cells into grades using the default thresholds recommended by the International Council for Standardization in Hematology (ICSH), that can be modified by the lab director.

The platelet clumps detection analyzes the entire monolayer and feathered edge regions of the scan to identify platelet clumps.

B Instrument Description Information:

1. Instrument Name(s):

   X100 with Full Field Peripheral Blood Smear (PBS) Application
   X100HT with Full Field Peripheral Blood Smear (PBS) 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_2EDTA or K_3EDTA 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:

   The daily QC involves testing a standard blood smear slide to verify image quality. 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):
X100 with Full Field Peripheral Blood Smear (PBS) Application, X100HT with Slide Loader with Full Field Peripheral Blood Smear (PBS) Application

B Predicate 510(k) Number(s):
K201301, K220013

C Comparison with Predicate(s):

Device & Predicate Device(s):	K243144	K201301	K220013
Device Trade Name	X100/X100HT with Full Field Peripheral Blood Smear Application	X100 with Full Field Peripheral Blood Smear (PBS) Application	X100HT with Full Field Peripheral Blood Smear (PBS) Application
General Device Characteristic Similarities			
Intended Use/Indications For Use	The X100/X100HT with Full Field Peripheral Blood Smear Application is intended	Same	Same

	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.		
Intended User	Skilled users, trained in the use of the device and in the identification of blood cells.	Same	Same
Sample Type	Stained blood film glass slides of peripheral whole blood	Same	Same
Sample Preparation	Romanowsky stain	Same	Same
Analysis Technique: White Blood Cells	WBCs 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	Same
Analysis Technique: Platelets estimation	Platelets are located/counted by moving according to the	Same	Same

	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 detect platelets. The user reviews the suggested estimate of the platelet concentration and accepts or modifies the result.		
Quality Control	The daily QC involves testing a standard blood smear slide. 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.	Same	Same
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.	Same	Same
General Device Characteristic Differences			
Analysis Technique: Red Blood Cells	The device presents an overview image to be reviewed by the user. The system presents to the user a dotted line around RBC	The device presents an overview image to be reviewed by the user. The examiner manually grades RBC morphology from the	The device presents an overview image to be reviewed by the user. The examiner manually grades RBC morphology from the

	morphology grading suggestions. The examiner manually grades RBC morphology from the image.	image.	image.
Analysis Technique: Platelets Clump presence	The device presents an overview image to be reviewed by the user. The system presents to the user a dotted line around a suggestion whether platelet clump was detected. The examiner manually marks if platelet clumps are present in the smear.	The device presents an overview image to be reviewed by the user. The examiner manually marks if platelet clumps are present in the smear.	The device presents an overview image to be reviewed by the user. The examiner manually marks if platelet clumps are present in the smear.

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
- IEC 62471 First edition 2006-07 Photobiological safety of lamps and lamp systems
- ANSI AAMI ISO 14971:2019 Medical Devices – Applications of risk management to medical devices
- ANSI UL 61010-1 3rd Ed 2012-05-12 Standard for Safety for Electrical Equipment for Measurement Control and Laboratory Use
- ANSI AAMI IEC 62304:2006/A1:2016 Medical device software – Software life cycle processes
- ANSI AAMI IEC 62366-1:2015+AMDI:2020 Medical devices Part 1: Application of usability engineering to medical devices

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Repeatability

Repeatability was conducted at three (3) clinical sites – two (2) US sites and one (1) OUS site, using 27 test samples representing different RBC morphological features as well as platelet clumping. Over the course of 20 testing days, two (2) daily runs were performed using two (2) replicates. The selected samples represented 23 morphological features in different grading levels. In total, 2160 scans were performed. The DSS suggestions from the scans were compared to the assigned reference grades as performed by laboratory professionals. The rate of agreement was calculated for each sample and each morphological feature separately, and each of the rate of agreement results was compared separately to a predefined acceptance criterion of 80%. All results met the pre-defined acceptance criteria.

Morphological Feature	Mean Agreement
Acanthocytes	99%
Anisocytosis	99%
Basophilic stippling	98%
Bite cells	98%
Blister cells	98%
Echinocytes	98%
Elliptocytes	100%
Helmet cells	99%
Howell-Jolly bodies	98%
Hypochromia	96%
Macrocytes	100%
Micro-organisms	100%
Microcytes	100%
Ovalocytes	99%
Pappenheimer bodies	98%
Poikilocytosis	97%
Polychromasia	97%
Schistocytes	99%
Sickle cells	100%
Spherocytes	98%
Stomatocytes	100%
Target cells	99%
Teardrop cells	99%
Platelet clumps	95%

Reproducibility

Reproducibility was performed using 16 test samples across three (3) clinical sites, two (2) US sites and one (1) OUS site, with the test samples representing different RBC morphological features as well as platelet clumping. The study was conducted over five (5) testing days with five (5) replicates per day on three (3) devices. All results met the pre-defined acceptance criteria of 80%.

Morphological Feature	Mean Agreement
Acanthocytes	99%
Anisocytosis	99%

Morphological Feature	Mean Agreement
Basophilic stippling	97%
Bite cells	97%
Blister cells	100%
Echinocytes	97%
Elliptocytes	99%
Helmet cells	99%
Howell-Jolly bodies	97%
Hypochromia	95%
Macrocytes	99%
Micro-organisms	99%
Microcytes	100%
Ovalocytes	98%
Pappenheimer bodies	97%
Poikilocytosis	97%
Polychromasia	96%
Schistocytes	99%
Sickle cells	99%
Spherocytes	99%
Stomatocytes	100%
Target cells	99%
Teardrop cells	99%
Platelet clumps	96%

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 (PBS) Application with the RBC and Platelet Clump Decision Support System (DSS) and without the RBC and Platelet Clump Decision Support System (DSS). A total of 1200 PBS slides were prepared, each from a different blood sample, from three (3) clinical sites – two (2) US sites and one (1) OUS site, representing RBC morphological features in different grading levels as well as platelet clumping. These samples were collected during routine laboratory workflow of the three sites, represented the range of clinical conditions expected in the target population, and were randomly assigned to the investigators at each site. The samples were split between six (6) investigators (200 samples per investigator) and analyzed in two (2) methods (reference

and test arms). First, in the reference arm, the samples were assessed using the previously cleared version of the application without DSS assistance. After a three-week washout period, sample anonymization and randomization, the investigators analyzed the same samples in the test arm, using the modified version of the Full Field PBS Application, with DSS suggestions presented to investigators for RBC morphology and platelet clumping. In both arms of the study, the qualified users were provided with a full field scan of their assigned samples, graded the same 23 RBC morphological features according to a predefined 4-graded scale, and evaluated the presence of platelet clumps in each sample. The same images were reviewed with and without the newly introduced DSS for RBC morphological features and indications concerning platelet clump presence. A washout period of three (3) weeks took place between finishing one study arm and starting the second.

The results were evaluated according to the categories of morphological features (RBC color, RBC inclusions, RBC shape, RBC size, PLT Clumping) with acceptance criteria applied for each category and each predictive value separately, including 95% confidence intervals measured using 1000 bootstrap iterations. All RBC categories and platelet clumping met the pre-defined acceptance criteria of 80% for overall agreement, PPA and NPA.

Multi-Center Performance by Morphological Features – All Sites Combined:

Category	PPA (95% CI)	NPA (95% CI)	Overall Agreement (95% CI)
RBC Color	98.33% (97.48%, 99.10%)	97.61% (96.81%, 98.33%)	97.88% (97.29%, 98.42%)
RBC Inclusions	86.73% (81.66%, 91.23%)	98.41% (98.06%, 98.78%)	97.90% (97.50%, 98.27%)
RBC Shape	95.35% (94.50%, 96.12%)	96.40% (96.06%, 96.71%)	96.22% (95.92%, 96.50%)
RBC Size	99.42% (99.03%, 99.75%)	92.72% (91.82%, 93.70%)	95.58% (95.06%, 96.13%)
PLT Clumping	86.11% (82.13%, 89.91%)	87.39% (85.39%, 89.3)	87.08% (85.25%, 88.92%)

Results evaluated for each morphological feature separately:

Morphological Feature	PPA (95% CI)	NPA (95% CI)	Overall Agreement (95% CI)
Hypochromia	99.31% (98.43%, 100.00%)	96.86% (95.58%, 97.99%)	97.75% (96.92%, 98.50%)
Polychromasia	97.40% (95.92%, 98.72%)	98.38% (97.48%, 99.20%)	98.00% (97.17%, 98.75%)
Basophilic stippling	96.55% (88.89%, 100.00%)	99.91% (99.74%, 100.00%)	99.83% (99.58%, 100.00%)
Howell-Jolly bodies	81.56% (74.82%, 87.82%)	93.96% (92.51%, 95.45%)	92.50% (91.00%, 93.96%)
Micro-organisms	85.71% (50.00%, 100.00%)	99.92% (99.75%, 100.00%)	99.83% (99.58%, 100.00%)
Pappenheimer bodies	100.00% (100.00%, 100.00%)	99.40% (98.89%, 99.83%)	99.42% (98.92%, 99.83%)
Platelet clumps	86.11% (82.13%, 89.91%)	87.39% (85.39%, 89.39%)	87.08% (85.25%, 88.92%)
Acanthocytes	100.00% (100.00%, 100.00%)	98.82% (98.10%, 99.37%)	98.91% (98.25%, 99.42%)
Bite cells	100.00% (100.00%, 100.00%)	99.91% (99.74%, 100.00%)	99.92% (99.75%, 100.00%)
Blister cells	88.89% (63.64%, 100.00%)	99.83% (99.58%, 100.00%)	99.75% (99.42%, 100.00%)
Echinocytes	99.48% (98.70%, 100.00%)	99.13% (98.37%, 99.64%)	99.24% (98.65%, 99.66%)
Elliptocytes	97.80% (94.19%, 100.00%)	99.64% (99.27%, 99.91%)	99.50% (99.08%, 99.83%)
Helmet cells	82.46% (72.22%, 92.23%)	94.23% (93.12%, 95.33%)	93.67% (92.50%, 94.75%)
Ovalocytes	100.00% (100.00%, 100.00%)	98.52% (97.47%, 99.35%)	99.24% (98.74%, 99.66%)
Poikilocytosis	98.61% (97.39%, 99.55%)	96.27% (94.99%, 97.46%)	97.13% (96.19%, 98.05%)
Schistocytes	77.17% (71.63%, 82.27%)	74.51% (71.44%, 77.40%)	75.17% (72.59%, 77.63%)
Sickle cells	98.00% (93.10%, 100.00%)	99.47% (99.03%, 99.83%)	99.41% (98.95%, 99.83%)
Spherocytes	97.59% (93.72%, 100.00%)	99.55% (99.11%, 99.91%)	99.42% (98.92%, 99.83%)
Stomatocytes	100.00% (100.00%, 100.00%)	99.30% (98.77%, 99.74%)	99.33% (98.83%, 99.75%)
Target cells	99.07% (97.84%, 100.00%)	99.17% (98.48%, 99.71%)	99.15% (98.55%, 99.57%)

Morphological Feature	PPA (95% CI)	NPA (95% CI)	Overall Agreement (95% CI)
Teardrop cells	84.78% (80.00%, 88.89%)	82.24% (79.68%, 84.85%)	82.89% (80.57%, 85.11%)
Anisocytosis	99.34% (98.66%, 100.00%)	97.98% (96.81%, 99.00%)	98.67% (98.00%, 99.33%)
Macrocytes	99.36% (98.59%, 100.00%)	88.49% (86.58%, 90.50%)	92.75% (91.58%, 94.00%)
Microcytes	99.57% (98.91%, 100.00%)	92.66% (90.82%, 94.43%)	95.33% (94.17%, 96.42%)

RBC Color

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	881	36	917
Test Method Negative	15	1468	1483
Total	896	1504	2400

RBC Inclusions

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	183	73	256
Test Method Negative	28	4516	4544
Total	211	4589	4800

RBC Shape

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	2606	493	3099
Test Method Negative	127	13184	13311
Total	2733	13677	16410

RBC Size

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	1531	150	1681
Test Method Negative	9	1910	1919
Total	1540	2060	3600

Hypochromia

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	432	24	456
Test Method Negative	3	741	744
Total	435	765	1200

Polychromasia

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	449	12	461
Test Method Negative	12	727	739
Total	461	739	1200

Basophilic Stippling

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	28	1	29
Test Method Negative	1	1170	1171
Total	29	1171	1200

Howell-Jolly Bodies

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	115	64	179
Test Method Negative	26	995	1021
Total	141	1059	1200

Micro-organisms

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	6	1	7
Test Method Negative	1	1192	1193
Total	7	1193	1200

Pappenheimer Bodies

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	34	7	41
Test Method Negative	0	1159	1159
Total	34	1166	1200

Acanthocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	97	13	110
Test Method Negative	0	1086	1086
Total	97	1099	1196

Bite cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	41	1	42
Test Method Negative	0	1158	1158
Total	41	1159	1200

Blister cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	8	2	10
Test Method Negative	1	1189	1190
Total	9	1191	1200

Echinocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	380	7	387
Test Method Negative	2	800	802
Total	382	807	1189

Elliptocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	89	4	93
Test Method Negative	2	1105	1107
Total	91	1109	1200

Helmet Cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	47	66	113
Test Method Negative	10	1077	1087
Total	57	1143	1200

Ovalocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	583	9	592
Test Method Negative	0	598	598
Total	583	607	1190

Poikilocytosis

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	426	28	454
Test Method Negative	6	723	729
Total	432	751	1183

Schistocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	196	194	390
Test Method Negative	58	567	625
Total	254	761	1015

Sickle cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	49	6	55
Test Method Negative	1	1136	1137
Total	50	1142	1192

Spherocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	81	5	86
Test Method Negative	2	1112	1114
Total	83	1117	1200

Stomatocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	56	8	64
Test Method Negative	0	1130	1130
Total	56	1138	1194

Target cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	319	7	326
Test Method Negative	3	841	844
Total	322	848	1170

Teardrop cells

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	234	143	377
Test Method Negative	42	662	704
Total	276	805	1081

Anisocytosis

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	602	12	614
Test Method Negative	4	582	586
Total	606	594	1200

Macrocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	467	84	551
Test Method Negative	3	646	649
Total	470	730	1200

Microcytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	462	54	516
Test Method Negative	2	682	684
Total	464	736	1200

Platelet clumps

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	248	115	363
Test Method Negative	40	797	837
Total	288	912	1200

Schistocyte Supplemental Study: RBC-DSS vs. manual light microscope

To supplement the results for schistocytes, the sponsor conducted a study in which the results for schistocytes using the DSS were compared to the results from manual light microscope. Two experienced operators analyzed 75 slides with a mixture of normal PBS samples without schistocytes and slides containing schistocytes in different grade levels. The slides were reviewed on both the DSS and the manual light microscope with a wash-out period between the two devices. The results are summarized below.

Schistocytes

	Reference Method Positive	Reference Method Negative	Total
Test Method Positive	29	7	36
Test Method Negative	6	33	39
Total	35	40	75

Morphological Feature	PPA (95% CI)	NPA (95% CI)	Overall Agreement (95% CI)
Schistocytes	82.86% (73.33%, 90.67%)	82.50% (69.57%, 94.44%)	82.67% (70.00%, 93.75%)

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.