



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

I Background Information:

A 510(k) Number

K240402

B Applicant

CytoChip Inc.

C Proprietary and Established Names

Cito CBC System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GKZ	Class II	21 CFR 864.5220 - Automated Differential Cell Counter	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

This submission is a Dual 510(k) and CLIA Waiver by Application (Dual Submission) tracked as K240402 and CW240006. CW240006 is for granting the CLIA Waiver by Application and K240402 is for clearance of a new device.

B Measurand:

WBC, RBC, HGB, HCT, MCV, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, and BASO%/#

C Type of Test:

Complete blood count (WBC, RBC, HGB, HCT, MCV, PLT) and leukocyte 5-part differential (NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, and BASO%/#)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Cito CBC system is a quantitative automated hematology analyzer intended for in-vitro diagnostic use to determine the following parameters with whole blood anticoagulated with K2EDTA (Venous):

- CBC parameters: white blood cell count (WBC), red blood cell count (RBC), platelet count (PLT), hemoglobin concentration (HGB), hematocrit (HCT), and mean corpuscular volume (MCV);

- 5-Part WBC Differential (WBC Diff): neutrophil count and percentage (NEUT and NEUT%), lymphocyte count and percentage (LYMPH and LYMPH%), monocyte count and percentage (MONO and MONO%), eosinophil count and percentage (EO and EO%), basophil count and percentage (BASO and BASO%).

It is not indicated for use in diagnosing or monitoring of oncology patients, critically ill patients, or children under the age of 2 years.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The Cito CBC System is intended to be used by operators with a minimum of an earned high school diploma or equivalent.

D Special Instrument Requirements:

Cito CBC Analyzer

IV Device/System Characteristics:

A Device Description:

The CytoChip Cito CBC System is an automated hematology analyzer that is intended to analyze K₂EDTA venous human whole blood, and report results of 16 hematology parameters (WBC, RBC, PLT, HGB, HCT, MCV, LYMPH #/%, NEUT #/%, MONO #/%, EO #/%, and BASO #/%). The system is comprised of an automated benchtop reader instrument (Cito CBC Analyzer), accessories, and disposable Cito CBC test kits. Each test kit includes 25 individually packaged test cartridges, alcohol wipes, a sample dispensing tips, one sealing card and package insert.

The Cito CBC Analyzer contains the essential hardware and software to perform a test with a disposable cartridge. It consists of 1) pneumatic module to actuate fluid transfer in the cartridge, 2) optical module to detect signals from the cartridge, 3) heating module to accelerate the

chemistry reaction in the cartridge, 4) control and signal board; 5) on-board computer for results computation and user interface. All reagents, sample and bio-waste are self-contained in the cartridge and has no physical contact with the analyzer.

B Principle of Operation:

The Cito CBC system uses two detection modules in the reader instrument for measurement of a test run: fluorescent flow cytometry and photometry. The Cito CBC system utilizes the principle of fluorescent flow cytometry for cell count and cell classification. A laser is used as the light source, and fluorescence and light scattering signals are detected for the measurements. For fluorescent labeling, blood cells are treated with a fluorescent dye that has high affinity binding to nucleic acid. Additionally, the analyzer utilizes the principle of two-wavelength photometry for the measurement of the hemoglobin. Blood cells are lysed to release hemoglobin. Meanwhile, the light scattering signal measured from the flow cytometry and the light absorption signals measured from the photometry are both used to quantify the hematocrit and the mean cell volume.

The Cito CBC Cartridge contains all the reagents needed for performing the test, including:

- A first reagent. It consists of a salt-based buffer solution to dilute a blood sample, which is used for downstream analysis and HGB/HCT testing.
- A second reagent. It consists of surfactants to lyse RBCs and release hemoglobin. It also contains a fluorescent dye to label the nucleic acids in the cells. This reagent mixes with a portion of the diluted blood to form a sample mixture for WBC, WBC Diff, and HGB/HCT testing.
- A third reagent. It consists of a salt-based buffer solution to further dilute the blood. It also contains a dye to label the nucleic acids in the cells. This reagent mixes with a portion of the diluted blood to form a sample mixture for RBC and PLT testing.

C Instrument Description Information:

1. Instrument Name:

Cito CBC Analyzer

2. Specimen Identification:

Barcode scanner or manual entry

3. Specimen Sampling and Handling:

Venous whole blood is collected in vacutainer tube with K₂EDTA anticoagulant as test specimen. The tube is inverted at least ten times to mix the sample before testing. A dispenser tip is inserted into the tube cap, and pressed against the inlet port of the test cartridge to dispense blood. The dispensed blood is drawn into the test cartridge by capillary force. Blood residue on the inlet port is wiped away with an alcohol pad, and the cartridge inlet seal is manually closed. The test cartridge is then inserted to the analyzer to complete the automatic measurement, and the result will be reported.

4. Calibration:

The Cito CBC System is factory calibrated. No user calibration is required.

5. Quality Control:

The system performance is evaluated using a commercial QC kit, Cito CBC Control. The QC materials are a tri-level (low, normal, high) whole blood control that contains human cells, mammalian cells and microspheres suspended in a plasma-like fluid with preservatives. The system guides users to test each level of the QC material in sequence, and determine automatically whether the QC test is passed or failed. If QC fails, the system software will deactivate the user access to perform a sample test. QC test is recommended: 1) when using the Cito CBC Analyzer for the first time; 2) with each new shipment of test kits; 2) when new operator to perform testing; 3) anytime an unexpected issue is encountered; 4) at least every 30 days.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Sysmex Xn-series

B Predicate 510(k) Number(s):

K112605

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K240402</u>	<u>K112605</u>
Device Trade Name	Cito CBC System	Sysmex XN-Series
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Cito CBC System is a quantitative automated hematology analyzer intended for in-vitro diagnostic use to determine the following parameters with whole blood anticoagulated with K2EDTA (Venous): - CBC parameters: white blood cell count (WBC), red blood cell count (RBC), platelet count (PLT), hemoglobin concentration (HGB),	The XN-Series modules (XN-10, XN-20) are quantitative multi-parameter automated hematology analyzers intended for in vitro diagnostic use in screening patient populations found in clinical laboratories. The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT,

	<p>hematocrit (HCT), and mean corpuscular volume (MCV);</p> <p>- 5-Part WBC Differential (WBC Diff): neutrophil count and percentage (NEUT and NEUT%), lymphocyte count and percentage (LYMPH and LYMPH%), monocyte count and percentage (MONO and MONO%), eosinophil count and percentage (EO and EO%), basophil count and percentage (BASO and BASO%).</p> <p>It is not indicated for use in diagnosing or monitoring of oncology patients, critically ill patients, or children under the age of 2 years.</p>	<p>NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, NRBC%/#, RET%/#, IPF, IRF, RET-He and has a Body Fluid mode for body fluids.</p> <p>The Body Fluid mode enumerates the WBC-BF, RBC-BF, MN%/#, PMN%/#, and TC-BF parameters in cerebrospinal fluid (CSF), serous fluids (peritoneal, pleural) and synovial fluids.</p> <p>Whole blood should be collected in K2 or K3EDTA anticoagulant and, Serous and Synovial fluids in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.</p>
Sample Type	Whole blood anticoagulated with K2EDTA (venous)	Whole blood anticoagulated with K2EDTA or K3EDTA Body fluid
Parameters	WBC, RBC, PLT, HGB, HCT, MCV, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, and BASO%/#	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, NRBC%/#, RET%/#, IPF, IRF, RET-He, WBC-BF, RBC-BF, MN%/#,

		PMN%/#, and TC-BF#
General Device Characteristic Differences		
Automated / robotic pipetting	No	Yes, multiple ways: Manual Open Cap Analysis Mode (Sample placed in tube holder position) Pre-dilute Analysis Mode (Dilute sample 1:7) Low WBC Mode (LWBC)
Testing Principle	Performs hematology analyses with flow cytometry method (using a semiconductor laser) to count and differentiate WBC, RBC and PLT cells. Use photometry method to quantify HGB. Use the flow cytometer method and the photometry method together to quantify HCT.	Performs hematology analyses according to the Hydro Dynamic Focusing (DC Detection), flow cytometry method (using a semiconductor laser), and SLS hemoglobin method.
Microfluidic cartridge	Yes	No
Sample Volume	15–20 µL	88 µL (aspiration volume)
Throughput	7 samples/hour	100 samples/hour maximum depending on mode used
Calibration and Quality Controls	Factory calibrated R&D Systems Cito CBC Controls – 3 Levels	XN CAL (XN-10/X-20 Calibrator) XN CAL PF (Platelet F Calibrator) XN-Check - 3 Levels

VI Standards/Guidance Documents Referenced:

IEC 60601-1-2 (2007): Medical Electrical Equipment Part 1-2: General Requirements for Basic Safety and Essential Performance Collateral Standard: Electromagnetic Compatibility

CLSI H20-A2 (2007): Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard - Second Edition

CLSI H26-A2 (2010): Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard - Second Edition

CLSI EP05-A3 (2014): Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition

CLSI EP06-A2 (2020): Evaluation of the Linearity of Quantitative Measurement Procedures - Second Edition

CLSI EP07 (2018): Interference Testing in Clinical Chemistry - Third Edition

CLSI EP09-c (2018): Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition

CLSI EP17-A2 (2012): Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second edition

CLSI EP21 (2016): Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures - second edition

CLSI EP25-A2 (2023): Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline - Second edition

CLSI EP27 (2022): Constructing and Interpreting an Error Grid for Quantitative Measurement Procedures - Second edition

CLSI EP28-A3c (2010): Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition

CLSI EP37 (2018): Supplemental Tables for Interference Testing in Clinical Chemistry - first edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

a) Repeatability with whole blood samples

Venous whole blood (K₂EDTA anticoagulated) was used to evaluate the precision of reported CBC parameters, including 5-part differential. Three CLIA-waived sites participated in this study, and each site used one analyzer and three untrained operators, totaling three analyzers and nine untrained operators overall. For the three sites, in total 45 blood samples were tested to cover the three sub-ranges (low, medium, high), including MDLs, for WBC,

RBC, PLT, HGB, HCT and MCV. Ten (10) consecutive tests were performed for each sample. The study calculates the SD (standard deviation) and %CV (coefficient of variation) for each reported parameter. The study results pool the SD and %CV together across the three sites, following the protocol of CLSI document EP05-A3. The pooled SD and pooled %CV meet the acceptance criteria for all reported parameters in the three sub-ranges (low, medium, high), as shown below.

Parameter	Level	Range	Sample Number	Mean	Pooled SD	Pooled %CV
WBC ($\times 10^3/\mu\text{L}$)	Low	3–4	5	3.66	0.08	2.3%
	Normal	4.3–7.9	19	6.11	0.14	2.3%
	High	10–50	11	25.21	0.82	3.3%
RBC ($\times 10^6/\mu\text{L}$)	Low	2–4	21	3.11	0.04	1.4%
	Normal	4.3–5.5	12	4.94	0.06	1.3%
	High	5.8–7.5	6	6.66	0.10	1.5%
PLT ($\times 10^3/\mu\text{L}$)	Low	100–170	6	135.34	3.01	2.2%
	Normal	180–350	21	251.05	5.69	2.3%
	High	400–600	8	468.55	11.75	2.5%
HGB (g/dL)	Low	10–11.5	10	10.67	0.11	1.0%
	Normal	12–16.2	10	12.31	0.15	1.2%
	High	16.9–24	10	18.48	0.21	1.1%
HCT (%)	Low	25–37	19	30.91	0.37	1.2%
	Normal	38–48	11	41.10	0.40	1.0%
	High	49.5–60	10	51.78	0.51	1.0%
MCV (fL)	Low	65–80	6	73.72	0.79	1.1%
	Normal	82–97	21	89.32	0.98	1.1%
	High	97.5–110	12	100.75	1.02	1.0%
NEUT ($\times 10^3/\mu\text{L}$)	Low	0–2.5	6	1.94	0.06	2.9%
	Normal	3–9	28	4.52	0.13	2.8%
	High	10–40	8	13.69	0.37	2.7%
LYMPH ($\times 10^3/\mu\text{L}$)	Low	0–1.1	14	0.86	0.04	4.8%
	Normal	1.3–1.9	9	1.62	0.07	4.1%
	High	2–10	11	2.92	0.12	4.0%
MONO ($\times 10^3/\mu\text{L}$)	Low	0–0.4	5	0.40	0.06	13.8%
	Normal	0.5–0.8	14	0.60	0.05	9.2%
	High	0.9–4.0	11	1.06	0.06	5.2%
EO ($\times 10^3/\mu\text{L}$)	Low	0–0.06	14	0.06	0.01	19.1%
	Normal	0.07–0.2	19	0.12	0.02	16.1%
	High	0.21–1	12	0.34	0.03	9.4%
BASO ($\times 10^3/\mu\text{L}$)	Low	0–0.02	9	0.02	0.01	50.0%
	Normal	0.03–0.04	9	0.03	0.03	76.2%
	High	0.05–0.2	21	0.07	0.02	34.0%
NEUT%	Low	NEUT < 2.5	6	52.52	0.95	1.8%
	Normal	NEUT 3–9	28	62.79	0.90	1.4%
	High	NEUT 10–40	8	72.21	0.62	0.9%
LYMPH%	Low	LYMPH < 1.1	14	11.88	0.55	4.6%
	Normal	LYMPH 1.3–1.9	9	25.82	0.94	3.6%
	High	LYMPH 2–10	11	32.39	1.25	3.9%
MONO%	Low	MONO < 0.4	5	6.87	0.81	11.8%
	Normal	MONO 0.5–0.8	14	8.60	0.78	9.0%

Parameter	Level	Range	Sample Number	Mean	Pooled SD	Pooled %CV
	High	MONO 0.9–4	11	10.66	0.57	5.4%
EO%	Low	EO < 0.06	14	0.69	0.19	26.8%
	Normal	EO 0.07–0.2	19	2.12	0.35	16.3%
	High	EO > 0.21–1	12	3.90	0.30	7.8%
BASO%	Low	BASO <0.02	9	0.43	0.23	52.8%
	Normal	BASO 0.03–0.04	9	0.50	0.29	58.4%
	High	BASO 0.05–0.2	21	0.88	0.31	35.1%

b) Cartridge lot-to-lot Precision

A study was performed to evaluate the lot-to-lot variability of the test cartridge. Three cartridge lots were used in the study, and venous whole blood (K₂EDTA anticoagulated) was tested to assess the between-lot component. A total of 19 samples were tested in this study. For each sample, 5 replicate tests were performed for each cartridge lot (15 tests for three lots). ANOVA analysis was performed according to CLSI EP05-A3 to calculate the between-lot %CV and total %CV, which meet the acceptance criteria, as shown below.

Parameter	Sample Range	Pooled Between-lot		Pooled Total	
		SD	%CV	SD	%CV
WBC ($\times 10^3/\mu\text{L}$)	Low 3.00–4.00	0.02	0.4%	0.08	2.2%
	Normal 4.30–7.90	0.06	0.2%	0.13	2.1%
	High 10.00–50.00	0.03	0.3%	0.52	2.7%
RBC ($10^6/\mu\text{L}$)	Low 2.00–4.00	0.01	0.4%	0.03	1.0%
	Normal 4.30–5.50	0.02	0.4%	0.04	0.9%
	High 5.80–7.50	0.01	0.5%	0.07	1.1%
PLT ($10^3/\mu\text{L}$)	Low 100 – 170	1.48	0.5%	3.42	2.3%
	Normal 180 – 350	2.45	0.1%	4.76	2.0%
	High 400 – 650	8.10	0.9%	18.76	3.3%
HGB (g/dL)	Low 8.0–11.5	0.04	1.0%	0.10	1.0%
	Normal 12.0–16.2	0.06	0.4%	0.13	0.9%
	High 16.9–24.0	0.04	0.2%	0.18	1.0%
HCT (%)	Low 25.0–37.0	0.09	0.3%	0.36	1.1%
	Normal 38.0–48.0	0.15	0.4%	0.42	1.0%
	High	0.22	0.4%	0.65	1.3%

Parameter	Sample Range	Pooled Between-lot		Pooled Total	
		SD	%CV	SD	%CV
	49.5–60.0				
MCV (fL)	Low 65.0–80.0	0.33	0.5%	0.72	1.0%
	Normal 82.0–97.0	0.43	0.5%	0.92	1.0%
	High MCV: 97.5–110.0	0.11	0.1%	1.02	1.1%
NEUT (10 ³ /μL)	Low 0.00–2.50	0.02	0.9%	0.06	3.0%
	Normal 3.00–9.00	0.05	1.0%	0.12	2.5%
	High 10.00–40.00	0.08	0.4%	0.51	2.6%
LYMPH (10 ³ /μL)	Low 0.00–1.10	0.01	1.1%	0.06	5.3%
	Normal 1.30–1.90	0.00	0.0%	0.07	3.8%
	High 2.00–10.00	0.03	0.8%	0.11	3.2%
MONO (10 ³ /μL)	Low 0.00–0.40	0.01	2.1%	0.03	8.6%
	Normal 0.50–0.80	0.00	0.0%	0.04	5.8%
	High 0.90–4.00	0.00	0.0%	0.07	4.1%
EO (10 ³ /μL)	Low 0.00–0.06	0.00	4.5%	0.05	71.9%
	Normal 0.07–0.20	0.00	3.5%	0.02	17.1%
	High 0.21–1.00	0.00	0.0%	0.04	15.6%
BASO (10 ³ /μL)	Low 0.00–0.02	0.00	2.5%	0.01	53.5%
	Normal 0.03–0.04	0.00	0.0%	0.02	72.4%
	High 0.05–0.20	0.01	15.4%	0.02	51.6%
NEUT% (%)	Low 0.00–2.50	0.00	0.0%	1.06	2.1%
	Normal 3.00–9.00	0.20	0.4%	0.72	1.2%
	High 10.00–40.00	0.39	0.5%	0.87	1.2%
LYMPH% (%)	Low 0.00–1.10	0.16	0.6%	1.34	4.6%
	Normal 1.30–1.90	0.12	0.4%	0.97	3.1%
	High 2.00–10.00	0.15	0.6%	0.64	2.4%
	Low	0.14	2.1%	0.59	8.4%

Parameter	Sample Range	Pooled Between-lot		Pooled Total	
		SD	%CV	SD	%CV
MONO% (%)	0.00–0.40				
	Normal 0.50–0.80	0.06	1.0%	0.45	7.0%
	High 0.90–4.00	0.04	0.5%	0.35	4.1%
EO% (%)	Low 0.00–0.06	0.07	7.5%	0.20	22.4%
	Normal 0.07–0.20	0.10	4.8%	0.27	12.5%
	High 0.21–1.00	0.00	0.0%	0.45	10.3%
BASO% (%)	Low 0.00–0.02	0.01	1.8%	0.22	52.2%
	Normal 0.03–0.04	0.04	8.2%	0.34	76.2%
	High 0.05–0.20	0.05	16.2%	0.18	54.5%

c) Reproducibility

The reproducibility performance was evaluated by testing QC materials. Three CLIA-waived sites participated in this study, and each site used one analyzer and at least two untrained operators. At each site, the study was performed for 5 days. In each day, 2 test runs were performed with 3 replicates per run. One lot of the QC materials (three levels: low, normal, and high) was used and a total of 90 replicates were performed for each control level over the study duration (3 sites×5 days×2 test runs×3 replicates per run). ANOVA analysis was performed according to CLSI EP05-A3 to calculate the SD and %CV for within-run (repeatability), between-run, between-day, between-site, and total precision for each control level. The total %CV of all parameters met the acceptance criteria, as shown below.

Parameter	Level	Mean	Within-run		Between-run/ between-operator		Between-day		Between-site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC (10 ³ /μL)	Low	2.34	0.07	2.79%	0.00	0.00%	0.00	0.00%	0.02	0.77%	0.07	2.89%
	Normal	5.92	0.10	1.70%	0.02	0.41%	0.00	0.00%	0.02	0.40%	0.11	1.79%
	High	13.18	0.22	1.67%	0.00	0.00%	0.10	0.78%	0.08	0.60%	0.26	1.94%
RBC (10 ⁶ /μL)	Low	2.78	0.03	1.00%	0.01	0.33%	0.01	0.51%	0.00	0.00%	0.03	1.17%
	Normal	3.14	0.04	1.15%	0.00	0.00%	0.00	0.00%	0.01	0.27%	0.04	1.18%
	High	4.01	0.05	1.32%	0.00	0.00%	0.02	0.50%	0.00	0.00%	0.06	1.41%
PLT (10 ³ /μL)	Low	54.01	1.46	2.71%	0.00	0.00%	0.84	1.55%	0.00	0.00%	1.69	3.12%
	Normal	101.87	2.56	2.51%	0.67	0.66%	0.31	0.30%	0.40	0.39%	2.69	2.64%
	High	178.37	4.41	2.47%	1.50	0.84%	1.58	0.88%	0.44	0.25%	4.94	2.77%
HGB (g/dL)	Low	8.10	0.08	1.02%	0.00	0.00%	0.03	0.42%	0.06	0.74%	0.11	1.33%
	Normal	10.67	0.12	1.10%	0.00	0.00%	0.02	0.22%	0.00	0.00%	0.12	1.12%
	High	14.63	0.17	1.17%	0.00	0.00%	0.05	0.35%	0.00	0.00%	0.18	1.22%
HCT (%)	Low	24.23	0.23	0.96%	0.00	0.00%	0.18	0.73%	0.20	0.82%	0.35	1.46%
	Normal	31.24	0.27	0.87%	0.10	0.33%	0.11	0.35%	0.00	0.00%	0.31	1.00%

Parameter	Level	Mean	Within-run		Between-run/ between-operator		Between-day		Between-site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
	High	42.09	0.43	1.03%	0.00	0.00%	0.17	0.40%	0.18	0.42%	0.50	1.18%
MCV (fL)	Low	87.08	1.05	1.21%	0.00	0.00%	0.72	0.83%	0.60	0.68%	1.41	1.62%
	Normal	99.45	1.08	1.08%	0.44	0.44%	0.30	0.30%	0.00	0.00%	1.20	1.21%
	High	105.01	1.43	1.36%	0.52	0.49%	0.48	0.46%	0.00	0.00%	1.60	1.52%
NEUT (10 ³ /μL)	Low	1.32	0.04	3.22%	0.00	0.00%	0.00	0.00%	0.00	0.00%	0.04	3.22%
	Normal	3.82	0.07	1.84%	0.01	0.21%	0.00	0.00%	0.02	0.59%	0.07	1.94%
	High	7.13	0.12	1.72%	0.00	0.00%	0.06	0.81%	0.03	0.39%	0.14	1.94%
LYMPH (10 ³ /μL)	Low	0.81	0.04	4.64%	0.01	0.85%	0.00	0.00%	0.02	2.49%	0.04	5.33%
	Normal	1.39	0.05	3.52%	0.00	0.00%	0.02	1.75%	0.00	0.00%	0.06	3.93%
	High	4.42	0.09	2.12%	0.00	0.00%	0.03	0.67%	0.05	1.19%	0.11	2.52%
MONO (10 ³ /μL)	Low	0.09	0.01	13.2%	0.00	0.00%	0.00	3.56%	0.00	0.00%	0.01	13.7%
	Normal	0.15	0.01	9.29%	0.00	0.00%	0.00	1.55%	0.00	0.00%	0.01	9.42%
	High	0.44	0.03	6.46%	0.00	0.79%	0.00	0.00%	0.00	0.00%	0.03	6.51%
EO (10 ³ /μL)	Low	0.09	0.02	15.9%	0.00	0.00%	0.00	4.20%	0.00	3.32%	0.02	16.8%
	Normal	0.47	0.03	5.78%	0.00	0.00%	0.00	0.00%	0.00	0.13%	0.03	5.79%
	High	1.00	0.04	4.38%	0.01	0.89%	0.00	0.00%	0.01	0.80%	0.05	4.54%
BASO (10 ³ /μL)	Low	0.04	0.01	20.5%	0.00	11.7%	0.00	0.00%	0.00	9.97%	0.01	25.6%
	Normal	0.08	0.01	12.6%	0.00	0.00%	0.00	0.00%	0.01	5.63%	0.01	13.8%
	High	0.19	0.02	7.75%	0.01	3.52%	0.01	3.90%	0.01	3.02%	0.02	9.84%
NEUT%	Low	56.33	1.22	2.17%	0.00	0.00%	0.07	0.13%	0.47	0.83%	1.31	2.33%
	Normal	64.59	0.62	0.95%	0.07	0.11%	0.20	0.31%	0.00	0.00%	0.65	1.01%
	High	54.10	0.46	0.85%	0.15	0.28%	0.03	0.05%	0.00	0.00%	0.48	0.89%
LYMPH%	Low	34.53	1.16	3.35%	0.16	0.47%	0.00	0.00%	0.57	1.66%	1.30	3.76%
	Normal	23.49	0.71	3.01%	0.00	0.00%	0.33	1.39%	0.00	0.00%	0.78	3.31%
	High	33.56	0.42	1.24%	0.22	0.64%	0.00	0.00%	0.18	0.52%	0.50	1.49%
MONO%	Low	3.67	0.45	12.2%	0.00	0.00%	0.13	3.57%	0.04	1.12%	0.47	12.8%
	Normal	2.55	0.24	9.31%	0.00	0.00%	0.02	0.82%	0.00	0.00%	0.24	9.34%
	High	3.30	0.21	6.26%	0.03	0.88%	0.00	0.00%	0.00	0.00%	0.21	6.32%
EO%	Low	3.94	0.59	15.0%	0.05	1.30%	0.15	3.79%	0.18	4.60%	0.64	16.2%
	Normal	8.00	0.42	5.20%	0.00	0.00%	0.00	0.00%	0.00	0.00%	0.42	5.20%
	High	7.60	0.27	3.55%	0.15	1.94%	0.00	0.00%	0.08	1.10%	0.32	4.19%
BASO%	Low	1.52	0.28	18.4%	0.17	11.4%	0.00	0.00%	0.10	6.73%	0.35	22.6%
	Normal	1.38	0.15	11.1%	0.00	0.00%	0.01	0.94%	0.08	6.01%	0.17	12.6%
	High	1.45	0.12	8.10%	0.03	2.00%	0.06	4.06%	0.05	3.57%	0.14	9.94%

2. Linearity:

The linearity interval of the WBC, RBC, PLT, HGB, and HCT were evaluated using fresh whole blood (venous blood anticoagulated with K₂EDTA). A 9-concentration sample panel was tested for each parameter. Linear regression was performed for data analysis, and all parameters met the allowable deviation from linearity within ±10% for the established ranges below.

WBC: 1.80 to 50.0×10³/μL

RBC: 2.00 to 8.25×10⁶/μL

PLT: 50 to 750×10³/μL

HGB: 6.0 to 25.0 g/dL
HCT: 24.0% to 70.0%
MCV: 65.0 to 115.0 fL

3. Analytical Specificity/Interference:

A study was conducted to determine the interference level for the following interfering substances: conjugated bilirubin, unconjugated bilirubin, intralipid, chyle, K₂EDTA, and hemolytic hemoglobin. The interference levels were evaluated by testing fresh whole blood (venous blood anticoagulated with K₂EDTA) spiked with the interferent at study concentration levels. For each interferent, blood samples were spiked with the interferent, and five replicate tests were performed with both control group (no spiking) and test group (with spiking) for comparison. A total of three blood samples were tested for each interferent. The non-significant %Interferences were defined as %Interferences within $\pm 10\%$. The results of the interference study demonstrated that:

- There was no significant conjugated bilirubin interference up to a concentration of 40 mg/dL for WBC, RBC, PLT, HGB, HCT, and MCV.
- There was no significant unconjugated bilirubin interference up to a concentration of 40 mg/dL for WBC, RBC, PLT, HGB, HCT, and MCV.
- There was no significant intralipid interference up to a concentration of 2000 mg/dL for WBC, PLT, and HGB, and up to a concentration of 500 mg/dL for RBC, HCT, and MCV. Samples with intralipid > 500 mg/dL are alerted by fail-alert mechanism and the impacted results (RBC, HCT, and MCV) are automatically suppressed.
- There was no significant chyle interference up to a concentration of 2524 FTU for WBC, RBC, PLT, HGB, HCT, and MCV.
- There was no significant hemolytic hemoglobin interference up to a concentration of 1.0 g/dL for WBC, RBC, PLT, HGB, and MCV; and up to a concentration of 0.5 g/dL for HCT.
- There was no significant K₂EDTA interference up to a concentration of 8 mg/mL for WBC, RBC, PLT, HGB, HCT, and MCV.

4. Reportable Range:

The measuring ranges for WBC, RBC, PLT, HGB, HCT and MCV are determined from the Linearity and the LoQ study results. After establishing the measuring ranges, the reportable ranges are chosen to be equal to or narrower than the measuring ranges, by applying a set of suppression levels for CLIA waived setting. After applying the suppression levels to the measuring ranges, the reportable ranges (with suppression) are established. Refer to submission CW240006 for detailed reportable range values for each parameter of this device.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a) Sample Stability

Sample stability of venous whole blood (K₂EDTA anticoagulated) was determined with 6 normal samples and 4 abnormal samples. The blood samples were stored at room temperature (15-25°C). At time zero (0 hour), the samples were tested in triplicates to establish the baseline. These samples were tested again in duplicate at the following time

points: 4.5 hours, 6.5 hours, and 8.5 hours. For each time point, the results were compared to the baseline results, and the mean percentage difference was calculated to meet the predefined acceptance criteria. The results support an 8-hour blood sample stability duration.

b) Cartridge Stability

A real-time stability study was conducted to establish shelf-life stability for the Cito CBC system cartridge when stored at the recommended storage conditions. Three lots of cartridges were tested. Each cartridge lot was stored at room temperature and tested at defined time points, and then evaluated using venous whole blood samples. Based on the results of this study, the Cito CBC cartridge shelf-life stability is 294 days at room temperature (15–25°C).

6. Detection Limit:

Four venous whole blood samples were diluted with homologous plasma to make low-level samples and were used in this study to evaluate LoQ of WBC, RBC, PLT, HGB, and HCT. One sample was tested on each day, and the LoQ study was conducted for four consecutive days. For each sample, 9 replicate tests were performed with each cartridge lot, and two cartridge lots were used to capture the reagent variability (in total 18 tests for each sample). For the four samples, a total of 72 tests were performed, with 36 tests for each cartridge lot. The LoQ was determined individually for two cartridge lots, and the greater LoQ between the two cartridge lots was taken as the LoQ for each parameter.

Parameter	LoQ
WBC	$1.79 \times 10^3/\mu\text{L}$
RBC	$1.68 \times 10^6/\mu\text{L}$
PLT	$44 \times 10^3/\mu\text{L}$
HGB	5.5 g/dL
HCT	17.5%
MCV	62.3 fL

7. Assay Cut-Off:

Not applicable.

8. Accuracy (Instrument):

See method comparison study.

9. Carry-Over:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was performed across three CLIA-waived testing sites (with nine untrained operators in total) to evaluate the performance of the Cito CBC System compared to the comparative method, Sysmex XN Automated Hematology Analyzer. A total of 481 subjects were included in the study (117 enrolled at the CW sites and 346 residual clinical samples). Of the 481 subjects, there were 197 female (41%) and 284 male (59%). One K₂EDTA venous whole blood sample was collected from each subject. Statistical analyses for the method comparison were performed based on correlation plots with Deming regression and difference plots for bias. For each reported parameter, the slope, intercept, and correlation coefficient from the Deming fittings, are shown in the table below.

Method Comparison Results for Cito CBC System vs. Sysmex XN				
Measurand	Range	r	Slope (95% CI)	Intercept (95% CI)
WBC ($\times 10^3/\mu\text{L}$)	3–49.28	0.999	1.00 (0.99, 1.01)	-0.02 (-0.07, 0.03)
RBC ($\times 10^6/\mu\text{L}$)	2.17–7.76	0.997	1.01 (1, 1.02)	-0.05 (-0.09, -0.01)
PLT ($\times 10^3/\mu\text{L}$)	101–706	0.994	0.99 (0.97, 1)	0.73 (-2.45, 3.9)
HGB (g/dL)	10–23.4	0.996	0.97 (0.97, 0.98)	0.29 (0.17, 0.42)
HCT (%)	25–67.2	0.986	0.96 (0.95, 0.98)	1.11 (0.56, 1.66)
MCV (fL)	65.2–112.4	0.935	1.05 (1.01, 1.09)	-4.91 (-8.77, -1.06)
NEUT ($\times 10^3/\mu\text{L}$)	0.56–38.21	0.998	0.96 (0.94, 0.99)	0.06 (-0.03, 0.15)
LYMPH ($\times 10^3/\mu\text{L}$)	0.14–17.42	0.996	0.99 (0.93, 1.05)	0.08 (-0.02, 0.18)
MONO ($\times 10^3/\mu\text{L}$)	0.05–3.92	0.979	1.04 (1.01, 1.07)	-0.04 (-0.05, -0.02)
EO ($\times 10^3/\mu\text{L}$)	0.01–2.02	0.983	0.90 (0.85, 0.96)	0.01 (0, 0.02)
BASO ($\times 10^3/\mu\text{L}$)	0–0.26	0.535	0.84 (0.65, 1.03)	0.00 (-0.01, 0.01)
NEUT%	11–92.2	0.993	0.98 (0.96, 0.99)	0.06 (-0.71, 0.84)
LYMPH%	2.7–84.1	0.991	1.01 (0.99, 1.02)	0.79 (0.39, 1.2)
MONO%	1.7–26.9	0.941	0.95 (0.89, 1)	0.21 (-0.19, 0.62)
EO%	0.1–20.6	0.982	0.89 (0.85, 0.93)	0.18 (0.09, 0.27)
BASO%	0–2.7	0.526	1.24 (0.96, 1.53)	-0.25 (-0.43, -0.06)

2. Matrix Comparison:

Not applicable.

3. Flagging Study:

A flagging study was performed across five CLIA-waived testing sites and one point-of-care site to evaluate the flagging agreement between Cito CBC System and the comparative method, Sysmex XN Automated Hematology Analyzer. Five hundred five (505) subjects were included in the study (247 male and 258 female), which consists of 74 children (≥ 2 to < 12 years old), 77 adolescents (≥ 12 to < 21 years old), and 354 adults (≥ 21 years old). One K₂EDTA venous whole blood sample was collected from each subject. Additionally, 577 leftover samples (K₂EDTA venous whole blood) were selected from a clinical lab and included in this study for increased coverage of abnormal samples. In total, 1082 samples were tested for the flagging comparison. Based on the reported flags, each sample was categorized as either Negative (no sample abnormalities) or Positive (with sample abnormalities). The positive percent agreement, negative percent agreement and overall agreement were calculated, and the results successfully met the acceptance criteria, as shown below.

		Sysmex XN-Series		
		Positive	Negative	Total
Cito CBC System	Positive	466	27	493
	Negative	41	548	589
	Total	507	575	1082
Positive Agreement: $466/507 = 91.9\%$ (95% CI: 89.2%, 94.0%)				
Negative Agreement: $548/575 = 95.3\%$ (95% CI: 93.3%, 96.8%)				
Total Agreement: $(466+548)/1082 = 93.7\%$ (95% CI: 92.1%, 95.0%)				

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

A reference interval study was performed to determine the reference intervals of adults and pediatrics on the Cito CBC System. Healthy subjects were enrolled at four CLIA-waived sites for the study, including 253 adults over 21 years old (127 male, 126 female), 46 adolescents between 12–21 years old (21 male, 25 female), and 41 children between 2–12 years old (20 male, 21 female). One K₂EDTA venous whole blood sample was collected from each subject and tested. For the adult group (over 21 years old), reference intervals are established by non-parametric method following CLSI EP28-A3c. For the adolescent group (12–21 years old) and the children group (2–12 years old), the reference intervals published in Pediatric Reference Intervals, AACC Press, Soldin, Brugnara and Wong, 8th edition 2021, were verified on the Cito CBC System.

Reference Intervals for Adult Group (≥21 years)			
Parameter	Adult	Adult Female	Adult Male
WBC (10 ³ /μL)	4.17–10.54	4.28–11.03	4.06–10.15
RBC (10 ⁶ /μL)	4.00–5.74	3.98–5.17	4.02–5.92
PLT (10 ³ /μL)	179–413	149–450	181–370
HGB (g/dL)	11.1–16.8	10.3–15.6	12.2–17.1
HCT (%)	35.5–49.8	32.9–46.3	36.1–50.6
MCV (fL)	82.4–96.8	81.2–96.8	82.9–96.7
NEUT (10 ³ /μL)	1.65–6.75	1.77–6.83	1.60–6.77
LYMPH (10 ³ /μL)	1.10–3.50	1.09–3.45	1.04–3.54
MONO (10 ³ /μL)	0.29–1.00	0.25–0.97	0.31–1.10
EO (10 ³ /μL)	0.04–0.42	0.04–0.36	0.03–0.43
BASO (10 ³ /μL)	0.00–0.11	0.00–0.12	0.00–0.11
NEUT% (%)	37.3–72.8	37.8–72.7	36.8–73.6
LYMPH% (%)	17.4–49.1	17.4–49.8	16.8–49.4
MONO% (%)	4.9–13.5	4.6–13.5	5.5–13.9
EO% (%)	0.6–5.8	0.6–5.0	0.5–6.0
BASO% (%)	0.1–1.6	0.1–1.7	0.0–1.6

Reference Intervals for Pediatric Groups		
Parameter	Adolescents (≥ 12 to < 21 years)	Children (≥ 2 to < 12 years old)
WBC (10 ³ /μL)	3.13–12.66	3.44–13.63
RBC (10 ⁶ /μL)	3.38–5.93	3.11–5.41
PLT (10 ³ /μL)	142–429	167–504
HGB (g/dL)	10.4–16.9	10.2–14.7
HCT (%)	32.9–50.8	32.7–44.8
MCV (fL)	70.7–96.9	67.8–92.7
NEUT (10 ³ /μL)	1.35–9.19	1.24–9.22
LYMPH (10 ³ /μL)	1.02–3.94	0.94–5.80

Reference Intervals for Pediatric Groups		
Parameter	Adolescents (≥ 12 to < 21 years)	Children (≥ 2 to < 12 years old)
MONO (10 ³ /μL)	0.26–1.15	0.28–1.33
EO (10 ³ /μL)	0.01–0.72	0.00–0.94
BASO (10 ³ /μL)	0.00–0.08	0.00–0.09
NEUT% (%)	32.2–74.7	23.2–71.3
LYMPH% (%)	14.0–53.3	13.8–66.4
MONO% (%)	4.5–15.1	4.3–15.3
EO% (%)	0.2–11.2	0.0–12.7
BASO% (%)	0.0–1.2	0.0–1.0

F Other Supportive Instrument Performance Characteristics Data:

In 2008 and 2009, the Hematology and Pathology Devices Panel of the Medical Devices Advisory Committee met to provide recommendations to the FDA regarding the CLIA waiver application of an automated WBC analyzer. The panel expressed several concerns. Below is a list of the panel concerns and the solutions implemented by CytoChip to mitigate these concerns.

Panel Questions/Concerns	Mitigation
Do clinically important but undetected interferences, such as NRBC or abnormal WBC, affect the system's status as a simple test?	The predicate device, Sysmex XN Series hematology analyzer, has been cleared for detection of pathological samples, such as samples with NRBCs or abnormal WBCs. This device uses a similar fluorescent flow cytometry technology, which is able to 1) provide appropriate flagging of these samples, and 2) either suppress results or does not report erroneous results from these samples. A sample challenge study with pathological samples, such as samples with abnormal findings including NRBCs and abnormal WBCs among many others, is included to verify the device performance and appropriate flagging capabilities.
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?	Reflex testing is triggered by flagging abnormalities (cell morphology or abnormal ranges). A flagging comparison study is included to compare this device with the predicate, Sysmex XN series analyzer, which represents the state-of-the-art in flagging abnormalities. For samples with the appropriate flagging, a message will be included in the test report to recommend a confirmation test by reference laboratory. Upon receiving the test report with the recommendation, 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	Mitigation
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) was defined utilizing the CLIA '88 42 CFR 493.941 ranges and an existing hematology analyzer device cleared for CLIA waiver use (Sysmex XW-100 hematology analyzer for CLIA waived use, CW170012/ CW210002). Refer to submission CW240006 for details on ATE criteria for Cito CBC System.
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	A method comparison study is included to verify that this device's accuracy in CLIA-waived setting by untrained operator and is substantially equivalent to the predicate device in CLIA compliance labs by trained users.
Quality control should be required	The analyzer has three built-in quality control (QC) mechanisms: 1) the analyzer automatically runs a self-check periodically to check hardware is in working condition, 2) the analyzer utilizes sensors to monitor the key steps of sample analysis during each test run, and 3) each test cartridge contains QC beads to check detection is working properly during sample test runs. Abnormalities detected in the mechanism 1) will lock out the analyzer for sample test. Abnormalities detected in mechanism 2) and 3) will suppress the test results. Additionally, external QC materials (3 levels) are provided for users to check the analyzer and cartridge lots. If measurements of the QC materials fail to meet the specifications, the analyzer can be automatically lock-out for sample test.
What do the error codes signify and how many error codes are there?	<p>There are five types of error codes in total.</p> <ul style="list-style-type: none"> - Operation error signifies errors caused by operators/human factors. - Sample error signifies low sample quality. - Test error signifies errors detected during the sample measurement. - Cartridge error signifies cartridge issues detected. - System error signified system issues detected. <p>If an error code is shown, simple on-screen instructions are provided to the operator for following actions:</p> <ul style="list-style-type: none"> - Retest with a new cartridge or cartridge lot. - Reboot the analyzer and/or run QC materials. - Test locked out. Run QC material to unlock. - Test locked out. Contact manufacturer to schedule trouble shooting service.

Panel Questions/Concerns	Mitigation
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?	This device does not require operator training. Onscreen prompts and Quick Reference Guides are available to direct the operator through instrument setup and testing.
What would happen if an EDTA sample is inadequately mixed?	A flex study was conducted to assess an K ₂ EDTA sample in blood tube is inadequate mixing prior to testing. It was found that samples settled for more than 15 minutes without proper mixing prior testing will impact results. Therefore, labeling (QRG) and on-screen prompt provides a reminder to mix the tube prior to testing. After the mixing reminder, a timer of 5 minutes will trigger the on-screen prompt to prevent testing and guide user to retest with a new cartridge.
Current cell counters are complicated. They require substantial maintenance and regular calibration.	There is no maintenance required other than basic cleaning of the external surfaces of the analyzer. No calibration is required for users. The device is factory calibrated. Test cartridge contains QC beads to provide internal calibration for each test run and check if the detection hardware has drift.
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 intervals for the indicated age of the patient by the system with no operator involvement. 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.
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 clinical study was conducted at multiple CLIA-waived sites in the U.S. and operated by multiple untrained CLIA-waived users at each site.
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 device is contraindicated for use in diagnosing or monitoring oncology patients.
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 device detects an abnormal specimen (cell morphology or abnormal ranges), the test report contains a message for the clinician that reads "Confirmation with reference lab".
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 analyzer produces a test report including the patient ID, date of birth, results, and any flags. The instrument instructs the operator to deliver the printout to the clinician. The

Panel Questions/Concerns	Mitigation
	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.	<p>Results are printed with the reference intervals for the indicated age of the patient by the system with no operator involvement. Clear indicators are provided if the device detects an abnormal sample:</p> <ul style="list-style-type: none"> • For samples out of reference interval, a “+” or “-” alert is provided for highlight. • For sample abnormalities that impact result accuracy, the impacted results are suppressed, and a flagging message is provided, which further recommends a confirmation test by reference laboratory. • For sample out of measurement ranges, the impacted results are suppressed plus a flagging message for “Too Low” or “Too High”, and a flagging message is provided, which further recommends a confirmation test by reference laboratory. <p>The results are stored on the analyzer and can be retrieved via Graphic User Interface. The results can also be printed out automatically by user setting selection.</p>

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.